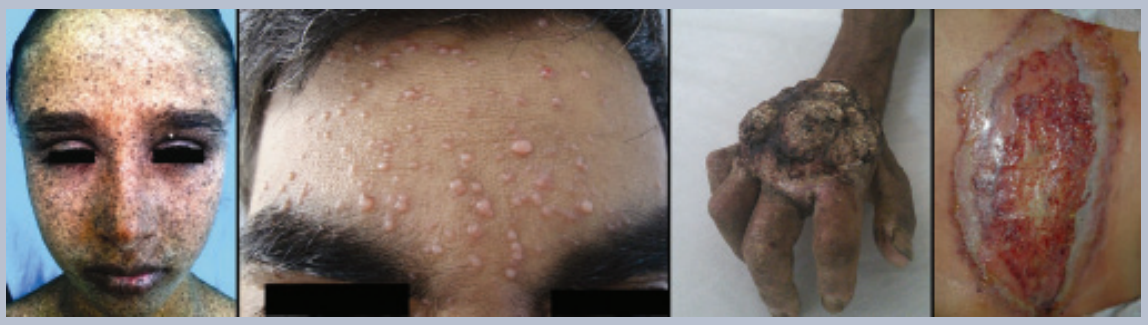
Volume 5, Number 4, October 2014
p. 333 - 447
Issue online since Friday, October 03, 2014

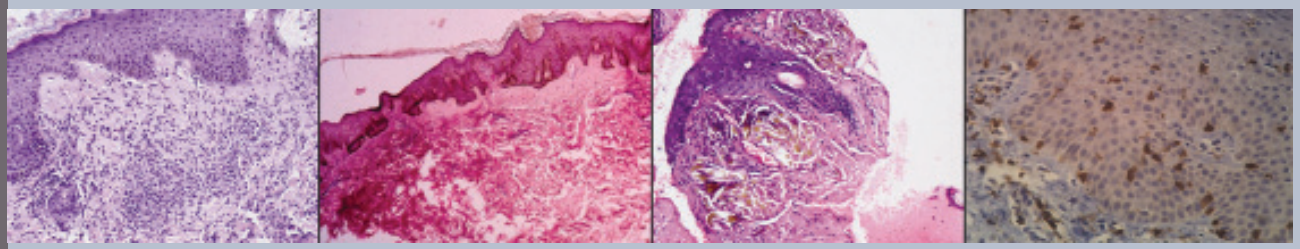
ISSN: 2081-9390
DOI: 10.7241/ourd
Universal Impact Factor {UIF} (= 0.7319)

NASZA DERMATOLOGIA ONLINE

www.odermatol.com

OUR DERMATOLOGY ONLINE





4 / 2014

Editorial Pages

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

e-ISSN: 2081-9390

DOI: 10.7241/ourd

Quarterly

published since 01/06/2010 years

Our Dermatol Online

www.odermatol.com

Indexed in:

Universal Impact Factor for year 2012 is = 0.7319
system of opinion of scientific periodicals INDEX COPERNICUS (6,70)
(Academic Search) EBSCO
(Academic Search Premier) EBSCO
MNiSW (kbn)-Ministerstwo Nauki i Szkolnictwa Wyższego (4.00)
DOAJ (Directory of Open Acces Journals)

Geneva Foundation for Medical Education and Research (GFMER), Google Scholar, Open J-Gate, NewJour, International Committee of Medical Journal Editors (ICMJE), Genamics JournalSeek, Hinari, Bielefeld Academic Search Engine (BASE), WorldCat, e-journal, WorldWideScience.org, National Science Library, LibSearch, Sciencegate, Virtual Science Library (VSL), Wanfang Data, COnnecting REpositories (CORE), CAB Abstracts, Global Health, Journal Indexed in Directory of Research Journals Indexing, OAIster: The Open Access Initiative, OAJSE - Open Access Journals Search Engine, Scirus

Previous website:	issue 1.2010	**www.ndermatol.like.pl**
	since issue 2.2010 to issue 3.2011	**www.odermatol.like.pl**
	since issue 4.2011	**www.odermatol.com**
Previous shortcut:	since issue 1.2010 to issue 3.2011	**N Dermatol Online**
	since issue 4.2011	**Our Dermatol Online**

Editorial Board:

CONTENTS

DOI: 10.7241/ourd.20144.85

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

TREATMENT OF ACTIVE ACNE VULGARIS BY CHEMICAL PEELING USING 88% LACTIC ACID

Khalifa E. Sharquie[1,2], Adil A. Noaimi[1,2], Entesar A. Al-Janabi[3]

[1]*Department of Dermatology, College of Medicine, University of Baghdad, Iraqi*
[2]*Arab Board for Dermatology and Venereology, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq*
[3]*Department of Dermatology and Venereology, Baghdad Teaching, Baghdad, Iraq*

Corresponding author: Prof. Khalifa E. Sharquie ksharquie@ymail.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 337-342 Date of submission: 17.07.2014 / acceptance: 26.08.2014

Abstract
Introduction: The etiopathogenesis of acne vulgaris is multifactorial, and its therapy is prolonged course that might be not accepted by many patients. Most recently TCA 35% one session peeling gave complete clearance and full remission for active acne vulgaris. Lactic acid has been used effectively as therapeutic topical agents for many skin diseases.
Aim: To evaluate the efficacy and safety of chemical peeling using 88% lactic acid solution in the treatment of active acne vulgaris.
Material and Methods: This clinical, interventional, therapeutic study was done at the Department of Dermatology, Baghdad Teaching Hospital, during the period from October 2012 to October 2013.
Twenty five patients with active acne vulgaris were included, 15 (60%) females and 10 (40%) males and their ages ranged from 16-36 (21.5000± 5.46279) years. Fifteen patients were associated with acne scars.
Three chemical peels using 88% lactic acid solution was carried out two weeks apart for patients with active acne vulgaris with or without scarring. Scoring for active acne vulgaris and acne scar was done for each case before and after operation to evaluate the severity of acne and the degree of scar before and after treatment.
All patients were with Fitzpatrick's skin types III and IV. Patients were followed up every two weeks during period of therapy and monthly for 3 months after stopping the treatment.
Results: Twenty five patients with active acne vulgaris were treated with 3 sessions of lactic acid, fifteen patients had associated acne scar. Scoring for active acne vulgaris including papules and pustules showed highly statistically significant reduction after 2 weeks of therapy (p=0.0001), after 4 weeks (p=0.0001)and after 6 weeks (p=0.0001), with percent reduction 87.2% for papules and 94% for pustules after end of sessions while after 3 months follow up the reduction rate for papules 93.8% and p-value (p=0.001) and for pustules 97.6% and (p=0.0001). While the scarring reduction was moderate in 3 (20%) patients, marked in 3 (20%) patients and excellent in 9 (60%) patients with statistically significant reduction (p=0.002).
All patients had full satisfaction about the results of peeling. Post inflammatory hyperpigmentation was observed few weeks after peeling but follow up for 3 months showed complete clearance of pigmentation with lightening and tightening of skin.
Conclusions: Chemical peeling using 88% lactic acid is an effective mode of therapy for active acne vulgaris and acne scar in patient with dark complexion.

Key words: Chemical peeling; lactic acid; active acne vulgaris; acne scarring; dark complexion

Cite this article:
Sharquie KE, Noaimi AA, Al-Janabi EA. Treatment of Active Acne Vulgaris by Chemical Peeling Using 88% Lactic Acid. Our Dermatol Online. 2014; 5(4): 337-342.

Introduction

Acne is a common chronic inflammatory skin disease experienced by most adolescents and young adults and the pathogenesis of acne vulgaris is a multifactorial.The four major identified factors that are involved in pathogenesis of active acne lesion formation and scarring are: excess sebum production, follicular epidermal hyperkeratinization, the proinflammatory effects of *propioni bacterium acnes* and other normal skin flora, and immunological reactions [1,2].
Although there are many topical and systemic agents that are used in treatment of acne vulgaris, still many patients don't use these therapies as the course of treatment is prolonged, other patients have no time to use drugs or they don't like to use it or they have phobia from their side effects [3-10]. Accordingly we are looking as a researcher for topical effective therapy that used for short time.

Lasers have been used in treatment of active acne vulgaris but there is controversy regarding their effectiveness as one study showed using Diod laser is an effective therapy in clearing lesions by application three sessions, two weeks apart. Also, another study using Pulse Dye Laser (PDL) showed clearance of inflammatory acne vulgaris lesions using one session while another study also using Diod laser didn't show significant improvement of facial acne [11-15].

Most recently one session trichloracetic acid (TCA) peel 35% had been used effectively in treatment of active acne vulgaris with or without scarring and the result were very encouraging as induced both clearance of the lesions and remission of disease, In addition, scarring was reduced tremendously. This stimulated us to conduct the present work using lactic acid 88%in treatment of active acne vulgaris [16-20].

Lactic acid is a member of alpha hydroxy acids (AHA) which has been used in treatment of many skin diseases [21] including: Lactic acid used in treatment of recurrent aphthous ulcer as oral gurgle by increasing spontaneous secretion of endothelial growth factor from keratinocytes and by its antibacterial action [22].

Also, lactic acid has antioxidant action and this might help in repigmentation of patch of vitiligo as topical 15% lactic acid solution has been use as new mode of therapy for the treatment of localized type of vitiligo [23].

Lactic acid cream 6% has been found effective in the treatment of melasma as topical therapy and also LA 88% has been tried as effective peeling agents for melasma [24]. Topical 15% lactic acid solution was found to be an effective therapy for alopecia areata [25].

The two major side effects of alpha hydroxy acids are irritation and sun sensitivity [26].

Hence, the aim of present work is to treat patients with active acne vulgaris with associated scars by 88% lactic acid as peeling agents and to compare its efficacy with TCA35% peels.

Material and Methods

This clinical, interventional, therapeutic study was carried out at the Department of Dermatology, Baghdad Teaching Hospital, during the period from October 2012 to October 2013. Twenty five patients with active acne vulgaris were included in this study, 15 (60%) females and 10 (40%) males and their ages ranged from 16-36 with mean and SD of 21.5000± 5.46279 years. Fifteen patients were associated with acne scars 10 (66.6%) females and 5 (33.4) males.

The nature and target of this study were explained for each patient and formal consent was taken for each patient before starting the therapy, after full explanation about the nature of the disease, course, the procedure of treatment, follow up, prognosis and the need for pre and post treatment photographs by Sony-Digital, high sensitivity, 16.1megapixels, 5 x optical zoom camera in the same place with fixed illumination and distance. Also, ethical approval was given by the scientific committee of the Scientific Council of Dermatology and Venereology-Iraqi Board for Medical Specializations. Statistical analysis was carried out using T test and Chi square.

History and dermatological examination were performed for all patients regarding all demographic points related to the disease. The severity of acne was graded using the following score:

- Mild acne in which the count of pustules is less than 20 and the count of papules is less than 10.
- Moderate acne in which the count of pustules is ranging between 20-40 and the count of papules is ranging between 10-30.
- Severe acne in which the count of pustules is more than 40 and the count of papules is more than 30.

Patients who had scarring in addition to active lesions the following score was used to evaluate the severity of scarring before and after peeling:

Score 0 = 0	No change or baseline.
Score 1 = 1%-25%	Mild reduction.
Score 2 = 26%-50%	Moderate reduction.
Score 3= 51%-75%	Marked reduction.
Score 4>75%-100%	Excellent reduction.

Patients satisfaction to response to therapy was evaluated according to satisfaction score that classified into:

1) Full satisfaction. 2) Partial satisfaction. 3) No satisfaction.

In addition to active lesions, some patients had white and black comedones. All patients were with Fitzpatrick's skin types III and IV.

Exclusion criteria are coexistence of any other dermatoses involving the face and allergy to medications, plus patients who had used any topical and systemic treatments in the previous one month, pregnant and lactating women, recurrent herpes infection, immunocompromised patients, diseases or drugs that interfere with clotting systems , patients with medical diseases like diabetes mellitus, epilepsy and patients with other types of acne like drug induced acne, cosmetic acne, post-hair epilation acne, occupational acne, peri-oral dermatitis, mechanical acne, and acne aestivalis.

Technique of peeling

Lactic acid (GAINLAND CHEMICAL COMPANY, UK) was used in concentration of 88%. Patients were prepared by cleansing and degreasing the whole face by using acetone or 70% alcohol soaked-gauze. The area was rubbed vigorously until it losses the greasy texture and becomes dry with faint erythema. Then the whole face was coated with lactic acid by using cotton-tipped applicator and generally rubbed in with pressure, and number of coating ranged from 1 - 3 applications with a mean 2, with three minutes apart, until fine frosting occurred. Three sessions of lactic acid peel was done for all 25 patients of active acne, even patients with scars, two weeks apart.

Post operative instructions and follow up

The skin of the treated area was washed with water immediately after the procedure, then cold wet compresses were applied immediately after the peel. After that hydrocortisone 1% ointment or zinc oxide ointment was applied for whole face. Patients were told that stinging will crescendo for 2 minutes and then will subside. All patients were given instruction leaflets that also specify dates for the patients follow up visit. For the entire first week, the patient is instructed to use topical fusidic acid (Leo-Pharma Company) ointment and systemic antibiotic include Augmentin (amoxicillin/ clavulanate potassium) 625mg /3times daily. In addition antihistamine were prescribed for patients, we asked the patients to wash the face 3-4 times/day with potassium permanganate solution (1/10000) or using an acetic acid solution (1 tea spoon white vinegar in 1 pint warm water) in the first five days following peeling.

And after five days onward, the patient could resume washing the face and scalp with non irritant soap and water. Also, the patients were advised to use sun screen at morning, this sunscreen contains titanium dioxide (ISIS, MADE IN FRANCE) and topical hydrocortisone at night. Follow up after 6 weeks, follow up was carried for 3 months to monitor the clearance of lesions and improvement in the scars and any relapse.

Results

Lactic acid peeling was used three times 2 weeks a part in patients with active acne vulgaris and scarring. Scoring for active acne vulgaris included papules and pustules showed highly statistically significant reduction after 2 weeks of therapy (p=0.0001), after 4 weeks (p=0.0001), after 6 weeks (p=0.0001) with percent reduction 87.2% for papules and 94% for pustules after end of sessions while after 3 months follow up the reduction rate for papules 93.8%, p-value (p=0.001) and for pustules 97.6%, p-value (p=0.0001), (Tabl I).

While the acne scar scoring reduction after 3 sessions of therapy was ranged from 26-50% in 3 patients (moderate reduction) and 51-75 % in 3 patients (marked reduction), while was more than 75% in 9 patients (excellent reduction), with statistically significant reduction (p=0.002) following peeling. There was mild post inflammatory hyperpigmentation. After 3 months of follow up the reduction of scars was not significantly different from the time after sessions but there was obvious tightening and whitening of the skin of whole face (Tabl. II).

	Pre therapy	(2nd visit) 1st session	(3rd visit) 2nd session	(4th visit) 3rd session	Percent redution**	Follow up	Percent redution**
papule	33.7±14.5	13.1±4.1	7.2±2.1	3.7±1.9	87.2%	2.1±0.8	93.8%
*p- value		0.0001	0.0001	0.0001		0.001	
pustule	33.1±10.7	13.6±5.1	6.5±2.2	2±0.9	94%	0.8±0.6	97.6%
P- value		0.0001	0.0001	0.0001		0.0001	

Table I. Results of patients with active acne vulgaris that was treated by 88% lactic acid peels.

*Percent Reduction = (A-B)/A*100,Ais an initial value, B is a final value

Reduction rate	No. of patients	%	P value
Excellent (75-100%)	9	60%	0.002
Marked (51-75%)	3	20%	
Moderate (26-50%)	3	20%	
Total	15	100	

Table II. Results of peeling of scarring that associated with acne lesions.

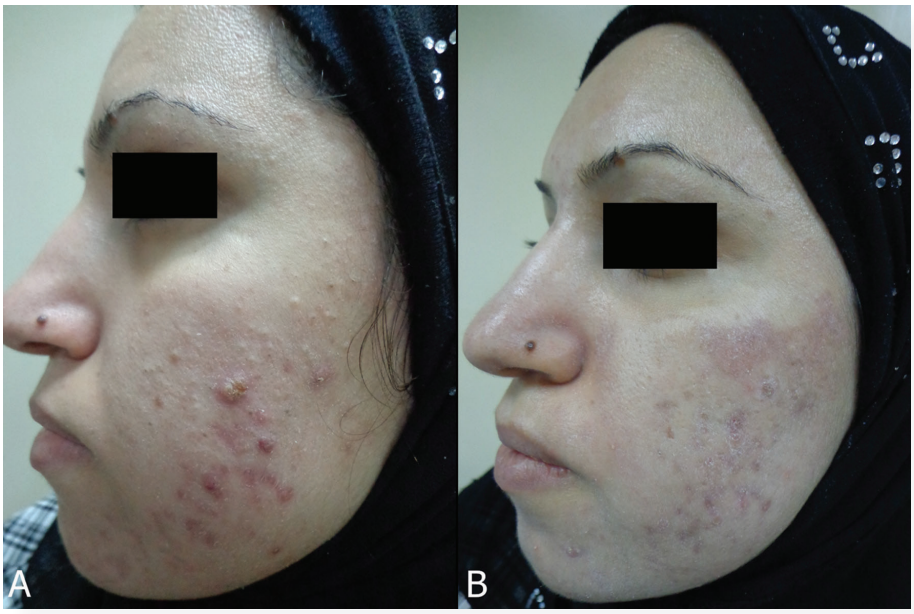


Figure 1. Twenty four years old female with active skin lesions. (A) Before treatment; (B) Showing clearance of active lesions after 88% lactic acid peels.

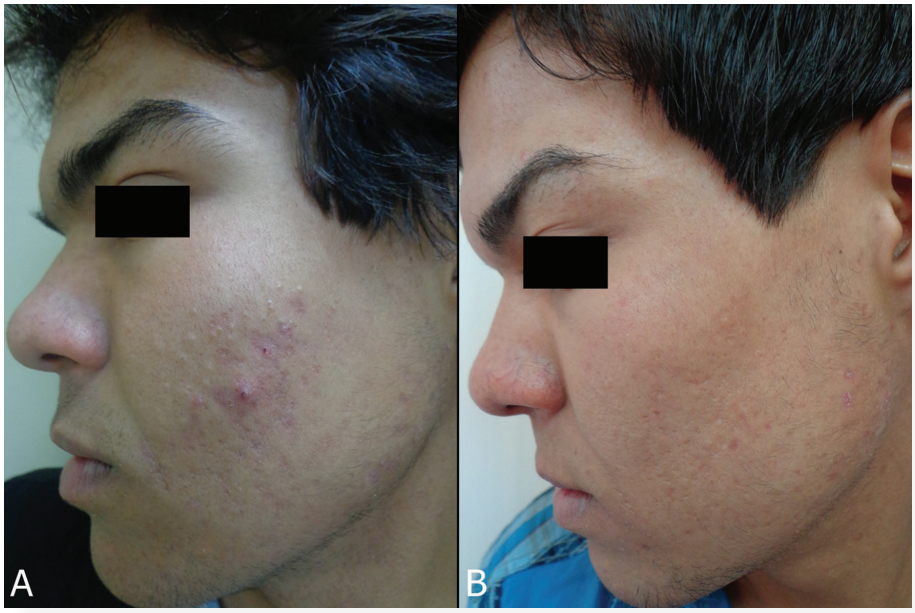


Figure 1. Twenty four years old female with active skin lesions. (A) Before treatment; (B) Showing clearance of active lesions after 88% lactic acid peels.

Discussion

There are many therapies for active acne vulgaris for clearance of lesions and preventing scars but all of these need long term of treatment at least 6 months. Still there are many non compliant patients for many reasons mainly because there are not ready to use treatment for long time or they are afraid from their side effects [3-8]. Accordingly researcher are looking for single therapy that used over short time in order to induce recovery from active lesions.

Laser sessions are effective for acne scars but give controversial results in treatment of active acne vulgaris in addition its high cost therapy and not available in centers [11-15].

Most recently, TCA 35% had been used in treatment of active acne vulgaris and the result very satisfactory for patients in inducing long term remission of acne lesions and reducing scarring [20].

The present work using 88% LA showed significant improvement of active acne vulgaris including papules and pustules after 3 session of peeling in patients with active acne lesion and the associated scarring was effectively reduced.

When the result of peeling of TCA compared with peeling result of lactic acid, we observed almost similar result both in the clearance of active lesions and reducing of scars at the end of course of therapy and at the end of 3 months follow up (Tabl. III).

Accordingly one session of TCA peeling is as effective as 3 sessions of lactic acid.

Hence the present study showed that LA peeling is a cost effective therapy for treatment of active acne vulgaris and its associated scarring that could be advised as treatment for patients that they don't like to use topical and oral therapy in a long term regimen.

Dermabrasion and peeling by lasers or acids are not well advised in patients with dark complexion as post inflammatory hyperpigmentation might be complication of these therapy but we have noticed from daily clinical practice that postinflammatory hyperpigmentation is not a complications of dermabrasion or peeling although all our patients have Fitzpatrick's skin types III and IV. In contrary these patients have whitening of their skin [18-20].

It is difficult to explain the mechanism of action of lactic acid peeling but we can suggest through the following actions: through reduction of microflora of acne lesions mainly Propioni bacterium acnes and other bacteria that causing acne, also might reduce the size of sebaceous glands that is involved in pathogenesis of the acne and thirdly LA might change the immunological reaction present in the acne lesions hence inducing clearance of lesions and reducing the scars.

In conclusion, lactic acid 88% peels is low cost mode of therapy for active acne vulgaris and associated scarring with no complications.

REFERENCES

1. William J, Harald PM. Acne diagnosis and management. Martin Dunitz Ltd, 1st ed, London, 2001;1-37.
2. Sommkr S, Bojar R, Cunliffe WJ, Hollanixf D, Holland KT, Naags H. Investigation of the mechanism of action of 2% fusidic acid lotion in the treatment of acne vulgaris Clin Exp Dermatol. 1997;22:211-5.
3. Ellis C, Krach K. Uses and complications of isotretinoin therapy. J Am Acad Dermatol. 2001;45:S150-7.
4. Leyden J. Current issues in antimicrobial therapy for the treatment of acne. J Eur Acad Dermatol Venereol. 2001;15(suppl 3):51-5.
5. Eaden E, Jones C, Tipper J, Cove J, Cunliffe W, Layton A. Antibiotic resistant propionibacteria in acne: need for policies to modify antibiotic usage. BMJ. 1993;306:555-6.
Leyden J, Shalita A. Rational therapy for acne vulgaris: an update on topical treatment. J AmAcad Dermatol. 1986;15:907-14.
7. Eady EA, Cove JH, Holland KT, Cunliffe WJ. Erythromvcin resistant propionibacteria in antibiotic treated acne patients: association with therapeutic failure. Br J Dermatol. 1989;121:51-7.
8. Leyden JJ, McGinley KJ, Cavalieri S, Webster GF, Mills OH, Kligman AM. Propionibacterium acnes resistance to antibiotics in acne patients. J Am Acad Dermatol. 1983;8:41-5.

	TCA35%			TCA35%			LA88%			LA88%		
	End of therapy			End of follow up			End of therapy			End of follow up		
papule	11.78±9.21	73.7%	>0.0001	2.50±1.98	94.4%	>0.0001	3.7±1.9	87.2%	0.0001	2.1±0.8	93.8%	0.001
pustule	21.89±14.54	52.5%	>0.0001	2.83±2.0	93.86%	>0.0001	2±0.9	94%	0.0001	0.8±0.6	97.6%	0.0001
scarring	66.66% (excellent)	16.6% (marked)	16.6% (moderate)	same	same	same	60% (excellent)	20% (marked)	20% (moderate)	same	same	same
Post inflammatory (tightening and whitening)	good			excellent			good			good		

Table III. Difference between results of peeling by TCA and LA.

9. Zaenglein AL, Thiboutot DM. Acne Vulgaris. Bolognia JL, Jorizzo JL, Schaffer JV. Dermatology, 3rd ed., China: Elsevier Saunders. 2012;36:545-60.
10. James WD, Berger TG, Eleston DM (eds.) Acne.Andrew's diseases of the skin Clinical Dermatology 11thed., Philadilphia: Saunders Elsevier. 2011;13:228-46.
11. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. J Am Acad Dermatol. 2001;45:109-17.
12. Moritz DL. Surgical corrections of acne scars. Dermatol Nurs. 1992;4:291-9.
13. Seaton ED, Charakida A, Mouser PE, Grace I, Clement RM, Chu AC. Pulsed-dye laser treatment for inflammatory acne vulgaris: Randomised controlled trial. Lancet. 2003;362:1347.
14. Orringer JS, Kang S, Hamilton T, Schumacher W, Cho S, Hammerberg C, et al. Treatment of acne vulgaris with a pulsed dye laser: A randomized controlled trial. JAMA. 2004;291:2834.
15. Friedman PM, Jih MH, Asadi AK, Goldberg LH. Treatment of inflammatory facial acne vulgaris with 1450-nm Diode laser :Apilot study. Dermatol Surg. 2004;30:147-51.
16. Garg VK, Sinha MS, AND Sarkar R. Glycolic Acid Peels Versus Salicylic–Mandelic Acid Peels in Active Acne Vulgaris and Post-Acne Scarring and Hyperpigmentation: A Comparative Study 2008 by the American Society for Dermatologic Surgery, Inc. _ Published by Wiley Periodicals, Inc._ ISSN: 1076-0512 _ Dermatol Surg. 2009;35:59–65.
17. Atzori L, Brundu MA, Biggio P, Orru A. Glycolic acid peeling in the treatment of acne. J Eur Acad Dermatol Venereol. 1999;12:119–22.
18. Al-Waiz MM, Al-Sharqi AI. Medium depth chemical peels in treatment of acne scars in dark-skinned individuals. Dermatol Surg. 2002;28:1-5.
19.Sh arquie KE, Noaimi AA. CO2 dermabrasion of acne scarring. J Iraqi Comm Mede. 2013;25:1.
20. Sharquie KE, Noaimi AA, Al-Janabi EA. Treatment of Active Acne Vulgaris by Chemical Peeling Using TCA 35%: J Cosm Dermatol Scienc Applicat. 2013;3:32-5.
21. Fox M, Helfrich Y, Kang S. Other topical medications in: In Bolognia JL,Jorizzo JL and Schaffer JV. Dermatology, 3rd ed., Spain: Mosby Elsevier 2012;129:2158.
22. Sharquie KE, AL-Tammimy SM. Lactic Acid 5% Mouthwash in the Treatment of Recurrent Aphthous Ulcerations. A Thesis Submitted To The Scientific Council Of Dermatology And Venereology As A Partial Fulfillment For The Degree Of Fellowship Of Iraqi Board For Medical Specialization In Dermatology And Venereology, coll. Med. Bagh. University. 2005.
23. Sharquie KE, Mohammed Y Saeed. Treatment of vitiligo with 15% lactic acid solution in comparison with other topical therapies in vitiligo.Thesis for fellow ship of Iraqi commission for medical specialization in Dermatology and Venereology, coll. Med Bagh Univ. 2002:36-46.
24. Sharquie KE, Al-Mashhadani SA, Al-Saadi AF. Topical Treatment of Melasma with Lactic Acid Cream: A comparative study with Glycolic Acid Cream. A Thesis Submitted to the Scientific Council of Dermatology and Venereology as a Partial Fulfillment for the Degree of Fellowship of Iraqi Board for Medical Specializations in Dermatology, coll. Med Bagh Univ. 2006.
25. Al-waiz MM, Al Mashhadani SA, Qadir NO. Treatment of patchy alopecia areata by using topical 15% lactic acid solution" is submitted to the Scientific Committee of Dermatology and Venereology as a partial fulfillment for the degree of Fellowship of Iraqi Board for Medical Specialization in Dermatology, coll. Med Bagh Univ. 2006.
26. Draelos ZD.Cosmotics and cosmeceuticals in: In Bolognia JL,Jorizzo JL and Schaffer JV. Dermatology, 3rd ed., Spain: Mosby Elsevier. 2012;153:2488.

DOI: 10.7241/ourd.20144.86

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

A STUDY ON THE PROFILE AND SEXUAL BEHAVIOUR OF PATIENTS IN AN ICTC CENTRE IN A DISTRICT HOSPITAL IN NORTH INDIA

Neerja Puri, Ashutosh Talwar, MRS Monika

Department of Dermatology and Venereology, Punjab Health Systems Corporation, Ferozepur, Punjab, India

Source of Support:
Nil
Competing Interests:
None

Corresponding author: Dr Neerja Puri *neerjaashu@rediffmail.com*

Our Dermatol Online. 2014; 5(4): 343-346 Date of submission: 21.07.2014 / acceptance: 08.09.2014

Abstract

Introduction: Integrated counseling and testing (ICTC) for HIV is a cost-effective intervention in preventing the spread of HIV transmission and is an integral part of HIV prevention program, which provides an opportunity to learn and accept the HIV status in a comfortable, convenient, and confidential manner.

Material and Methods: A retrospective study of 3600 attendees visiting the ICTC centre from April 2010 to April 2011was undertaken. The study included 3600 attendees who came either voluntarily or referred by various department of this institute. Dominant reason for visiting ICTC was the history/presence of high risk behavior (HRB).

Results: 60% indulged in heterosexual route; other HRB including men having sex with men or MSM were 5% and injecting drug users or IDU) were 15%. There were more positive among males, 21-40 years of age group, those living singly, unmarried, divorcee, widow(er) and separated. Similarly positives were more amongst illiterates, less educated and those engaged in unskilled and semi skilled jobs. Adolescent students (>14 years) accounted for one-fifth of the total positives. Direct walk in clients were more positive compared to those referred by doctors. Overall sero positivity was 4.8%; high in males, 21-40 years age, unmarried and divorcee etc.

Conclusions: Sero prevalence decreased with improvement in education and also with improvement in job nature. It was also high in those living alone compared to those staying with their family.

Key words: HIV; AIDS; sexual; behavior; high risk behavior; truckers

Cite this article:
Puri N, Talwar A, Monika MRS. A study on the profile and sexual behaviour of patients in an ICTC Centre in a District Hospital in North India. Our Dermatol Online. 2014; 5(4): 343-346.

Introduction

HIV was first identified in the gay community in the United States in the early 1980s, but the origin of the virus is in Africa, likely around the Democratic Republic of the Congo (former Zaire) [1]. There are large differences in HIV prevalence across the world, with Africa sustaining much higher HIV rates than elsewhere [2].

In India, about 2.47 million people are infected. As per the PSACS, the infection prevalence in Punjab is 0.11 per cent as against the national figure of 0.36 per cent. The state has so far reported 17,820 HIV positive cases; AIDS cases on ART are 7,567 and reported deaths are 786 [3]. Due to easy availability of drugs and high purchasing power in the state, injection drug users (IDUs) are emerging as the major problem. The latest mapping study and surveillance data has indicated at increasing HIV positive cases in IDUs category. PSACS is focusing on IDUs through 15 targeted intervention (TI) projects. Sexual, especially the heterosexual, transmission is the main driver of the epidemic in most of India, accounting for nearly 90% of nationwide prevalence [4]. In order to implement the desired intervention, the epidemiology of modes of transmission (HIV/AIDS) in a particular region has to be understood with regard to sociodemographic factors, level of awareness, as well as risk behavior of the population. It is so because the effective approach for the prevention and control of infection/disease is through awareness generation and lifestyle changes.

Integrated counseling and testing (ICTC) for HIV is a cost-effective intervention in preventing the spread of HIV transmission and is an integral part of HIV prevention program, which provides an opportunity to learn and accept the HIV status in a comfortable, convenient, and confidential manner [5]. Integrated counseling testing center (ICTC) network is the first interface between a person willing to get tested and the public health system. Further, it is an entry point to care.

In the NACP phase III, HIV testing facilities have been segregated in A and B categories by district and are now available at all medical colleges, district hospitals, and subdistrict hospitals (Community Health Centers). At subdistrict level, earlier ICTCs and facilities providing prevention of Parent to Child Transmission of HIV and AIDS (PPTCT) services are now remodeled as a hub to deliver integrated services to all clients. Presence of infection everywhere highlights spread from urban to rural areas; from high risk to general population via bridge population, and from permissive to conservative societies. Migration of labor, low literacy levels, gender disparities, and prevalent RTI/STI have contributed to this spread. The data generated in ICTC provides an important clue to understand the epidemiology of the disease in a particular region [6,7].

There are four subgroups of single men for each age category: those with no partners, those with casual partners, those with female sex worker partners, and those with both casual and female sex worker partners [8]. Casual partners are drawn at random from the female population, and female sex worker partners are drawn at random from the sex worker population. In parallel, married men of any age are in one of four subgroups: spouse only, spouse and casual partners, spouse and female sex worker partners or spouse, casual, and female sex worker partners. viral transmission rates from men to women are higher (by a factor of 2) than from women to men. In addition, due to the extremely short length of partnerships with female sex workers, it is assumed that the transmission rate is lower in these partnerships than in casual or spousal partnerships. Condom use differs by gender, marital status, and partnership type. There is assumed to be no condom use in spousal partnerships, and higher condom use in partnerships with female sex workers than in other premarital or extramarital sex.

Aims

1. To find out the profile of those who come to avail the ICTC services
2. To know the profile of those found positives.
3. An additional objective was to find out sero positivity in subsamples of the attendee in terms of various socio-demographic and epidemiological characteristics.

Material and Methods

A retrospective study of 3600 attendees visiting the ICTC centre from April 2010 to April 2011was undertaken. The epidemiological and clinical aspects of each patient were recorded in the computer and then analysed in detail. The study included 3600 attendees attendees for a period of one year, who came either voluntarily or referred by various department of this institute. Anonymous and unlinked information was collected (as per NACO guidelines) on predesigned schedule by the counsellor who interviewed the attendees under strict confidentiality. After the pretest counseling and obtaining the consent from the attendees, blood samples were collected. As per the policy prescribed by NACO, HIV was confirmed by performing enzyme-linked immunosorbent assay (ELISA), by using two different antigens and a rapid test. The prior approval was taken from the appropriate authorities from the institute.

Results

The data was collected, tabulated and the results were analyzed (Tabs I - III).

Sr No	Age Group	Number	Percentage
1	10-20	360	10%
2	21-30	144	40%
3	31-40	108	30%
4	41-50	360	10%
5	51-60	288	8%
6	>60	72	2%
	Total	3600	100%

Table I. Age group of ICTC attendees.

Sr No	Occupation	Number	Percentage
1	Farmers	864	24%
2	Unemployed youth	966	26%
3	Manual workers	506	14%
4	Students	720	20%
5	Housewives	360	10%
6	Truck drivers	216	6%
	Total	3600	100%

Table II. Occupation of the ICTC attendees.

Sr No	Routes of Transmission	Number	Percentage
1	Heterosexual	2160	60%
2	Homosexual	180	5%
3	Blood transfusion	252	7%
4	Intravenous drug users	540	15%
5	Mother to child transmission (mct)	108	3%
6	Unknown causes	360	10%
	Total	3600	100%

Table III. The various routes of transmission.

Out of total 3600 patients, 2160 (60%) were males, 1440 (40%) females. The maximum number of patients (40%) were seen in the age group 21-30 years, followed by 30% patients in the age - group 31-40 years, 10% patients in the age - group 10-20 years, 10% patients in the age - group 41-50 years, 8% patients in the age - group 51-60 years, 2% patients were more than 60 years (Tabl. I). All subjects were adults (>15 years). Majority were married (82%), literates (72%), urbanites (56%), and natives (55%). Male: Female was 1.5:1. Regarding their occupational status, 26% were unemployed youth, 24% were farmers, 14% were manual workers (including mechanics, labourers, tailors and carpenters), 10% were housewives, 20% were students and 6 % were truck drivers (Tabl. II). Half of them came to know their HIV status from ICTC , followed by physicians (30%) and rest from RNTCP (9%), PPTCT (3%), self-referral (5%), and accidentally detected (2%). Large number informed their spouse (85%) and family (76%). Based on self-reporting, 60% clients acquired it by heterosexual and 5% by homosexual route (man having sex with man), blood transfusion was the cause in 7% cases, intravenous drug abuse was noted in 15% clients, mother to child transmission was seen in 3% of the attendees and no cause could be elicited by the counsellor in 10% cases (Tabl. III). Sexual route needs to be targeted because 21-40 years age group accounted for 70% cases. In 90% couples, the husband was the source of the infection and in 10% couples, the wife was the source of the infection. 60% patients had unprotected sexual contact while 40% patients had at least one contact protected by the usage of condom. 30% patients had premarital contact (PMC), 45% patients extramarital contact (EMC) and 25% patients had both PMC and EMC. The remaining patients denied any history of PMC or EMC. The source of contact was commercial sex workers (CSW) in 40% patients in 35% cases a known friend was the source of contact, while in 25% cases the contact was casual.

Discussion

The ICTC is an ideal point for prevention, where HIV negative individuals learn to use full array of existing services and interventions to adopt and maintain risk reduction behaviors, and HIV positive individuals use quality prevention services to adopt and sustain lifelong protective behaviors and avoid the virus transmission. ICTC services cater to those who come to the center either from referral (care providers) or direct walk in clients; some times it can be referral from the targeted interventions by NGOs running in the area [9]. So the profile of attendees depends upon the characteristics of the catchment areas and the population residing therein [10]. Many people do not know that they are/may be HIV positive and the challenge is to make these people aware to come forward for the testing and adopt a healthy lifestyle, thereafter for the access to care and treatment and help in preventing further transmission. Counselling and testing are important for prevention and control of HIV/AIDS; however, it is neither desirable nor feasible to counsel and test everyone in the general population. The subpopulations which are vulnerable or practice high risk behavior (HRB) or have high HIV prevalence shall be the target group for these services.

An alarming fact was observed in this study that the prevalence is catching up in 21-30 years of age group, indicating that AIDS still threatens the most productive segment of society in the prime of their working life [11]. It emphasizes the need of some youth specific interventions or some school or college-based interventions whereby these people can be prepared beforehand. Education and job status showed the inverse relationship with the prevalence. In fact none of the positive was educated beyond 12th standard. It seems that overall development (reflected by better education and job opportunities) will provide some protection. As such the people who are educated or placed in better jobs (mostly go together) are more receptive to IEC and amenable to interventions. India's vulnerability to the AIDS epidemic can be attributed to pervasive poverty, huge illiteracy, less awareness, promiscuous behavior, and adverse attitude towards condom use. The route of transmission reported among HIV-positive male and female clients of ICTC is mainly heterosexual contact [12]. Therefore for behavioral change communication (BCC) and effective positive prevention, it is essential to explore HRB of each and every client. Another important bridge population is the long-route truck drivers of India; 70% of them have sexually transmitted infections and on an average they have 200 sexual encounters per year [13].

Therefore it was not surprising to find 95% PLHA truck driver in this study to have acquired the infection through heterosexual route (remaining 5% did not mention the route). Present study reinforces the need to work more intensively with this population. One-forth clients in present study were from rural areas, which confirm that the epidemic is moving from urban to rural areas; better surveillance can explore more clients. Migration itself is not a risk factor for HIV but the circumstances in which migration occurs increases vulnerability to infection. Blood transfusion is second established route of transmission after sexual route, which has reduced but is still around 2%, much lower than present study (7%). Those who acquired it form blood route informed their spouse as well as family, while those who acquired it from sexual route did not inform to their spouse and family . Because of stigma associated with sexual route, a PLHA (infected through sexual route) finds it difficult to share HIV status with his/her spouse/family [14]. Same is not the case when it is acquired through blood route. The present study indicates that 90% of the infected males and 98% of the infected females were living with their families. The information regarding their disclosure of the test to their family members is not available and hence it is difficult to say whether such a high level of acceptance by the family, especially towards females will be maintained even after the disclosure or not.

Current study is subjected to certain limitations since it was conducted in a district hospital with a predesigned schedule, therefore, results are based on the reporting and data collection by the personnel employed in the ICTC. Information regarding socioeconomic status, substance abuse and condom use were not available in all the cases. Timely and relevant use of data to guide decision making (though challenging) is critical. Program needs to invest resources not just to gather data, but also to create and stimulate a culture that emphasizes appropriate data analysis and use at all levels. All these variables could have unmasked certain behavior pattern and given new dimension to this study. This study setting being a hospital decreased its external validity. Results observed are subjected to bias arising from rate of reporting in the counseling and testing centre. A community based study though resource intensive would have been better to avoid such bias. All four modes of transmission were associated with typical epidemiological determinants and have impact on accessibility of preventive/curative services and treatment-seeking behavior.

Also, the medical fraternity should take a stand and fight against the discrimination of sufferers , rather than ostracizing them to have a positive attitude for the HIV sufferers.

Conclusion

Prevention of HIV infection should theoretically be easier than prevention of water and air borne pathogens. HIV/AIDS is spread as much by human behavior and ignorance as by the virus. The wider clinical setting itself can provide enabling environment and reduce the stigma and discrimination. The empowerment of attendees and empathic attitude of staff at center is crucial, as clinical staff can set an example by exhibiting stigma free attitudes.

Improvement of IEC and HIV/AIDS awareness is one of the most effective strategies to control HIV/AIDS [15,16]. A successful communication program helps to promote behavioral change, in addition to increasing knowledge regarding the disease. Such programs will be more effective if conducted in local languages and using the locally derived data. At the same time, they must keep in mind the following: social norms, cultural beliefs, and sensitivities of the community. Such intensive IEC will improve the uptake of VCT services by the target population. Even if the country's epidemic does not match the severity of those in southern Africa, it is clear that HIV and AIDS will have a devastating effect on the lives of millions of Indians for many years to come. It is essential that effective action is taken to minimise this impact.

REFERENCES

1. Anderson J, Santelli J, Mugalla C. Changes in HIV-Related Preventative Behavior in the U. S. Population. J Acquir Immune Defic Syndr. 2003;34:195-202.
2. Carael M, Cleland JC, Deheneffe BF, Ingham R. Sexual Behavior in Developing Countries: Implications for HIV Control. AIDS. 1995; IX:1171–5.
3. Kadri SM. Determinants of HIV/AIDS in India. Indian J Pract Doc. 2008;5:73.
4. Sayal SK, Gupto CM, Songhi S. HIV infection in patients of sexually transmitted disease. Indian J Dermatol Venereal Leprol. 1999;65:131-3.
5. Joardar GK, Sarkar A, Chatterjee C, Bhattacharya RN, Banerjee P. Profile of attendees in the voluntary counseling and testing centre of North Bengal Medical College in Darjeeling District of West Bengal. Indian J Community Med. 2006;31:241.
6. Kumar A, Kumar P, Gupta M, Kamath A, Maheswari A, Singh S. Profile of Client Tested HIV Positive in a Voluntary Counseling and Testing Center of District Hospital, Udupi, South Kannada. Indian J Community Med. 2008;33:156.
7. Sanjay M. HIV infection amongst persons with high risk behavior in Pune City: Update on findings from prospective Cohort study. AIDS Research Review. 1998;1:2.
8. Muzaffar A, Gaash B. Awareness of HIV/AIDS in a remotely located conservative district of Jand K (KARGIL): Results of a community based study. Indian J Community Med. 2002;28:12.
9. Sharma AK, Guptha A, Agarwal OP. HIV/ AIDS related knowledge, risk perception attitude and sexual behaviour of working women staying in hostels. Indian J Dermatol Venereol Leprol. 2001;67:21-4.
10. John TJ, Babu PG, Saraswathi NK, Jayakumari H, Selvaraj R, Kaur A, et al. The epidermiology of AIDS in Vollore region Southern India. AIDS. 1993;7:421-4.
11. Karibasappa NA, Prosanna Babu N. Incidence of HIV seropositivity in STD cases. Indian J Dermatol Venereal Leprol. 1999;65:214-5.
12. Saggurti N. HIV risk behaviours among contracted and non-contracted male migrant workers in India: potential role of labour contractors and contractual systems in HIV prevention. AIDS. 2008; 22:127-36.
13. Pandey A. Risk behaviour, sexually transmitted infections and HIV among long-distance truck drivers: a cross-sectional survey along national highways in India. AIDS. 2008;22:81-90.
14. Newmann S. Marriage, monogamy and HIV: a profile of HIV-infected women in south India. Int J STD AIDS. 2000;11:250-3.
15. Reza-Paul S. Declines in risk behaviour and sexually transmitted infection prevalence following a community-led HIV preventive intervention among female sex workers in Mysore, India. AIDS. 2008;22:91-100.
16. Mahanta J1, Medhi GK, Paranjape RS, Roy N, Kohli A, Akoijam BS, et al. Injecting and sexual risk behaviours, sexually transmitted infections and HIV prevalence in injecting drug users in three states in India. AIDS. 2008;22:59-68.

DOI: 10.7241/ourd.20144.87

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

TOPICAL ERYTHROMYCIN-ZINC ACETATE COMPLEX LOTION VERSUS TOPICAL ERYTHROMYCIN GEL IN TREATMENT OF MILD TO MODERATE ACNE VULGARIS

Hayder R. Al-Hamamy[1], Khalifa E. Sharquie[2,3], Adil A. Noaimi[2,3], Wajeeh N. Hussein[4]

[1]*Scientific Council of Dermatology and Venereology - Iraqi Board for Medical Specializations, Baghdad, Iraq*
[2]*Department of Dermatology, College of Medicine, University of Baghdad, Baghdad, Iraq*
[3]*Iraqi and Arab Board for Dermatology and Venereology, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq*
[4]*Department of Dermatology and Venereology, Baghdad Teaching Hospital. Baghdad, Iraq*

Corresponding author: Prof. Khalifa E. Sharquie ksharquie@ymail.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 347-351 Date of submission: 07.08.2014 / acceptance: 18.09.2014

Abstract
Introduction: Topical antibiotics are the main step in the treatment of mild to moderate acne vulgaris. Erythromycin is one of the effective topical therapies for this disease. Zinc sulfate 5% solution was reported to be effective in treatment of acne vulgaris and rosacea.
Aim: To compare the effectiveness and side effects of topical erythromycin in combination with zinc and erythromycin alone in treatment of mild to moderate acne vulgaris.
Material and Methods: This single, blind, therapeutic, comparative study was done in the Department of Dermatology – Baghdad Teaching Hospital, Baghdad, Iraq; from May 2012 - August 2013.Scoring of acne was carried out and the patients were examined every two weeks for 10 weeks of treatment. One month after stopping drugs, patients were evaluated for drug complications and disease recurrence.
Eighty patients fulfilling enrollment criteria were included in this study. Patients were divided into two groups: Group A (40 patients) treated twice daily with topical erythromycin-zinc complex lotion and Group B (40 patients) treated twice daily with topical 2% erythromycin gel.
Results: Both topical erythromycin-zinc lotion and erythromycin gel were statistically an effective therapy starting after 6 weeks treatment and up to 4 weeks after stopping treatment. Erythromycin-zinc lotion was more effective and act earlier than erythromycin gel starting from 4 weeks of therapy till the end of treatment (after 10 week) and even after 4 weeks after stopping the treatment (p value <0.0001).
Conclusions: Erythromycin-zinc complex lotion was an effective and well tolerated topical therapy for mild to moderate inflammatory acne vulgaris and was more effective than erythromycin gel alone.

Key words: acne vulgaris; inflammatory; erythromycin, zinc acetate

Cite this article:
Al-Hamamy HR, Sharquie KE, Noaimi AA, Hussein WN. Topical erythromycin-zinc acetate complex lotion versus topical erythromycin gel in treatment of mild to moderate acne vulgaris. Our Dermatol Online. 2014; 5(4): 347-351

Introduction

The pathogenesis of acne vulgaris is multifactorial. The four major identified factors are: excess sebum production, follicular epidermal hyperkeratinization, the proinflammatory effects of propioni bacterium acnes and other normal skin flora, and inflammation [1].

Many topical agents have been used to target the known pathogenic factors like benzoyl peroxide, topical retinoids, azelaic acid, salicylic acid and topical antibiotics, such as erythromycin, clindamycin, and nadifloxacin. Topical antibiotics are the most commonly used therapeutic agents for the treatment of mild to moderate inflammatory acne [1,2].

Erythromycin is a macrolide antibiotic that has long been used topically for acne. It is one of the most common prescribed topical antibiotics.

Erythromycin has favorable effects in resolving inflammatory acne lesions not only by reducing the *Propioni bacterium acnes* density but also by directly inhibiting neutrophil chemotactic factors and reactive oxygen species production [1-3].

Zinc is a metallic element with bacteriostatic activity against *Propioni bacterium acnes*; it also inhibits neutrophils chemotaxis and reduces tumor necrosis factor production [4]. If used topically, zinc reduces sebum production [5], has keratolytic activity [6], increases tissue healing [7]. It also has anti-oxidant [8], antibacterial [9], antiviral [10], antiprotozoal [11], antifungal [12], immunomodulatary [13], anti-inflammatory activities [14]. If combined with antibiotics, it will reduce antibiotic resistance and increase antibiotic absorption efficiently into the skin [6].

Therefore the present work was arranged to evaluate the effectiveness of erythromycin-zinc complex compared to erythromycin alone in treatment of mild to moderate acne vulgaris.

Material and Methods

This single, blind, therapeutic, comparative study was carried out in the Department of Dermatology – Baghdad Teaching Hospital, Baghdad, Iraq from May 2012 to August 2013.

Eighty patients were included in this study, 19 (23.8%) males and 61 (76.3%) females and their ages ranged from 13-29 years with a mean ±SD of 19.97 ± 3.93 years.

Full history was taken from each patient including: age, gender, duration of disease and previous treatment. Physical examination was done to evaluate the severity of acne

Scoring of severity of acne was carried out by counting the inflammatory lesions (papules and pustules) according to Habif [3]. Side effects were recorded at each visit.

Acne was defined as mild acne in which the count of pustules is less than 20 and the count of papules is less than 10, moderate acne in which the count of pustules is ranging between 20-40 and the count of papules is ranging between 10-30 and severe acne in which the count of pustules is more than 40 and the count of papules is more than 30.

Inclusion criteria into this study were mild to moderate inflammatory acne vulgaris.

Exclusion criteria were severe and nodulocystic acne, and coexistence of any other dermatoses involving the face and allergy to medications, plus patients who had used any topical and systemic treatments in the previous two months, pregnant and lactating women. Patients with other types of acne like drug induced acne, cosmetic acne, post-hair epilation acne, occupational acne, perioral dermatitis, mechanical acne, and acne aestivalis were also excluded.

Formal consent was taken from each patient before starting the trial of treatment, after full explanation for the nature of the disease, course, treatment, prognosis and its complications, the target of the present work regarding the drug, its efficacy, side effects, the method and duration of treatment and follow up. Ethical approval was confirmed from scientific council of Dermatology and Venereology Iraqi Board for Medical Specializations.

Color photographs for each patient were performed by using Sony-digital, high sensitivity, 16.1 megapixel camera in the same place with fixed illumination and distance.

Patients were divided into two groups according to the mode of treatment, Group A treated with erythromycin-zinc complex [(Zineryt)^{R} produced by: Astellas Pharma Europe B.V, Leiderdorp, The Netherlands; which contains erythromycin 40mg and zinc acetate 12mg per ml on concentration] and Group B treated with 2% erythromycin gel [(Erythromycin)^{R} Produced by: Al-Shifa Company, Damascus, Syria, 2% gel].

Patients were instructed to apply the treatment twice daily for 10 weeks. The clinical evaluation was done every two weeks till the end of the ten weeks. Then the patients were asked to stop the use of medication to be re-evaluated again after one month without any treatment to review the relapse rate, local and systemic side effects. Satisfaction of patients to treatment is classified into full satisfaction, partial satisfaction and no satisfaction.

Statistical analysis were done using SPSS version 20 (Statistical Package for Social Sciences). Comparison between both groups was done by using independent sample t-test. Comparison before and after treatment in each group was done by using paired t-test, comparison of reduction rate of the lesions in both groups done by using chi- square, and P-value < 0.05 was considered as level of significance.

Results

The mean ages± SD of patients in Group A were 19.95 ± 3.6 years, 10 were males and 30 were females with female to male ratio 3:1. The mean ages± SD of patients in Group B were 20 ± 4.26 years, 9 were males and 31 were females with female to male ratio 3.4:1.

The mean ± SD of duration of acne in patients within Group A were 18.70 ± 14.50 (range from 4-60 weeks), and the mean ± SD for those in Group B were 16.10 ± 12.66 (range from 4-60 weeks). Both groups were statistically matched regarding age, gender and duration of the disease.

In Group A the papules started to be reduced significantly after 4 weeks of treatment (p value= 0.0001), while the number of pustules started to be reduced after 2 weeks (p value= 0.019). In Group B the papules and pustules started to be reduced significantly after 6 weeks of treatment (p value <0.0146, and 0.0049 respectively).

Comparison of Group A with Group B revealed that reduction in number of papules and pustules was significantly more in Group A starting from the 4th week and increased at each visit till the end of the treatment (Tabl. I; Figs 1 - 2).

The percent reduction rate from baseline visit up to 10 weeks of treatment for Group A were 77.2% and 85.5% for papules and pustules respectively. And for Group B were 35% and 23.25% for papules and pustules respectively (Tabl. II).

After one month of follow up, there was no significant relapse in both groups as the number of papules and pustules did not increased significantly (p value= 0.90 for papules and 0.92 for pustules in Group A, 0.85 for papules and 0.91 for pustules in Group B) (Tabl. III).

The assessment of local side effects for Group A showed: burning sensation in 20 (50%) patients, flare-up at the beginning of treatment 5 (12.5%), erythema 12 (30%), scaling 13 (32.5%), dry skin 30 (75%) and pruritus in 8 (20%) patients. All these symptoms and signs were disappeared after 10 weeks from starting treatment except dry skin which persists in three patients (7.5%).

The assessment of local side effects for Group B revealed: burning sensation in 2 (5%) patients, erythema in 1 (2.5%), scaling in 2 (5%), dry skin in 4 (10%) and pruritus in 3 (7.5%) patients. All these symptoms disappeared after 10 weeks from starting treatment. For both groups, the side effects did not necessitate stopping the treatment.

The assessment of systemic side effects for Group A showed 3 (7.5%) of patients suffered gastrointestinal upset, 1 (2.5%) from headache at 2nd visit. These complain resolved at next visit without discontinuation of treatment. Patients in Group B showed no systemic side effects along the course of treatment.

In Group A; 30 (75%) patients were fully satisfied, 7 (17.5%) patients were partially satisfied and 3 (7.5%) patients were not satisfied. In Group B; 20 (50%) patients were fully satisfied, 10 (25%) patients were partially satisfied and 10 (25%) patients were not satisfied. Hence the patients in Group A were significantly satisfied with treatment more than patients in Group B (*p* value= 0.043).

	Papules (Mean ±SD)			Pustules (Mean ±SD)		
	Group A	Group B	P value	Group A	Group B	P value
Baseline visit	11.40 ± 4.07	11.50 ± 3.29	0.904	20.58 ± 7.25	19.65 ± 4.88	0.505
After 2 weeks	9.55 ± 4.74	10.82 ± 3.16	0.161	*16.65 ± 7.39	19.00 ± 4.80	0.096
After 4 weeks	*7.32 ± 4.15	10.15 ± 3.29	#0.001	*9.88 ± 4.95	17.98 ± 4.60	#0.0001
After 6 weeks	*5.38 ± 3.93	*9.68 ± 3.25	#0.0001	*6.50 ± 4.91	*16.75 ± 4.03	#0.0001
After 8 weeks	*3.15 ± 3.32	*7.88 ± 2.84	#0.0001	*3.30 ± 3.70	*16.20 ± 4.26	#0.0001
After 10 weeks	*2.52 ± 2.73	*7.38 ± 2.37	#0.0001	*2.90 ± 3.26	*14.98 ± 3.87	#0.0001

Table I. The mean ± SD of papules and pustules in both groups during the course of treatment.

***Statistically different from the 1st visit within the same group (paired t test).**

#Statistically different between both groups (independent t test).

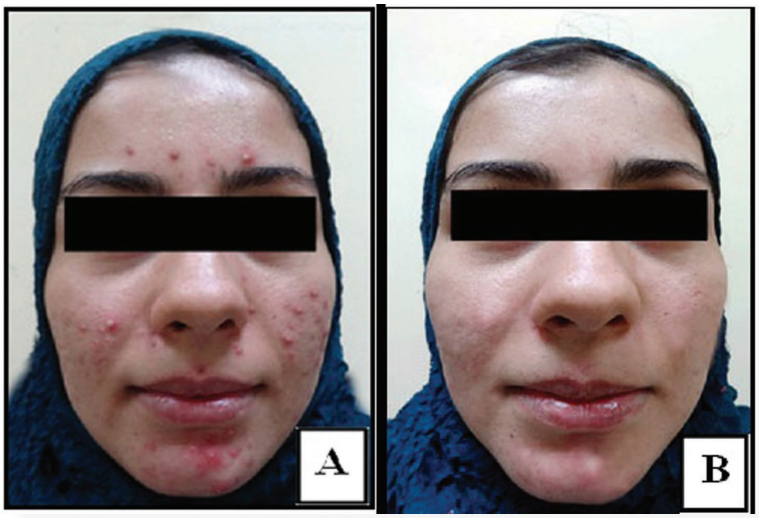


Figure 1. Twenty three years old female with moderate acne vulgaris (A). Before treatment and (B). Complete healing six weeks after treatment with topical erythromycin-zinc lotion.

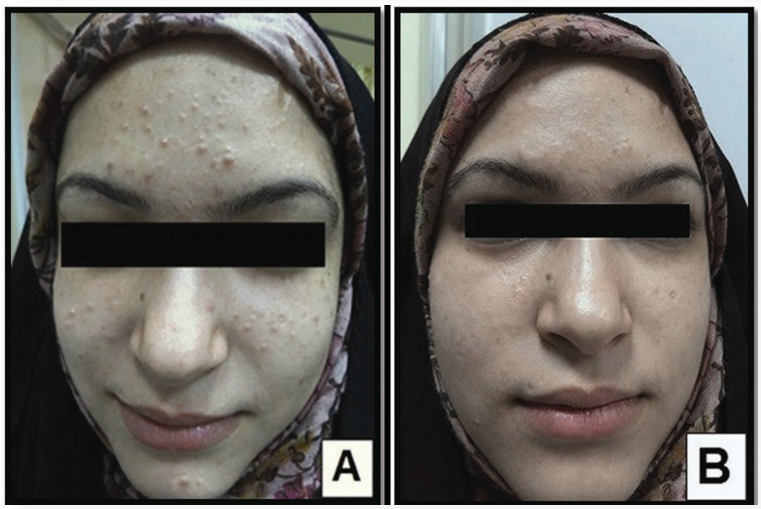


Figure 2. Sixteen years old female with moderate acne vulgaris (A) Before treatment and (B). Complete healing ten weeks after treatment with topical erythromycin gel 2%.

Visits	Group A		Group B	
	Papules	Pustules	Papules	Pustules
(Baseline visit)	0	0	0	0
After 2 weeks	16.2%	19%	6%	3.3%
After 4 weeks	35.8%	52%	11.7%	8.5%
After 6 weeks	52.8%	68,4%	15.8%	14.75%
After 8 weeks	72.36%	84%	31.5%	17.5%
After 10 weeks	77.9%	85.9%	35.8%	23.75%
4 weeks after stopping treatment	77.2%	85.5%	35%	23.25%

Table II. Percent reduction rate for both groups at each visit.

***Percent Reduction = (A-B)/A*100, A is an initial value, B is a final value.**

Group	Type	End of the 10 wks.	4wks following Stopping the R	P-value
Group A	Papules	2.52 ±	2.60 ± 2.82	0.90*
	Pustules	2.90 ±3.26	2.98 ± 3.43	0.92*
Group B	Papules	7.38 ± 2.37	7.48 ± 2.41	0.85*
	Pustules	14.98 ± 3.87	15.08 ± 3.83	0.91*

Table III. Comparison of the number of papules and pustules (mean ±SD) of both groups after one month follow up with that at 10 weeks of therapy.

***p- value not significant ≥ 0.05**

Conclusion

Acne is a common disease and a lot of patients require treatment for relatively long time [1,2]. Topical antibiotics are the main stay for mild to moderate inflammatory acne vulgaris. Erythromycin is widely used antibiotic in acne vulgaris and Zinc sulfate solution 5% has been used successfully in the treatment of acne vulgaris [15].

In present study, the effect of the addition of zinc acetate to erythromycin was assessed. This combination was proved to be effective as the number of papules and pustules were recorded to be reduced significantly from second week onward. Side effects were mild and well tolerated and did not necessitate stopping the treatment. No relapse was recorded after one month follow up.

This study has proved that erythromycin-zinc complex was highly effective in treatment of acne vulgaris, act earlier and much more effective than erythromycin gel alone.

These results are comparable to other studies in which the treatment with Zineryt lotion was found to be more effective than with 2% erythromycin [16], clindamycin lotion [17] and placebo [18,19] as regards the reduction in number of the acne lesions and the severity grade of the acne. There was a significant decrease (77.9%) in inflammatory lesions (papules and pustules) shown for the erythromycin/zinc treatment group at week 8. The reduction rate in other literature for the same period was 69% which is slightly lower than the present study [20].

The mechanism of action of erythromycin in inflammatory acne vulgaris is due to its antibacterial action effects against *Propioni bacterium acnes* and other bacteria that causing acne, while zinc has multiple actions as it has keratolytic [6] anti-oxidant [8], antibacterial [9], immunomodulatary [13], anti-inflammatory [14] and sebosuppressiveactivities [5] and prolong the action of topical antibiotics [6].

In conclusion, erythromycin-zinc complex is highly effective topical combination in treatment of mild to moderate acne vulgaris.

REFERENCES

1. Habif TP. Acne and related disorder. In Clinical Dermatology: A color guide to diagnosis and therapy, 5th ed. Edinburgh, UK, Mosby, 2010; 7; 217-247.
2. James WD, Berger TG, Elston DM. Acne In : Andrew's diseases of the skin, clinical dermatology, 11th ed. WB Sounder Company Philaelphia, 2011; 13: 228-246.
3. Jain A, Sangal L, Basal E. Anti-inflammatory effects of erythromycin and tetracycline on Propionibacterium acnes induced production of chemotactic factors and reactive oxygen species by human neutrophils. Dermatol Online J. 2002;8:2.
4. Capitanio B, Sinagra J. Role of clindamycin and zinc acetate in topical acne therapy. Esperienze Dermatol. 2012;14:21-4.
5. Piérard-Franchimont C, Goffin V, Visser JN, Jacoby H, Piérard GE. A double-blind controlled evaluation of the sebosuppressive activity of topical erythromycin-zinc complex. Eur J Clin Pharmacol. 1995;49:57-60.
6. Van Hoogdalem EJ, Terpstra J, Baren AL. Evaluating the effect of zinc acetate on stratum corneum penetration kinetic of erythromycin in healthy male volunteers. Skin Pharmacol. 1996;9: 104-10.

7. Mirastschijski U, Martin A, Jorgensen LN, Sampson B, Ågren MS. Zinc, copper, and selenium tissue levels and their relation to subcutaneous abscess, minor surgery, and wound healing in humans. Biol Trace Elem Res. 2013;153:76-83.
8. Powell SR. The antioxidant properties of zinc. J Nutr. 2000;130:1447S-54S.
9. Fluhr JW, Bösch B, Gloor M, Höffler U. In-vitro and in-vivo efficacy of zinc acetate against propionibacteria alone and in combination with erythromycin. Zentralbl Bakteriol. 1999;289:445-56.
10. Merluzzi VJ, Cipriano D, McNeil D, Fuchs V, Supeau C, Rosenthal AS, et al. Evaluation of zinc complexes on the replication of rhinovirus 2 in vitro. Res Commun Chem Pathol Pharmacol. 1989;66:425-40.
11. Sharquie KE, Najim RA, Farjou IB. A comparative controlled trial of intralesionally-administered zinc sulphate, hypertonic sodium chloride and pentavalent antimony compound against acute cutaneous leishmaniasis. Clin Exp Dermatol. 1997;22:169–73.
12. Geovana D. Savi, Adailton J. Bortoluzzi, Vildes M. Antifungal properties of Zinc-compounds against toxigenic fungi and mycotoxin. Int J Food Scienc Technol. 2013;48:1834–40.
13. Sharquie KE, Noaimi AA, Shwail ER. Oral Zinc Sulphate in Treatment of Alopecia Areata (Double Blind; Cross-Over Study). J Clin Exp Dermatol Res. 2012;3:150.
14. Clermensen OJ, Siggaard J. Psoriatic Arthritis Treated with Zinc Sulphate. Br J Dermatol. 1980;103:411-5.
15. Sharquie KE, Noaimi AA, Al-Salih MM. Therapeutic Evaluation of 2% Tea Lotion in Comparison with 5%Zinc Sulphate Solution in the treatment of Acne Vulgaris and Rosacea. Saudi Med J. 2008;29:1757-61.
16. Habbema L, Koopmans B, Menke HE, Doornweerd S, De Boulle K. A 4% erythromycin and zinc combination (Zineryt) versus 2% erythromycin (Eryderm) in acne vulgaris: a randomized, double-blind comparative study. Br J Dermatol. 1989;121:497-502.
17. Schachner L, Pestana A, Kittles C. A clinical trial comparing the safety and efficacy of a topical erythromycin-zinc formulation with a topical clindamycin formulation. J Am Acad Dermatol. 1990;22:489-95.
18. Schachner L, Eaglstein W, Kittles C, Mertz P. Topical erythromycin and zinc therapy for acne. J Am Acad Dermatol. 1990;22:253-60.
19. Feucht CL, Allen BS, Chalker DK, Smith JG Jr. Topical erythromycin with zinc in acne. A double-blind controlled study. J Am Acad Dermatol. 1980;3:483-91.
20. Strauss JS, Stranieri AM. Acne treatment with topical erythromycin and zinc: effect of Propionibacterium acnes and free fatty acid composition. J Am Acad Dermatol. 1984;11:86-9.

TOPICAL ERYTHROMYCIN-ZINC ACETATE COMPLEX LOTION VERSUS TOPICAL ERYTHROMYCIN GEL IN TREATMENT OF MILD TO MODERATE ACNE VULGARIS

by Hayder R. Al-Hamamy, Khalifa E. Sharquie, Adil A. Noaimi, Wajeeh N. Hussein

comment:

Ass. Prof. Antonio Chuh MD FRCP FRCPCH[1], Prof. Vijay Zawar MD DNB DV&D FAAD[2]
[1]*School of Public Health, The Chinese University of Hong Kong and Prince of Wales Hospital, Shatin, Hong Kong*
[2]*Department of Dermatology, Godavari Foundation Medical College and Research Center, DUPMCJ, India*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 352 Date of submission: 16.09.2014 / acceptance: 20.09.2014

Cite this article:
Chuh A, Zawar V. Comment: Topical erythromycin-zinc acetate complex lotion versus topical erythromycin gel in treatment of mild to moderate acne vulgaris . Our Dermatol Online. 2014; 5(4): 352.

Hayder et al [1] described a well-conducted clinical trial comparing topical erythromycin-Zinc acetate complex lotion against topical erythromycin get in treating patients with acne vulgaris of mild to moderate severity.

This study bears several limitations, such as its being single-blinded, a predetermined recruitment period not clearly delineated, the response rate and completion rate unclear, and the randomisation process, if any, not being explicit. However, the authors courageously admitted some of these limitations. We agree that their analyses and conclusions are largely valid, statistically significant, and clinically pertinent.

We have previously conducted studies on similar groups of patients with acne of mild to moderate severity [2,3]. At that time, we found that equipments on patient-assessed outcomes were readily available [4,5], and validly translated several instruments [6,7]. With such instruments, we have been able to determine how patients judged their clinical response to different treatment modalities. We could also quantitatively evaluate how different treatments for acne can exert different impacts on the quality of life to patients, and which of the many aspects of such including their self image, their moods, their activities of daily living, adverse impacts of treatments, and effects on their social activities.

We thus advise future investigators on acne vulgaris to consider the inclusion of patient-assessed data as primary outcome variables. We would highly recommend, a qualitative branch in such clinical trials, so that the novel and original opinions from the patients would be realised and analysed in depth. After all, patients are the bosses in the enterprise which we call clinical medicine.

REFERENCES

1. Hayder R Al-Hamamy, Khalifa E Sharquie, Adil A Noaimi, Wajeeh N Hussein. Topical erythromycin-Zinc acetate complex lotion versus topical erythromycin gel in treatment of mild to moderate acne vulgaris. Our Dermatol Online. 2014;5:347-51.
2. Law MP, Chuh AA, Molinari N, Lee A. An investigation of the association between diet and occurrence of acne: a rational approach from a traditional Chinese medicine perspective. Clin Exp Dermatol. 2010;35:31-5.
3. Chuh AA, Zawar V, Wong WC, Lee A. The association of smoking and acne in men in Hong Kong and in India: a retrospective case-control study in primary care settings. Clin Exp Dermatol. 2004;29:597-9.
4. Motley RJ, Finlay AY. Practical use of a disability index in the routine management of acne. Clin Exp Dermatol. 1992;17:1-3.
5. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19:210-6.
6. Law MP, Chuh AA, Lee A. Validation of a Chinese version of the Cardiff Acne Disability Index. Hong Kong Med J. 2009;15:12-7.
7. Chuh AA, Chan HH. Effect on quality of life in patients with pityriasis rosea: is it associated with rash severity? Int J Dermatol. 2005;44:372-7.

DOI: 10.7241/ourd.20144.88

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

SKIN INFECTIONS AMONG INFANTS AND PARENTAL AWARENESS: IS THERE ANY RELATIONSHIP?

Zoya Hossenbaccus, Rajesh Jeewon

Department of Health Sciences, Faculty of Science, Reduit, University of Mauritius, Mauritius

Source of Support:
Nil
Competing Interests:
None

Corresponding author: Dr Rajesh Jeewon, PhD r.jeewon@uom.ac.mu

Our Dermatol Online. 2014; 5(4): 353-358 Date of submission: 17.08.2014 / acceptance: 25.09.2014

Abstract
Introduction: In Mauritius, studies on skin infection are limited to adults only and no reports are available on skin health of infants and toddlers. The aim of this study is to determine the prevalence of skin infection among infants and toddlers and to investigate whether there is an association between socioeconomic status and education level of parents on skin infection of infants and toddlers.
Material and Methods: Survey data was collected from 500 parents that have children between the age of 1 month till 5 years. A questionnaire was distributed to elicit information on family history, socioeconomic and education details of parents, hygiene level and level of awareness of parents on skin infections and data was analysed using SPSS.
Results: Skin infections were mostly nappy rashes, eczema and skin rashes. Itching has been noted to be the most prevalent among infants and toddlers with a prevalence of 22%. Socioeconomic status and education level of parents have an effect on prevalence of skin infection. A high percentage of parents possess good knowledge on hygiene, risks factors and concern towards the skin health of the child.
Conclusions: There is a high prevalence of skin infection noted among infants and toddlers. Children having parents with low socioeconomic status and low education level have a higher incidence of skin infection. The majority of parents show high concern on skin health of their children.

Key words: prevalence; skin; infection; infants; toddlers; awareness level

Cite this article:
Hossenbaccus Z, Jeewon R. Skin infections among infants and parental awareness: Is there any relationship? Our Dermatol Online. 2014; 5(4): 353-358.

Introduction

Skin problem is a major health problem in the paediatric age group [1]. Several studies have been done across the world to determine factors that can have an impact on the prevalence of skin problem among paediatric age group. It is found that skin diseases contribute to the total morbidity presenting at different level of health and medical care [2]. Skin diseases form a substantial part (10-24 %) of the total childhood morbidity that is encountered [3] and hence, the evaluation of skin disorders forms an important part of primary health care practice in case of children [4]. According to Mostafa et al. [5], the epidemiological data of skin infections provide us with information about prevalence, age and gender differences in affected groups and their regional distribution. In many parts of India, it has been found that the patterns of skin diseases are consequences of poverty, malnutrition, overcrowding, poor hygiene, illiteracy and social backwardness. As a result, status of health, hygiene and personal cleanliness of a society can be judged while assessing the prevalence of skin infections in children of the community [4].

It is also stated by World Health Organization 2005 [6] that a high prevalence rate of skin infections is strongly linked to low socioeconomic level where incidences of skin infections like climatic factors, poor hygiene, interpersonal transmission have been shown to be positive. Moreover, Mostafa et al. [5] postulated that genetic background, geographical area, climate, season, socioeconomic status, living conditions and medical resources are the most important factors that can result in an increase in the prevalence of skin infections. For instance, it has been demonstrated that good hygiene may prevent the occurrence of impetigo and social crowding may increase the risk of developing the disease [3]. Among these, Mostafa et al. [5] stated that the most frequent and prevalent skin infections in infants were bacterial skin infections (23.4%) which have also been attributed to hot humid and climate, overcrowding, low socioeconomic status and widespread use of tropical antibiotics leading to resistant strain.

Among the factors affecting skin infections, family size makes an important contribution. It is suggested by World Health Organization [6] that the occurrence of severe scabies epidemics increases in places like jails with close interpersonal contact. There is a high level of interpersonal contact in developing countries where households are often crowded [6]. In Egyptian villages studies were done that revealed that sharing bed among children is a factor that increases the prevalence of scabies in families [6].

Balai et al. [4] stated that the pattern of skin infections varies from country to country with pyoderma and malnutrition being more common in developing countries, while eczemas are more common in developed countries. This has been attributed to different climatic, cultural and socio-economic factors. As far as dermatoses in children are concerned, dermatoses are more influenced and are associated with socioeconomic status, climatic exposure, dietary habits and external environment [1]. Based on school surveys, Jain and Khandpur [1] stated that the prevalence of paediatric dermatoses in various parts of India ranged from 8.7% to 35%. The prevalence of dermatoses in children of school age ranged from 34% to 87.7% in developing countries whereas in countries such as Romania and Turkey, dermatoses accounted for 22.8% and 77% respectively [7]. The latter also showed that atopic dermatitis is more common in developed countries. This accounts for 25% to 33% of all consultations, followed by melanocytic nevi, (3% to 20%) and viral warts (5% to 13%). Concerning the level of awareness of parents on impetigo, a child with impetigo brings about attention, concern and inconvenience since children with impetigo are barred from schools and kindergartens [3].

In Mauritius, current data pertaining to skin problem are limited to mostly adults. There is no published data on the prevalence of skin problems in infants and toddlers.

The objectives of this study are as follows:

1) To investigate the prevalence of skin problems among infants and toddlers in Mauritius.

2) To determine any association between socioeconomic status and education level of parents on the prevalence of skin problem among infants and toddlers.

3) To assess the level of awareness among parents with respect to level of hygiene, nappy change, regular bath, use of products like cream and their concern to the skin health of the child.

Material and Methods

Participants: Using a stratified random sampling method, data was collected from 500 parents all around the island from different regions and occupational categories.

Inclusion criteria: The only inclusion criteria included those parents having one or more child/children of 1 month till > than 3 years up to 5 years.

Exclusion criteria: Children greater than 5 years were not taken into consideration and those suffering from any type of disease.

Settings: The survey was carried out in 2012 and 2013. The questionnaires were randomly distributed in day-care centres of children and pre-primary schools from all over the island. The parents were explained that all their answers will be dealt with strict confidentiality and the survey was strictly anonymous with no name and address of the participants. Appropriate informed consent was obtained from parents and all participants. Research was approved by appropriate Research Ethics Committee. Information sheet in which all details about the project, the participant's rights and the researcher's statement were enclosed, accompanied the questionnaire. The parents in the pre-schools and day-care centres were given verbal explanation in Creole, the most spoken language in Mauritius and as much time was allotted to them to answer the questions so that they could respond correctly.

Contents of the questionnaire

Two questionnaires were used:

One of them dealt with:

a) Family history: Details of family history, the number of family members, the number of children in the family their specific age group;

b) Socioeconomic status: The total monthly family income, parental education attainment, parental care, mother's care;

c) Lifestyle and hygiene: The number of baths given daily, the types of nappies that were used and the number of nappies used daily. Questions on whether products like body lotion, powder and cream used were asked;

d) Awareness: The level of awareness of parents on regular bath, increase change of nappies, using products like creams, keeping the baby dry, sharing of infected towels. Open ended questions were asked on the precautions the parents usually take to prevent skin problems in their child.

The second questionnaire dealt with the Life Quality Index:

Questions on the dermatitis severity were asked, the degree of itching and scratching of the child and whether there has been effect of skin problem on his daily activities and life. A validated questionnaire based on DLQI (Dermatology Life Quality Index) (Lewis-Jones and Finlay, 2000) [8] was used. Prior permission from authors was obtained beforehand.

Results

Prevalence of skin problem and the relationship with sociodemographic factors

Figure 1 shows that 22% of infants and toddlers suffered from itching. 17% from nappy rashes; 5% from eczema, 5% from skin problems other than itching, eczema and nappy rashes; 3% are from skin rashes.

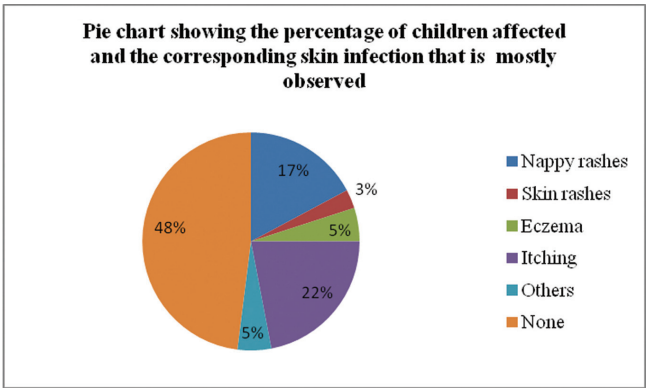


Figure 1. Percentage of children affected and the corresponding skin problem mostly observed.

It can be observed that in this study parents having a total monthly salary scale of < 500 USD have a high percentage (77.3%) of children who are affected with skin problem whereas, for those having monthly salary scale of 500-1000 USD, only 54% of children are affected. Parents that have total monthly salary scale of > 1000 USD, have children with less prevalence of skin problem (40.4%).

For nappy rashes, 54% of children come from family with a total monthly income of 500-1000 USD. 71% of children with skin rashes come from middle class family with a total monthly salary scale of 500-1000 USD. 56% of affected children with eczema come from family with total monthly salary scale of 500-1000 USD compared to that of low family income, where none comes from family with salary scale of < 500 USD. Similarly, 53% of affected children come from family with total monthly income of 500-1000 USD compared to 13% that come from family with a total monthly salary scale < 500 USD. There is a positive correlation (r =0.251) showing that there is a link between total monthly family income and children being affected with skin problem (Fig. 2).

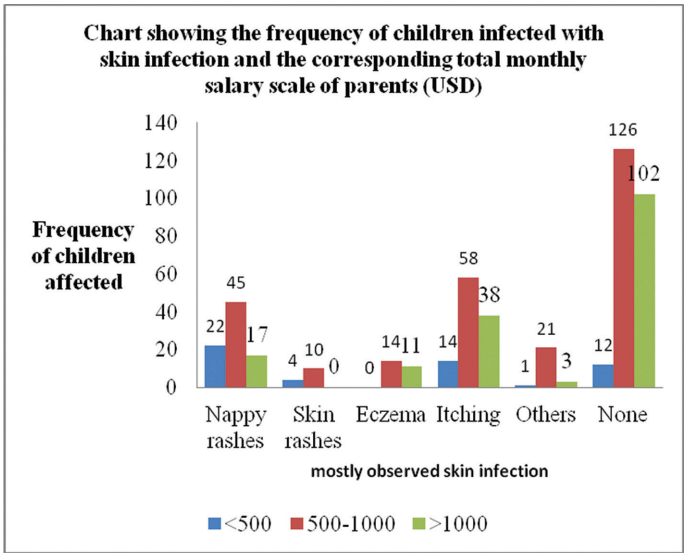


Figure 2. Frequency of children affected with skin problems and the corresponding total monthly salary scale of parents (USD).

For children having parents with no formal education level, it can be seen that there is a high prevalence (100%) of children being affected with skin problem while parents that have studied till primary level, 79% of children are affected with skin problems. Parents who have studied till secondary level have 60% children that are affected with skin problem while those who have studied till tertiary level show less prevalence of (44.8%) of skin problem. However, it should be mentioned that out of 500 participants interviewed, 308 children have parents that are tertiary education holders. The correlation coefficient is 0.099 nearly 0.1, showing a positive relationship between education level and number of children affected with skin problem. However, the relationship is rather weak as the coefficient is of low value (Tabl. I).

Level of education	% children infected with skin infection	% children not infected with skin infection
None	100	0
Primary	79.0	21
Secondary	60	40
Tertiary	44.8	55.2

Table I. The level of education of parents and % of children infected with skin infection.

Prevalence of skin problem with relation to hygienic practices and level of awareness of parents

Results indicate that the majority of children have 2 baths per days but still have a high frequency of skin problem. Even those who did not have skin problem also have 2 baths a day. There is no statistical significant difference and also no relationship between the number of baths and mostly observed skin problem (p value=0.356) (r= 0.041). A high prevalence (65%) of the Mauritian population strongly agrees on the fact that increase use of nappies helps to decrease skin problem while 29% of Mauritian population only agree to the increase use of nappy change. Hence, majority of the parents are conscious on the increase use of nappies.

A high prevalence of the Mauritian population (52%) strongly agrees on the use of products like powders and lotion that contributes in the decrease of skin problem. 35 % of parents only agree on the use of products like powders and lotion that helps in the decrease of skin problem.

A high prevalence of Mauritian population (62%) strongly agrees on the use of towels to dry a child can help to decrease skin problem while only 1 % of the population has a disagreement over the use of towels. A high prevalence of parents (94%) is aware of the fact that sharing of infected towels may contribute to skin problem in children.

Among the population, 80% of parents are very much concerned on the skin health of their child, while the rest 20% are only concerned.

Quality of Life Index: Assessment of dermatitis severity of children

45% of parents admitted that that there has been no dermatitis severity on the children. 4% of extremely severe cases have been reported among children (Tabl. II).

52% of infants and toddlers have been scratching and itching a little only as compared to 40% who have not been scratching. Only a little (8%) have been scratching a lot. According to the Figure 3, 45% of children show a slightly fretful mood while 40% show a happy mood.

	Frequency	Percent	Valid Percent	Cumulative Percent
Extremely Severe	11	2.2	4.3	4.3
Severe	10	2.0	3.9	8.2
Average	58	11.6	22.7	31.0
Fairly good	61	12.2	23.9	54.9
None	115	23.0	45.1	100.0
Total	255	51.0	100.0	

Table II. The frequency of children and the corresponding dermatitis severity level.

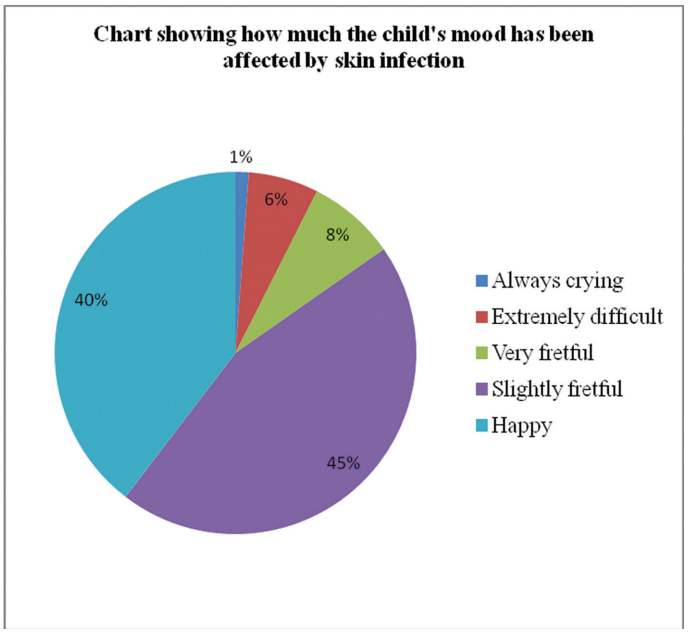


Figure 3. Percentage of child's mood affected by skin problem.

Discussion

Given the increased prevalence of skin problem in many developing countries and the lack of published data pertaining to the prevalence of skin problems among infants in Mauritius, this study was done in order to investigate the prevalence of skin problems among infants and toddlers and assess the level of awareness among parents.

Prevalence of skin infections and sociodemographic factors

48% of the Mauritian population is not affected by any skin problem. The remaining 52% of the population suffer from the following: itching (22%), nappy rashes (17%), eczema (5%), others (5%) and skin rashes (3%) (Figure 1). Studies in Ethiopia have shown similar frequencies. Oyedeji et al. [9] reported a prevalence of 49.2% of skin problem. In other countries, however, the prevalence of skin problem has been lower. For instance, in Iraq, the overall skin problem is reported to be 40.9%, Jordan (19.3%), Malaysia (34.4%) and Nigeria (35.2%) as outlined in [10].

In Mauritius, itching has been observed to be the most common with a percentage of 22% while in countries like Nigeria, impetigo was observed in a higher prevalence (19.4%) [9]. Studies from Uttar Pradesh, India have shown that in children less than 14 years, pediculosis capitis (22.6%) was the most common dermatosis [1]. Itching as reported in this study, is mostly due to mosquito bites that cause inflammation and redness on exposed areas such as hands and forearms, ankles and neck.

Wenk and Itin [2] revealed that in Switzerland, atopic dermatitis was the most common dermatosis in all age groups, with the highest prevalence (33.5%) in the infant group followed by hemangioma (7.5%) and eczema (4.1%) which were the second and third most common skin disorders in infants. This study also shows that the frequency of occurrence of eczema (5%) is quite similar to that reported in Switzerland whereas nappy rash (17%) is the second most common skin problem [2].

The impact of socioeconomic status of parents on the prevalence of children was also assessed. Parents having total monthly family income of less than (<500 USD) have a high prevalence of skin problems (77.3%) as compared to 54% from those with a monthly middle class income (500-1000 USD) and 40.4% respondents from the high monthly income category (> 10000 USD) had skin problems. A higher frequency of skin problems among low socioeconomic status is quite well documented. This finding is in line with other studies where the majority of skin problems were observed in families with low occupation group [9]. The latter reported 43% skin problem among low socioeconomic status as compared to 22.5% among high social class. Results indicate that there is a significant difference but positive relationship between total monthly family income and children having skin problem. Other studies have demonstrated an association between socioeconomic status and poor skin health of children. Ete-Rasch [11] stated that socioeconomic factors for example unemployment and low income are risk factors that have a negative impact on children's health. In Iraq, a high prevalence of skin problems was reported in regions of low socioeconomic status [10]. One major explanation for the association between income and child health is that families with a high income are able to provide their children with more goods, services and resources that can benefit their children and prevent them from experiencing adverse health outcomes [12].

An association of level of education of parents on prevalence of skin problem is also well documented. Parents who have no formal school education level at all have the highest prevalence of skin problem (100%) while primary education holders have 79% children being affected. Less percentage (60%) of affected cases is seen with parents that have studied till secondary level while the least prevalence (44.8%) is observed in parents with tertiary education. These findings are consistent with other studies that state that high prevalence of skin problems are due to poor parental supervision, child neglect or ignorance [9] and these can be judged by parents who were illiterate and have no education attainment [9]. Correlation between education level of parents and prevalence of skin problem has shown there is statistically significant difference between the two variables with a very weak positive relationship between education level of parents and occurrence of skin problem. Ete-Rasch [11] postulated that poor parental education attainment and low occupation group are associated with a high prevalence of skin problems. However, this is not always the case as children of highly educated parents may be more prone to an irritating skin disorder than those from less educated families [13]. The authors tried to explain this discrepancy with the "hygiene hypothesis" which states the fact that some educated parents provide a germ free environment for their child, hence, they are less prone to problems. As a result, following the "hygiene-hypothesis" theory, they have an improperly trained immune system due to less exposure to pathogenic agents [13]. This hypothesis suggests that if the environment is "too clean" the immune system will not mature properly and may not react properly while encountering germ [14].

Relationship between hygiene level and parental awareness on the prevalence of skin infections

Nappy rashes were linked to level of hygiene [15]. 43% of children suffering from nappy rashes use four nappies daily while only 2% of children use two nappies daily. Results also indicate that the majority of children use four nappies on a daily basis and this category has a higher frequency of nappy rash conditions. A high prevalence (65%) of the Mauritian population strongly agrees on the fact that increase use of nappies helps to decrease skin problems. Despite this, high prevalence of nappy rashes is observed in children using more nappies. Contradictory to what has been observed in the study, Borkowski [16] stated that entailing frequent diaper changes is an ideal way for both treating and preventing nappy rashes.

It should be noted that while doing the survey many parents cited the importance of keeping the children dry, that is without nappies for some time during the day to prevent nappy rashes. Many parents acknowledged that using products like creams and powders and the most common one is sudocream (15.25% zinc oxide). The baby powder and lotions act as barriers between the skin and the diaper, hence, block the moisture and help in producing some degree of lubrication [15].

It has been shown that a high prevalence of the Mauritian population (52%) strongly agrees on the use of products like powders and lotions that help to decrease the occurrence of skin problem. During this survey, it has been found that most parents use moisturizing cream. According to Larson [17], moisturizing is beneficial for skin health and reducing microbial dispersion from the skin.

The majority of children are given baths twice daily. Among children affected with skin problem, the highest frequency of children take two baths daily but number of baths do not have any effect on the frequency of skin problem. Moreover, there is a weak positive relationship between the two variables (r =0.041). Furthermore, a high prevalence of parents (94%) is aware that the fact that sharing infected towels may contribute to skin problems in children.

Life Quality Index

Skin diseases are known to have major impact on the lives of patients and the families and several validated patient completed questionnaire have been used to assess its impact Basra et al. [18]. While assessing the dermatitis severity of the child in the Quality Life Index [8], it has been found that a low percentage of children (4%) shows extremely severe dermatitis while the majority of children (45%) are not affected at all. This can be attributed to the prompt treatment given to the child as most parents are very much concerned of the skin health of the child. As far as the reaction of parents on skin problem of the child is concerned, 80% of parents are very much concerned on the skin health of their child. Only 20% affirmed to be concerned only. Hence, Mauritian parents are well informed of skin problems and the level of awareness is high which results in proper skin care of the child. Amoran et al. [19] reported school children sought low level of medical care due to the assumption that skin diseases are not important and not merit any treatment. Another part of the Life Quality Index was the nature of the frequency of itching and scratching whereby 52 % of the population has been scratching and itching a little. A high prevalence (22 %) of the infants and toddlers suffered from itching. This is due to tropical climate (25-33 degrees Celsius) prevailing in Mauritius and many respondents reported mosquito bites as the major cause of itching. The Life Quality Index also investigated the mood of the child under criteria like, always crying, extremely difficult, very fretful, slightly fretful and happy. 45% of the children have a slightly fretful mood while 40 % show a happy mood. Hence, the mood of the child is slightly affected due to skin problems.

Conclusion

More than half of the participants suffer from skin problems with itching and and nappy rashes were more common. Those infants and toddlers from low socioeconomic status were more prone to skin problems. Parents with low level of education have children with more skin problems. Parents have a high level of awareness on hygienic practices. Skin problem has little impact on quality of life of children.

REFERENCES

1. Jain N, Khandpur S. Pediatric dermatoses in India. Indian J Dermatol Venereol Leprol. 2010;76:451.
2. Wenk C, Itin, H. Epidemiology of Pediatric Dermatology and Allergology in the Region of Aargau, Switzerland. Pediatr Dermatol. 2003;20:482–7.
3. Mohammedamin RSA. Infectious Skin Diseases in Children in General Practice. Epidemiology and management. Doctoral thesis, Erasmus University Medical Center Rotterdam. 2007;1-57.
4. Balai M, Khare AK, Gupta LK, Mittal A, Kuldeep CM. Pattern of paediatric dermatoses in a Tertiary Care Centre of South West Rajasthan. Indian J Dermatol. 2012;57:275-6.
5. Mostafa FF, Hassan AAH, Soliman MI, Nassar A, Deabes RH. EDOJ. 2012;81:2-25.
6. World Health Organisation. Epidemiology and management of common skin diseases in developing countries. Department of Child and Adolescent Health and Development. 2005;2-14.
7. Casanova JM, Sanmartin V, Soria X, Baradad M, Marti RM, Font A. Childhood dermatosis in a dermatology clinic of a General University Hospital in Spain. Actas Dermosifiliogr. 2008;99:112-5.
8. Lewis-Jones MS, Finlay AY. Children's Dermatology Life Quality Index. The Cardiff University, Wales, UK. 2000.
9. Oyedeji OA, Okeniyi JAO, Ogulensi O, Oyedeji GA, Oyelami OA. Parental factors influencing the prevalence of skin infections and infestations among Nigerian primary school pupils. Dermatol Online J. 2006;3:2.
10. Khalifa KA, Al-Hadithi TS, Al-lami FH, Al-Diwan JK. Prevalence of skin disorders among primary-school children in Baghdad governorate, Iraq, East. Mediterr Health J. 2010;16:209-12.
11. Ete-Rasch E. 'I thought it was just a pimple' A study examining the parents of pacific children's understanding and management of skin infections in the home. Thesis (Masters of Arts (Applied) in Nursing), Victoria, University of Wellington. 2009;12-120.
12. Victorino C, Gauthier AH. The social determinants of child health: variations across health outcomes – a population-based cross-sectional analysis. BMC Pediatr. 2009;9:53.
13. Haidinger G, Weber A. Scientists say educated parents more likely to have children with skin conditions. Natural Beauty News. 2013.
14. Davis CP, Stoppler MC. „Yaws". MedicineNet.com [serial online] 2013. Available from: URL: http:// http://www.medicinenet.com/yaws/page4.htm
15. Li CH, Zhu ZH, Dai YH. Diaper Dermatitis: A Survey of Risk Factors for Children Aged 1 – 24 Months in China. J Int Med Res, 2012;40:1752-60.
16. Borkowski S. Diaper rash care and management. Pediatric Nursing, 2004;30:467-8.
17. Larson E. Hygiene of the Skin: When is clean too clean? Emerging Infectious Diseases. 2001;7:200-27.
18. Basra MK, Sue-Ho R, Finlay AY. The Family Dermatology Life Quality Index: measuring the secondary impact of skin disease. Br J Dermatol. 2007;156:528-38.
19. Amoran OE, Runsewe-Abiodun OO, Mautin AO, Amoran IO. Determinants of dermatological disorders among school children in Sagamu, Nigeria. Educ Res. 2011;2:1743-8.

DOI: 10.7241/ourd.20144.89

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

NON MELANOMA SKIN CANCER TRENDS IN TRIPOLI / LIBYA

Amani Tresh[1], Omimma El Gamati[2], Nihal Elkattabi[1], Abd Alrazak Burshan[3]

[1]Department of Dermatology, Ber usta Milad Dermatology Hospital, Lecturer at Tripoli University, Alsyahea street Gergaresh, Tripoli, Libya
[2]Department of Pathology, Tripoli Medical Centers, Lecturer at Tripoli University, Alsyahea street Gergaresh, Tripoli, Libya
[3]Department of Pathology, Burn and Plastic Surgery Hospital, Lecturer at Tripoli University, Alsyahea street Gergaresh, Tripoli, Libya

Corresponding author: Dr Amani Tresh *treshamani@yahoo.co.uk*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 359-361 Date of submission: 10.06.2014 / acceptance: 30.07.2014

Abstract
Introduction: The incidence of skin cancer is increasing at an alarming rate. Non melanoma skin cancer (NMSC) is the most common cancer affecting white individuals. Skin Cancer registration in Northern Africa is still limited and, until now, there have been no population-based data available for Libya. We perform the first epidemiological analysis of non melanoma skin cancer (NMSC) in Tripoli/ Libya during 5years period between 2006-2010.
Aim: To discuss current epidemiologic data concerning incidence and demographic variation. To compare our findings with those of published reports from other regions.
Material and Methods: All histopathologically proven cases of (NMSC) reported during the years 2006 through 2010 were retrieved and reviewed. 70% of the data were electronically stored. Information regarding tumor type, age, gender, and anatomical location were collected.
Results: A total of 579 cases of (NMSC) were diagnosed between the years 2006 and 2010. Basal cell carcinoma (BCC) was the commonest type, representing 76.9% of all skin cancers. Males were more frequently affected than female.
Conclusions: We concluded that (NMSC) in Tripoli/Libya is not uncommon problem. Ascertainment of NMSC should improve since the advent and use of electronic pathology data. Ongoing increases in age-adjusted incidence, combined with ageing of the population, will have major implications for the clinical workload associated with (NMSC) for the foreseeable future.

Key words: Non melanoma skin cancer; Basal cell cancer; squamous skin cancer; cancer registry

Abbriviation: Nonmelanoma skin cancer (NMSC)

Cite this article:
Tresh A, El Gamati O, Elkattabi N, Burshan AA. Non melanoma skin cancer trends in Tripoli /Libya. Our Dermatol Online. 2014; 5(4): 359-361.

Introduction

Nonmelanoma skin cancer (NMSC) is one of the most common malignant cancer in Caucasian populations around the world, and usually refers to either basal cell carcinoma (BCC) or squamous cell carcinoma (SCC) [1].
Epidemiologic studies of these tumours have been limited by the fact that most patients are usually seen and treated in private clinics.
The primary source of data is usually from cancer registries, yet in Tripoli /Libya there is no cancer registry. In Benghazi they established cancer registry on 2003 however information about (NMSC) was limited [2].
There are considerable geographic and racial variations [3]. The incidence of (NMSC) is highest in Australia [4], Finland BCC is the second most common type of cancer [5].
In Jordan which is a Middle Eastern country, it is the sixth most common type of cancer in males and the fourth most common type in females [6].

We report the frequency and pattern of NMSC in Tripoli /Libya between 2006-2010, a country with a total population of around 1,5 million. The report is based on the data-analysis of all histological confirmed skin cancers. The results are compared to those obtained from the other countries with regard to frequency, sex distribution, anatomical location, histological types.

Methods

All histopathologically proven cases of (NMSC) reported during the years 2006 through 2010, were retrieved and reviewed.70% of the data was electronically stored. Information regarding tumor type, age, gender, and anatomical location were collected. The study was performed at main Tripoli / Libya teaching Hospitals: Tripoli medical center, Tripoli Central hospital, Burn and plastic Hospital and Beer Usta Milad dermatology hospital.

Results

A total of 579 cases of (NMSC) were diagnosed between the years 2006 and 2010. On 2006 there were just under 80 case reported, this number doubled on 2007 to around 160 case with no clear explanation, thereafter the number reported reduced to 100 cases per year in the last 2years of the study (Fig. 1)

Basal cell carcinoma (BCC) was the commonest type, representing 76.9% of all skin cancer. Nodular BCC was the commonest clinical and histopatholgical type (Fig. 2)

Males were more frequently affected than females; Male represented 61.5% of all (NMSC). The incidence of both BCC and SCC increased with age. The median age at onset was 70 years (Fig. 3).

The head and neck region was the commonest site affected by both types of cancer. With >70% of the documented site were at the face and scalp area.

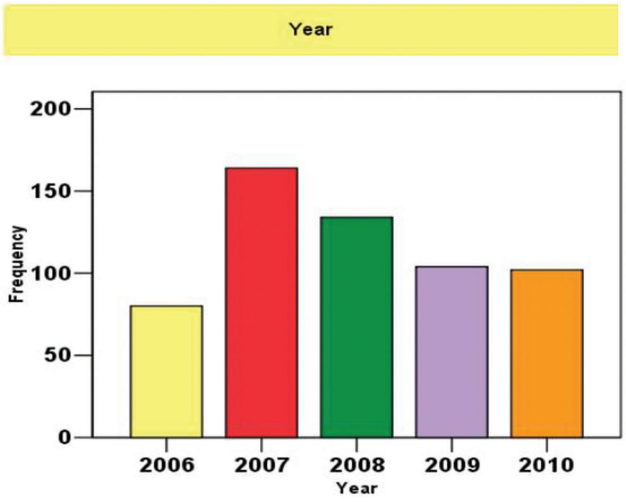


Figure 1. Reported cases per year.

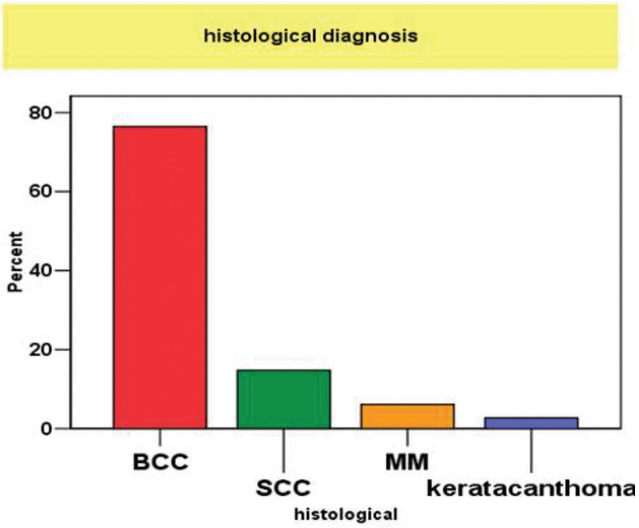


Figure 2. Histological confirmed cases.

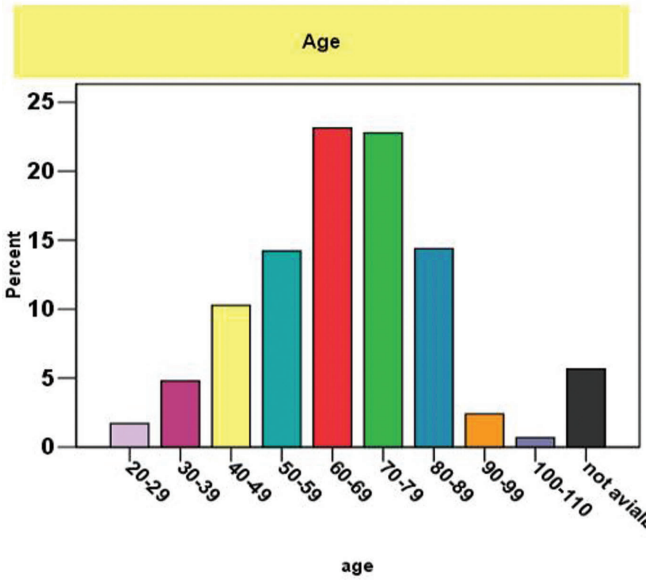


Figure 3. Median age of onset.

Discussion

The total number of our reported cases was more than twice the number in similar study done in Egypt the study duration was for 15 years (1989–2004) and they report a 241 cases [7].
In Algeria (1993–1997), PubMed age-standardised incidence for NMSC was eight per 100,000 in men and three per 100,000 in women [8].
In northern Jordan, 34 per 100,000 in men and 29 per 100,000 in women [6].
We could not calculate age-standardised incidence rates; however our frequency revealed a higher incidence than Egypt, Algeria and Jordan. The high risk of second and further tumours in patients with NMSC can increase the sensation of epidemic. It must be remembered that only the first occurrence of each histologically different subtype of NMSC must be reported in registers [9].
Increased awareness by dermatologists, general practitioners and the population can influence the detection of tumours that would have passed unnoticed before. Public health campaigns can also contribute. Recent evidence suggesting that almost all clinically diagnosed NMSCs in hospitals are verified histologically, coupled with the increasing availability of electronic histopathology data, raises the possibility that Cancer registry in Tripoli/Libya can establish.

Conclusion

In our country, sun-related skin cancers have relatively high frequency and a rather stable pattern, compared with other areas with similar climate and skin phenotypes.
Increased awareness, better registration, ageing of the population and diagnosis of multiple tumors can give the impression of a higher increase in cases than there really is. Accurate and up-to-date records on (NMSC) are necessary for quantification of changes in its incidence to allow for research and planning of services.

REFERENCES

1. Weinstock MA. Epidemiology of nonmelanoma skin cancer:clinical issues, definitions, and classification. J Invest Dermatol. 1994;102:4S–5S.
2. El Mistiri M1, Verdecchia A, Rashid I, El Sahli N, El Mangush M, Federico M. Cancer incidence in eastern Libya: The first report from the Benghazi Cancer Registry, 2003. Int J Cancer. 2006;120;392–7.
3. Harris RB, Griffith K, Moon TE. Trends in the incidence of nonmelanoma skin cancers in southeastern Arizona, 1985–96. J Am Acad Dermatol. 2001;45:528–36.
4. Marks R. Epidemiology of non-melanoma skin cancer and solar keratosis in Australia: a tale of self-immolation in Elysian Fields. Australas J Dermatol. 1997;38:S26–S29.
5. Cancer Statistics of the National Research and Development Center for Welfare and Health, Publication 58. Helsinki: Cancer Society of Finland. Cancer incidence in Finland 1995.
6. Omari A, Khammash M, Matalka I. Skin Cancer trends in northern Jordan. Int J Dermatol. 2006;45:384-8.
7. Hussein MR. Skin Cancer in Egypt, Cancer Biol Ther. 2005;4:593–5.
8. http://www.iarc.fr/IARCPress/pdfs/ci5v8/ci5v8-tabafrica.pdf
9. Non-melanoma Skin Cancer in the Mediterranean Area report by Jordi Graells Estrada© T O U C H B R I E F I N G S 2 0 0 7

DOI: 10.7241/ourd.20144.90

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

AN EPIDEMIOLOGICAL ANALYSIS OF CHILDREN AND ADOLESCENTS PSORIASIS IN A TERTIARY REFERRAL DERMATOLOGY INSTITUTE IN THE DOMINICAN REPUBLIC

Manuel Valdebran, Martha Miniño

Instituto Dermatológico y Cirugía de Piel "Dr. Huberto Bogaert Díaz", C/Federico Velásquez, esq. Albert Thomas, Santo Domingo, República Dominica

Source of Support: Nil
Competing Interests: None

Corresponding author: Dr Manuel Valdebran *investigacion@valdebran.com*

Our Dermatol Online. 2014; 5(4): 362-365 Date of submission: 12.08.2014 / acceptance: 20.09.2014

Abstract
Introduction: Psoriasis is one of the most common chronic inflammatory diseases, affecting about 3.5% of the population. Despite psoriasis carries a high risk of morbidity, few epidemiological studies provide estimates on the prevalence of psoriasis in children.
Aim: The objective of this study is to report the frequency of children and adolescents diagnosed with psoriasis at Instituto Dermatologico y Cirugía de Piel "Dr. Huberto Bogaert Díaz" (IDCP-DHBD) between March 2007 and March 2012.
Material and Methods: Examination were done on 76 children and adolescents with psoriasis confirmed by histopathological examinations at the IDCP DHBD in the Dominican Republic between March 2007 and March 2012. The data was retrospectively reviewed to assess age, gender, clinical localization, treatment modalities and delay in diagnosis.
Results: The frequency of children and adolescents with psoriasis among dermatological patients was 0.96 cases for every 10,000 patients seen in the Institute. There were 43 (56.6%) girls and 37 (43.4%) boys. The mean age of onset was 14 years. Children from 0-2 years, were the least affected with 3% of the cases. The most frequent site of onset were the trunk (28.8%) and the scalp (27.4%). 67% of the patients had 2 or more sites involved. The mean delay in diagnosis was 6 months. Topical therapy was the treatment of choice in all the patients except one.
Conclusions: Even though psoriasis may cause a profound impact on the quality of life of children and adolescents the epidemiological data in the countries of Central America and the Caribbean is scarce.

Key words: psoriasis; children; Dominican Republic

Cite this article:
Valdebran M, Miniño M. An epidemiological analysis of children and adolescents psoriasis in a tertiary referral dermatology institute in the Dominican Republic. Our Dermatol Online. 2014; 5(4): 362-365.

Introduction

Psoriasis is one of the most frequent chronic inflammatory diseases in the world, affecting around 3.5% of the population [1]. It presents in the first two decades of life [2-5] in more than 33% of the cases; 10% of which will develop psoriasis before the age of 10 [6].

Besides being affected physically a child can potentially be affected socially and emotionally [7]. In fact, it has been reported that the quality of life of the children suffering psoriasis is worse than those suffering from other chronic diseases such as diabetes mellitus or epilepsy [8].

Epidemiology

Despite being a matter of concern, there are a few epidemiological studies that provide estimates of the prevalence of psoriasis in children worldwide, most of the available data we have at the present time comes from European countries where the prevalence is relatively high as opposed to what is seen in southern countries [9-13] as described in Figure 1.

Etiology

Psoriasis is a chronic inflammatory condition probably mediated by T lymphocytes, endothelial cells, dendritic cells, monocytes, neutrophils, keratinocytes and cytokines and chemokines characterized by hyperproliferation of keratinocytes, endothelial vascular proliferation and an infiltrate of inflammatory cells. The IL-23/Th17 seems to be crucial in the pathogenesis of psoriasis, mediating the host's inflammatory response [14].

It has been demonstrated that the PSORS1 gene is determinant in the early onset of non-pustular type 1 psoriasis [5,15]. The HLA-Cw6 is the most important allele in the PSORS1 locus which confers susceptibility for the early onset of the disease [2,5,16,17].
Contrary to what has been described in adults, infections such as pharyngitis or skin trauma may trigger the disease [5,18]. Additionally, the onset of new lesions in periods of emotional stress is seen more frequently in children [18].

Aim

To report the number of diagnosed cases of psoriasis in children and adolescents at Instituto Dermatológico y Cirugía de Piel "Dr. Huberto Bogaert Díaz" (IDCP-DHBD) between March 2007 and March 2012

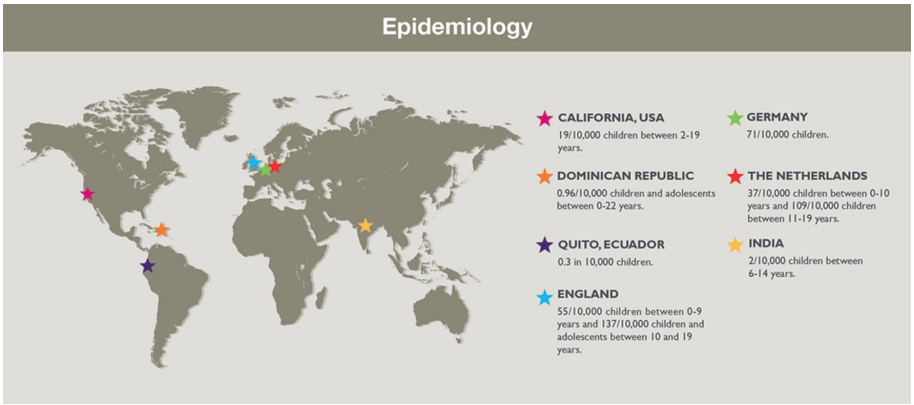


Figure 1. Frequency of children and adolescents psoriasis around of the world.

Material and Methods

This is a retrospective epidemiologic study from 76 children and adolescents with psoriasis confirmed by histopathological examinations at the IDCP DHBD in the Dominican Republic between March 2007 and March 2012.
Information data was obtained from the clinical and histopathology records of the patients seen at the Institute. The data was retrospectively reviewed to assess age, gender, clinical localization, treatment modalities and delay in diagnosis.

Results

In total 76 children and adolescents with psoriasis were included in the study. The center registered a total of 789,558 patients seen in the clinical dermatology division in the period of time of the study. The frequency of children and adolescents with psoriasis among dermatological patients was 0.96 cases for every 10,000 patients seen in the Institute (Fig. 2). There were 43 (56.6%) girls and 37 (43.4%) boys, with a female to male ratio of 1.3:1 (Fig. 3). The mean age of onset was 14 years, with a peak age of onset seen in the group of adolescents from 12-18 years with 40.2% of the cases. Children from 0-2 years, were the least affected with 3% of the cases (Fig. 4).
The most frequent site of onset were the trunk (28.8%) and the scalp (27.4%) (Fig. 5). It was found that 67% of the patients had 2 or more sites involved, while 32% of patients were affected in one body site.
The period between the onset of the first skin lesions and the final diagnosis was designated as the delay in diagnosis. The mean delay in diagnosis was 6 months.
Topical therapy was the treatment of choice in all the patients except one. Antralin was prescribed for 42% of the patients followed by betamethasone combined with calcipotriol, cade emulsion, topical corticosterioids and salicylic acid ointments. Systemic therapy with methotrexate was used in only one patient.

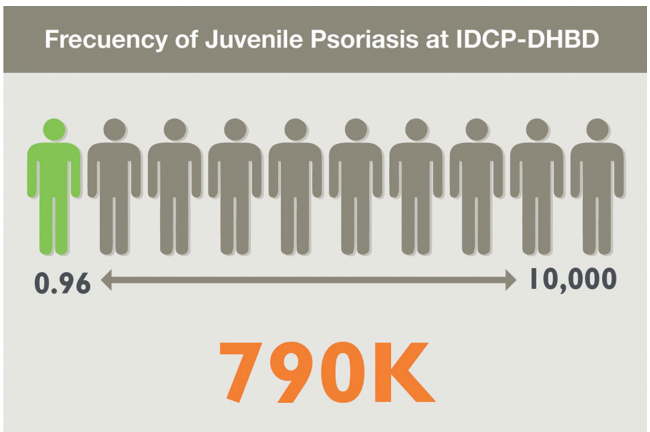


Figure 2. Frecuency of juvenile psoriasis at IDCP in the Dominican Republic.

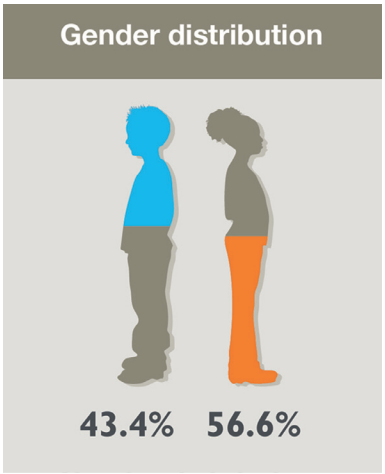


Figure 3. Gender distribution of patients.

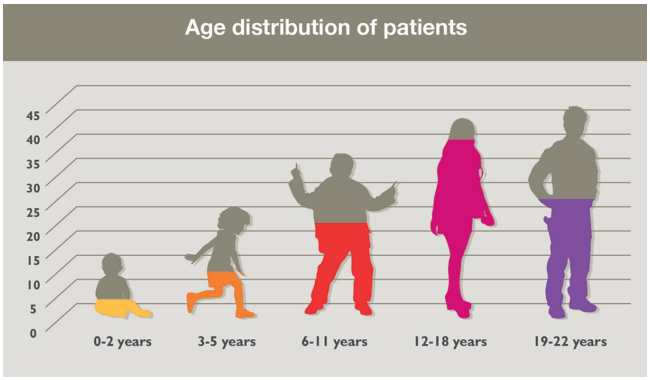


Figure 4. Age distribution of patients.

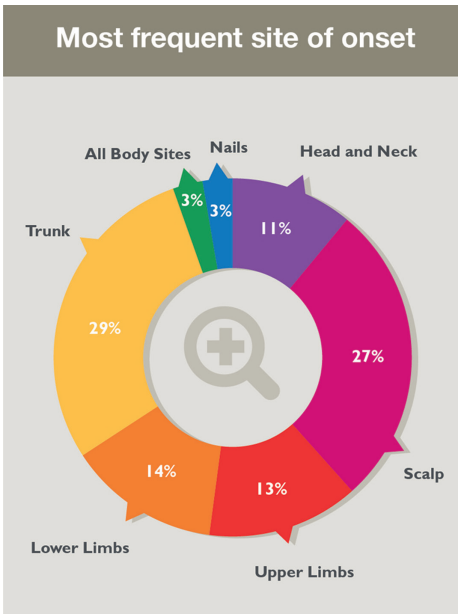


Figure 5. Most frequent site of onset.

Discussion

In terms of age of onset our data shows that 3.4% of patients were infants of 0-2 years, 12.6% less than 5 years and 54% less than 15 years. This results differs to the data of other regions of the world, for example in Australia, where 27% of the cases of psoriasis in children were reported in the group of patients of 0 - 2 years. But they are similar to areas like California which reports 2% of affected patients less than 2 years, 7% in 5 years or less, and 45% in the group of 12 years or less [12].

There have been reported racial differences on the groups affected by psoriasis; White and Asians seem to be the most affected while Hispanics and blacks are the least affected [12]. Our data reflects a low frequency of children and adolescents psoriasis. There is a mixture of races in the Caribbean area where there is a significant African American population.

In the present series, girls were slightly more affected than boys in a 1.3:1 ratio. It was interesting to see that 67% of the patients presented with 2 or more body segments involved, which could correlate with a delay in the diagnosis found of 6 months. There is a need to educate the population about what is psoriasis, how the symptoms may be found in children and adolescents and how they may differ from the typical presentation of the adults.

Treatment

It is important to consider certain facts that in children could alter the course of the disease, for instance, infections may trigger the onset of psoriasis or may perpetuate it. [19] In this young age it is essential to verify the weight and height of the children and adolescents, especially to detect metabolic syndrome risk factors [20,21], and also search for sign and symptoms of psoriatic arthritis. The objective of the treatment is to improve the physical symptoms minimizing the effect of the disease in the psychosocial development of the child. When choosing a therapy it is imperative to think in the future health of the child as well as in his growth and development [7].

Based on the European consensus on the management of juvenile psoriasis [22] we propose that the first line of treatment for induction to remission on mild psoriasis defined as PASI $\leq$ 10, or BSA $\leq$ 10 or DLQI $\leq$ 10 should be topical steroids class II- IV; for transitional therapy topical steroids class IV-VI or calcipotriol plus steroids; and for maintenance therapy it should be considered the use of mild potency steroids, calcipotriol, tacrolimus and finally tar, antraline and salicylic acid compounds.

In cases of moderate-to-severe psoriasis, defined as PASI $\geq$ 10 or BSA $\geq$ 10 or DLQI $\geq$ 10, it is indicative of the use of systemic therapy such as methotrexate, cyclosporine, oral retinoids or biologic agents. Alternatively narrow band ultraviolet B phototherapy could be considered for older children and adolescents. It is important to take into consideration the rotation, combination and sequential strategies when using these agents in order to improve the effectiveness of the treatment, its tolerance and to minimize the long term side effects of these agents (Fig. 6).

Conclusions

Even though psoriasis may cause a profound impact in the quality of life of children and adolescents the epidemiological data in the countries of Central America and the Caribbean is scarce. Psoriasis may impact the quality of life of children and adolescents and their parents in different ways than in adults, thus requiring separate studies. Many times the initial clinical presentation, the different trigger factors, and the different associations may be unrecognized by the parents and thus contribute to the delay in the diagnosis therefore more education should be given to the general population regarding this entity and specific therapeutic guidelines should be proposed.

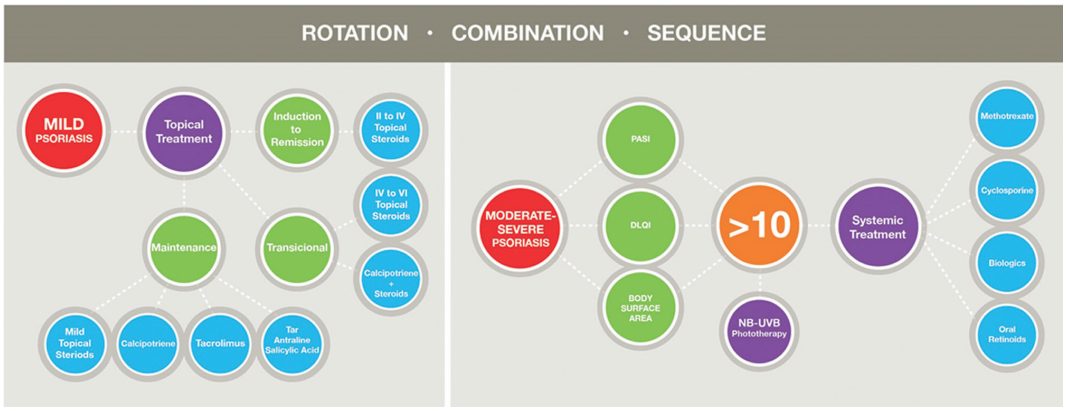


Figure 6. Therapeutic algorithm.

REFERENCES

1. Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. J Am Acad Dermatol. 2009;60:218-24.
2. Benoit S, Hamm H. Childhood psoriasis. Clin Dermatol. 2007;25:555-62.
3. Romiti R, Maragno L, Arnone M, Takahashi MD. Psoriasis in childhood and adolescence. An Bras Dermatol. 2009;84:9-20.
4. Rogers M. Childhood psoriasis. Curr Opin Pediatr. 2002;14:404-9.
5. Cordoro KM. Management of childhood psoriasis. Adv Dermatol. 2008; 24:125-69.
6. Farber EM, Jacobs AH. Infantile psoriasis. Am J Dis Child. 1977;131:1266-9.
7. Dogra S, Kaur I. Childhood psoriasis. Indian J Dermatol Venereol Leprol. 2010;76:357-65.
8. Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. Br J Dermatol. 2006;155:145-51.
9. Agustin M, Glaske G, Radtke MA, Christophers E, Reich K, Schafer I. Epidemiology and comorbidity of psoriasis in children. Br J Dermatol. 2010;162:633-6.
10. Gelfand JM, Weinstein R, Porter SB, Neimann AL, Berlin JA, Margolis DJ. Prevalence and treatment of psoriasis in the United Kindom: a population-based study. Arch Dermatol. 2005;141:1537-41.
11. De Jager ME, Van de Kerhof PC, De Jong EM, Seyger MM. Epidemiology and prescribed treatments in childhood psoriasis: a survey among medical professionals. J Dermatolog Treat. 2009;20:254-8.
12. Wu J, Helen-Black M, Smith N, Porter A, Jacobsen S, Koebnick C. Low prevalence of psoriasis among children and adolescents in a large multiethnic cohort in southern California. J Am Acad Dermatol. 2011;65:957-64.
13. Dogra S, Kumar B. Epidemiology of skin diseases in school children: A study from Northen India. Pediatr Dermatol. 2003;20:470-3.
14. Coimbra S, Figueiredo A, Castro E, Rocha-Pereira P, Santos-Silva A. The roles of cells and cytokines in the pathogenesis of psoriasis. Int J Dermatol. 2012.51:389-398.
15. Sticherling M, Augustin M, BoehnckeW, Christophers E, Domm S, GollnickH, et al. Therapy of psoriasis in childhood and adolescence - a German expert consensus. J Dtsch Dermatol Ges. 2011;9:815-23.
16. Sticherling M. Children and adolescents with psoriasis. What therapy is recommended? Hautarzt. 2012;63:192-201.
17. Silverberg NB. Pediatric psoriasis: an update. TherClin Risk Manag. 2009;5:849-56.
18. Leman J, Burden D. Psoriasis in children: a guide to its diagnosis and management. Paediatr Drugs. 2001 3:673-80.
19. Raychaudhuri SP, Gross J. A comparative study of pediatric onset psoriasis with adult onset psoriasis. Pediatric Dermatol. 2000;17:174-78.
20. Zindancı I, Albayrak O, Kavala M, Kocaturk E, Can B, Sudogan S, et al. Prevalence of Metabolic Syndrome in Patients with Psoriasis. Scientific World J. 2012;2012:312463.
21. Langan SM, Seminara NM, Shin DB, Troxel AB, Kimmel SE, Mehta NN, et al. Prevalence of Metabolic Syndrome in Patients with Psoriasis: A Population-Based Study in the United Kingdom. J Invest Dermatol. 2012;132:556-62.
22. Ståhle M, Atakan N, Boehncke WH, Chimenti S, Daudén E, Giannetti A, et al. Juvenile psoriasis and its clinical management: a European expert group consensus. J Dtsch Dermatol Ges. 2010;8:812-8.

DOI: 10.7241/ourd.20144.91

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

SECRET AND LATENT DANGERS HIDDEN UNDERNEATH THE GLAZED COVER OF THE MODERN ORGANIC COSMETIC

Lorenzo Martini

University of Siena, Department of Pharmaceutical Biotechnologies, Via A.Moro 2, 53100 Siena, Italy

Corresponding author: Lorenzo Martini, M.Sc. *martinil163@libero.it*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 366-369 Date of submission: 21.06.2014 / acceptance: 17.08.2014

Abstract
Amongst the principal targets the New Organic Cosmetic (and peculiarly the modern "Juice Beauty Care" based on the use of juices from fruits and polychrome herbs) heralds, there is the fact that it is advisable that the extraction must be done "naturally" from all vegetables, randomly collected and these vegetables may contain degraded chlorophyll and its derivative phylloeritrin, that is a very important photosensitizing agent, since the ripening of most fruits and some vegetables is characterized by rapid decrease of chlorophyll levels coupled with rapid increase of pigments.
This involves the presence of extreme severe photosensitising agents in natural cosmetics belonging to the category of the "make up and decorative" ones, as eye-shadows, foundations, pencils, fards aux paupiers, coloured creams and pastes.
Aims of my study is to determine how much the presence of these photosensitising agents in Organic cosmetics may damage human skin, when covered by natural maquillage products and then exposed to sun. For this purpose I have recruited 20 women in a government prison that decided voluntarily to undergo my experiments, based on the simple application of natural make up cosmetics before to have their out of cell time, during summer days at noon. Final evaluations of photosensitization have been carried out along with the clinical scoring scale drawn up by the International Contact Dermatitis Research Group (ICDRG).

Key words: photosensitization; phylloeritrin; organic cosmetic; ICDRG score

Cite this article:
Martini L. Secret and latent dangers hidden underneath the glazed cover of the modern Organic Cosmetic. Our Dermatol Online. 2014; 5(4): 366-369.

Introduction

Photosensitization occurs when skin (especially areas exposed to light and lacking significant protective hair, wool, or pigmentation) becomes more susceptible to ultraviolet light due to the presence of photodynamic agents. Photosensitization differs from sunburn and photodermatitis, as both of these conditions result in pathologic skin changes without the presence of a photodynamic agent. The trend of the new Organic cosmetic (and peculiarly the modern "Juice Beauty Care") need to use manifold plants for extracting the most ample selection of natural juices that are useful as pigments in order to display eye-shadows, foundations, pencils, fards aux paupiers, coloured creams and pastes, but even for yielding biological colorants to render more attractive and delicate many kinds of cosmetics to apply onto safe skin.
The simplest and most common natural colorants allowed by the International Procedural Guidelines are Annatto (orange derived from a shrub that grows in a number of places in the southern hemisphere) beta-Carotene (yellow to orange, that can be used for cosmetics around the world), Caramel (brown that comes from the burning of sugars like sucrose, dextrose, malt syrup, molasses; highly stable, can be used for formulating products around the world) Carmine (bright, red colorant which has a bluish shade, derived from female cochineal beetles that are collected primarily in Peru and can be used in cosmetic products around the world). Chlorophyll and Chlorophyll Cu Complexes (green colorant obtained from several evergreen plants.
Moreover, approved throughout the world, are numbered Henna(a brown dye derived from the Henna plant. It primarily comes from India and is allowed in the US for all kinds of cosmetics, in China and EU only for hair treatment, since it is specifically prohibited for use in colouring eyelashes and eyebrows due to its known ability to cause irritation.

The primary photosensitization occurs when the photodynamic agent is absorbed through the skin. The agent enters thus the systemic circulation in its native form where it results in skin cell membrane damage after the subject is exposed to ultraviolet light. We have to stress though that too many others are the photosensitizing agents that can be retrieved in cosmetics, in addition to the aforesaid colorants, and include hypericin (from Hypericum perforatum [St. John's wort]), active substances from certain Umbelliferae and Rutaceae, as furocoumarins (psoralens), but several other principles from species of Trifolium (pratense and repens, both admitted in INCI) Medicago (clovers and alfalfa), species of Polygonum (aviculare, bistorta, fagopyrum, filiforme, falcatum, hydropiper, multiflorum, odoratum, persicaria, punctatum, tataricum, tinctorium that are all included in INCI, COLIPA and CTFA), apium graveolens, petroselinum crispum, species of Brassica (alba, campestris, juncea, napus and nigra). Bermudagrass (Cynodon dactylon) (CAS 84649-95-6) generally used as skin conditioning contains a very dangerous photosensitizing toxin.

The Organic Cosmetic prescribes that the extraction must be done "naturally" from fruits and vegetables that have been "organically and biologically" cultivated and many botanizers, naturopaths and herbalists agree upon the fact that the most part of fruits, randomly collected, that are used for yielding juices for cosmetics, contain degraded chlorophyll and its derivative phylloeritrin, that is a very important photosensitizing agent, since the ripening of most fruits and some vegetables is characterized by rapid decrease of chlorophyll levels coupled with rapid increase of pigments. I have to add that the same European procedural guidelines for Organic Cosmetics forecast the possibility of employ of xanthophyllines as natural colours and it is well known that these are yellow derivatives of carotenes, extremely photosensitizing and the most commonly used are:

Criptoxanthine (extracted from papaya, paprika, corn, orange), zeaxanthine (from marigold and corn), Violaxanthine (from viola tricolour, ranunculus ficaria, tulipa darwin or genseniana) canthaxanthine (from mushrooms and corynebacterium), astacin (from lobsters), astaxanthin (from green algae).

Errera [1] referred that all the photosensitizing substances (in our specific case, biologic substances) can behave as protein-photo-oxidizing and/or photo-hemolyzing agents.

The A. asserted that substances that are able to photo-oxidize and photo-hemolyze, may provoke erythemas after 6 days of exposure to light, visible or invisible (among these substances furocoumarins are to be numbered).

Besides, the same A. asserted that all the substances that do not photo-oxidize but are able to photo-hemolyze, do not provoke erythemats or hyperpigmentations, or sometimes reveal very light but reversible erythemas.

Finally, all the substances that are able to photo-oxidize, but are not able to photo-hemolyze, evoke erythemas and hyperpigmentations absolutely irreversible.

Here follows a research I have conducted, that intends to demonstrate how the inappropriate use of natural colours for make up products, may be extremely risky for human skin and organism.

Aims of our study is to demonstrate that too many are the cosmetics for maquillage (especially natural based eye-shadows, foundations and nail lacquers) are extremely perilous to human health, that are strenuously declared safe and non toxic.

I have recruited 20 women in a government prison that decided voluntarily to undergo our experiments, based on the simple application of natural make up cosmetics before to have their out of cell time, during summer days at noon.

Finally, evaluations of photosensitization have been carried out along with the clinical scoring scale drawn up by the International Contact Dermatitis Research Group (ICDRG).

Material and Methods

We have selected two samples of cosmetics publicised and merchandised as "pure Juice beauty care products" (Organic and natural Cosmetics); the first (one) was a juice foundation (the following is the CTFA-ingredients:peach, apricot, cucumber, carrot, pomegranate, goj berry, tomato, white tea, aloe juice.

The latter (two) was an organic eye-shadow (the following is the INCI names: rosa damascena buds, jasminum officinale buds, chamomilla recutita flower, aloe barbadensis powder, equisetum arvense (horsetail) extract, urtica dioica (nettle) leaf extract (simmondsia chinensis (jojoba) seed oil, magnesium stearate, alpha tocopherol. ascorbyl palmitate, caprylic/capric triglycerides). The ingredients in italic are merely excipients and do not contribute to the phenomenon of the photosensitization at all.

Ten of the 20 volunteers were gently requested to spread the eye-shadow before to walk around under the summer sun for the out-of-cell-time (one hour) for seven days, everyday at midday, meanwhile the other 10 were requested to spread the foundation on cheek and décolleté and to do all the same of the first panel group's volunteers

I have had to exclude several volunteers that presented the typical jail dermatological illnesses, that may be, along with Roodsari et al. [2] and Hall [3] sycosis vulgaris, dermatitis papillaris, follicular hyperkeratotic papules, follicular pustules, acneform facial eruptions, intracutaneous hemorrhages and xerosis (surely produced by hypovitaminosis), facial scabies, facial pyoderma, melasma, frictional melanosis, neurodermatitis and urticaria; notwithstanding the group was well assorted (age and race).

Besides, women with couperose, rosacea, teleangectasiae on the face, breastfeeding accoucchées and subjects taking hormones, FANS and antipsychotic drugs have been excluded.

An informed consent was rigorously required and gently obtained from each volunteer prior to participate to the experiment.

The evaluation of the effects of the photosensitization onto face skin and eyelids after during the entire week of periodical walks under the sun rays, was carried out by scrupulous examinations effectuated using magnifying glass under the same lamp light in the same period of time, during daylight every afternoon at 2.00 p.m. and have been carried out along with the clinical scoring scale drawn up by the International Contact Dermatitis Research Group (ICDRG).

Results

Score	Appearance	Diagnosis
0	Negative	Negative
0.5	Macular erythema	Barely perceptible macular erythema
1	Weak (non-vesicular) reaction, induration, possible papules	Mild erythema
2	Strong (edematous or vesicular) reaction, erythema, induration, papules, vesicles	Moderate-intense uniform erythema
3	Extreme (spreading, bullous or ulcerative) reaction	Intense erythema and edema, vesiculation or erosion

Table I. The Plot of Photosensitization (by ICDRG).

Case	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
01e	0	0	0.5	0.5	0.5	1	1
02e	0	0.5	0	0.5	1	0.5	1
03e	0.5	1	1	1	0.5	2	1
04e	0	0.5	0.5	0.5	0	0.5	0.5
05e	0.5	0.5	0.5	0	0.5	1	1
06e	0	0.5	0	0.5	0.5	1	0.5
07e	0	0	0	0	0	0	0.5
08e	0	0	0.5	0.5	0.5	0.5	1
09e	0	0.5	0.5	0	0.5	1	1
10e	0	0	0	0.5	0	1	1
11F	0.5	0.5	0	0.5	0.5	0.5	1
12F	0.5	0.5	0.5	0.5	0.5	1	0.5
13F	0.5	0.5	0	0.5	0	1	0.5
14F	0	0.5	0.5	0	0	1	0.5
15F	0	0.5	0	0.5	0.5	0.5	1
16F	0.5	0	0.5	0	0.5	0.5	1
17F	0.5	0.5	0.5	1	1	2	2
18F	0	0.5	0	0.5	0	1	1
19F	0.5	0	0	0	0.5	0.5	1
20F	0	0.5	0.5	0.5	0	1	0.5

Table II. Scores of Photosensitization recorded during a week of experiments on volunteers.

Legenda: "e" corresponds to the volunteers using the eye-shadow, "F" the ones using the foundation).

Conclusion

It is suggestive to stress that the theory referred first by Errera in 1954 is amply confirmed: objectively an increase in photosensitization effect is always noticeable at the or after the 6th day.

Only appropriate chemical investigations on the final make up product could provide the entire list of pigments and the percentages of phylloeritrines, chlorophylls and antocyanins included, in order to predict a photo-toxicological profile, albeit it is important to demonstrate that make up products based on fruit juices, when exposed to sun rays for prolonged and reiterated times, evokes always progressive manifestations of adverse skin reactions and hyperpigmentations.

Case 4e and Case 7e were coloured-skin individuals, and it is noteworthy that even if Case 7e appears more resistant than the other white skin individuals, the final rash at the 6th day is always evident.

Surely Case 4e presents a more thin and delicate skin than Case 7e, anyway the final rash at the 6th day is less severe than all the others.

This may induce to deem that black coloured-skin subject are less prone to photosensitization by fruit juices in make up products.

REFERENCES

1. Errera M. Protoplasmatologia - Handbuch der Protoplasmaforschung. 3rd ed.Wien:Springer; 1957.
2. Roodsari R, Malekzad F, Ardakani ME. Skin diseases in male prisoners. Indian J Dermatol Venereol Leprol. 2007;73:55-6.
3. Hall TB. Dermatitis papillaris capillitii and sycosis vulgaris with hypovitaminosis:report of a case. Arch Derm Syphilol. 1936;33:880-4.
4. Gokilamani N, Muthukumarasamy N, Thambidurai M, Ranjitha A, Velauthapillai D. Utilization of natural anthocyanin pigments as photosensitizers for dye-sensitized solar cells. J Sol-Gel Sci Technol. 2013;66:212–9.
5. Souad AM, Al-Bat'hi L, Iraj A, Sopyan I. Natural Photosensitizers for Dye Sensitized Solar Cells. Int J Renewable En Res. 2013;3:111.
6. Kushwaha R, Srivastava P, Bahadur L. Natural Pigments from Plants Used as Sensitizers for TiO2 Based Dye-Sensitized Solar Cells. J Energy. 2013;654953:8.
7. Anthony TT. Handbook of Natural Toxins.Vol. 7: Food Poisoning, CRC, London 1992.
8. Yamazaki E, Murayama M, Nishikawa N, Hashimoto N, Hoyama M, Kurita O. Utilization of natural carotenoids as photosensitizers for dye-sensitized solar cells. Solar Energy. 2007;81:512–6.

DOI: 10.7241/ourd.20144.92

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

UNIQUE PSORIATIC LESION VERSUS MULTIPLE LESIONS

Anca Chiriac,[1,2] Piotr Brzezinski[3], Liliana Foia[4], Anca E Chiriac[4], Tudor Pinteala[4], Caius Solovan[5]

[1]*Apollonia University Iasi, Dermato-Physiology Department, Strada Muzicii nr 2, Iasi-700399, Romania*
[2]*Nicolina Medical Center, Department of Dermatology, Iasi, Romania*
[3]*Department of Dermatology, 6th Military Support Unit, os. Ledowo 1N, 76-270 Ustka, Poland*
[4]*Universityof Medicine and Pharmacy „Gr. T Popa" Iasi, Romania*
[5]*University of Medicine and Pharmacy „V Babes" Department of Dermatology, Timisoara, Romania*

Corresponding author: Prof. Anca Chiriac anca.chiriac@yahoo.com

Source of Support: Nil
Competing Interests: None

Our Dermatol Online. 2014; 5(4): 370-373 Date of submission: 18.07.2014 / acceptance: 02.09.2014

Abstract
Aim: To evaluate the number of lesions of psoriasis and to find risk factors for multiple lesions.
Material and Methods: 1,236 patients (male 54.13%, female 45.87%) with psoriasis were seen over a period of 8 years in an Outpatient Clinic. Patients filled out questionnaires containing age at onset, number of lesions and location at the beginning of the disease, gender, type and localization of psoriasis at the time of clinical examination, psoriasis family history, previous treatment, comorbidities, and social status.
Results: The number of psoriasis lesions correlates with: onset age of psoriasis (F=8.902, p=0.0029); age at the moment of clinical examination (F=8.902, p=0.0029); residence in rural area (χ^2=8.589, p=0.00338, 95%CI); alcohol intake (χ^2=16.47, p=0.00005, 95%CI); smoking (χ^2=8.408, p=0.00373, 95%CI); occupation: workers/pupils/students (χ^2=14.11, p=0.0069, 95%CI).
Conclusions: There is a correlation between number of psoriatic lesions and some factors. Multiple lesions were observed in older patients, smokers and drinkers, coming from rural area and social active (workers and pupils/students). No correlation was statistically proved between number of lesions and gender, comorbidities and family history of psoriasis.

Key words: psoriasis; number of lesions; Romania; statistical analysis; statistical correlation; large clinic-based sample

Cite this article:
Chiriac A, Brzezinski P, Foia F, Chiriac AE, Pinteala T, Solovan C. Unique psoriatic lesion versus multiple lesions. Our Dermatol Online. 2014; 5(4): 370-373.

Aim

The aim of the work was a evaluate the number of lesions of psoriasis and to find risk factors for multiple lesions.

Material and Methods

At the end of 2011, we initiated a project which intended to evaluate the number of lesions of psoriasis at the moment of clinical examination and to find correlations between clinical characteristics of lesions and other factors: onset age, present age, gender, residence, smoking, alcohol intake, severity index, comorbidities, work status, family history of psoriasis.
1,236 patients (male 54.13%, female 45.87%) with psoriasis were seen over a period of 8 years in an Outpatient Clinic in Romania, by the same dermatologist, the diagnosis was certified by clinical features and, when necessary, by skin biopsies. The subjects were also asked about other medical problems, the presence of similar lesions among other members of the family.

Results

The distribution of psoriasis was clearly recorded. Active lesions were noted on the scalp, face, trunk, anogenital area, arms, legs, hands, feet or nails, i.e. in 10 different locations (Tabl. I).

The most common finding was s psoriasis on the arms and legs, followed by scalp psoriasis. Less common locations were the trunk and palmo-plantarregion. The facial area was affected in 4.45% of all the examined persons.

Majority of patients (82.85%) had multiple skin lesions at the moment of clinical inspection.

Of 1236 patients enrolled in the study an approximately equal distribution was observed among patients with solitary lesion or 2, 3 or 4 body areas involved (Tabl. II).

More generalized forms were very rare.

	Nr of cases	%
Nail psoriasis	165	13.35%
Psoriatic arthritis	309	25.00%
Koebner	173	14.00%
Scalp psoriasis	681	55.10%
Gutate psoriasis	146	11.81%
Superior limbs	788	63.75%
Inferior limbs	736	59.55%
Trunk	462	37.38%
Face	55	4.45%
Palmo-plantar	205	16.59%
Others	265	21.44%
Total	1236	

Table I. Clinical aspect of psoriasis.

Location	Nr. cases	%
Unique lesions	212	17.15%
Multiple lesions	1024	82.85%
2 body areas	266	21.55%
3 body areas	244	19.74%
4 body areas	240	19.41%
5 body areas	155	12.54%
6 body areas	76	6.15%
7 body areas	30	2.43%
8 body areas	12	0.97%
10 body areas	1	0.08%
Total	1236	

Table II. Evaluating the number of psoriatic lesions at the moment of clinical examination.

A few patients (1.21%) with multiple onset lesions turned to have later unique lesions; 7.61% of them preserved the initial multiple lesions (Tabl. III).

A small percentage (15.94%) of onset single lesion patients in time remained with unique (the same or different) cutaneous psoriasis stigma.

Vast majority of cases (75.24%) with declared unique psoriatic lesion at the onset of the disease developed multiple skin manifestations over short or long period of time.

Statistical report shows no marked relationship between locations of the lesions at the first diagnosis of psoriasis and at the moment of onset evaluation. ($r= 0.1406$, $\chi^2=1.018$, $p=0.312$, 95%CI).

Evaluation of risk factors associated with multiple psoriatic lesions was done and the results are sumarrized in Table IV.

Table V presented PASI vs number of lesions.

1. Onset age vs number of lesions

Median onset age of psoriasis does not show significant differencies related to location of the psoriatic lesions: unique vs multiple. ($F=12.93$, $p=0.000337$, 95%CI)

2. Age at the moment of clinical examination vs. number of lesions

The median age of patients with multiple lesions (45.55 years ± 15.72 SD) was significant higher ($F=8.902$, $p=0.0029$) than the same parameter calculated for patients with unique lesion (41.99 years ± 15.72 SD).

Onset location	Location at the moment of examination		%
	unique location	multiple location	
unique location -onset	197 / 15.94%	930 / 75.24%	1127
multiple location -onset	15 / 1.21%	94 / 7.61%	109
Total	212	1024	1236

Table III. Comparison between unique onset lesion ad multiple lesions at the moment of clinical examination.

3. Residence vs. number of lesions
The risk for multiple lesions is 2.05 higher in rural area. A moderate association is evidenced between residence and multiple location (χ^2=8.589, p=0.00338, 95%CI)

4. Gender vs. number of lesions
There is no association between gender of psoriasis patients and number of the lesions (χ^2=3.164, p=0.0752, 95%CI)

5. Psoriasis severity index and number of lesions
It is obvious that a very strong correlation is proved (and attest our study) between the severity of the disease and number of psorasis lesions (r=0.414, p<<0.01, 95%CI).

6. The presence of comorbidities vs. number of lesions
There is no correlation between the presence of comorbidities and multiple locations (χ^2=2.103, p=0.146, 95%CI). Patients with psoriasis and comorbidities have a very low risk of developing multiple skin lesions. (OR=1.25).

7. Alcohol intake(by declaration) vs. number of lesions
A strong association is confirmed among alcohol intake and multiple location (χ^2=16.47, p=0.00005, 95%CI). The risk for disseminated psoriasis lesions in alcohol consumers is 2.06 higher compared to non-drinkers (OR=2.06).

8. Smoking vs number of lesions
Smoking and multiple location are correlated (χ^2=8.408, p=0.00373, 95%CI). Risk found in smokers to multiple lesions is 1.71 higher compared to non-smokers. (OR=2.06).

9. Occupation vs number of lesions
Multiple lesions of psoriasis were noted in workers (50.32%) and pupils/students (11.08%) Only 2.18% of people, those with no income had multiple lesions. A strong association links the occupation and location of lesions (χ^2=14.11, p=0.0069, 95%CI).

10. Family history of psoriasis vs number of lesions
Statistically there is no correlation between the presence of family history of psoriasis and number of lesions. (r= 0.0017, χ^2=2.06, p=0.724, 95%CI).

	Location	
	unique lesionnr patients / %	**multiple lesionsnr patients / %**
Urban residence	192 / 18.53%	844 / 81.47%
Rural residence	20 / 10.00%	180 / 90.00%
Male gender	103 / 15.40%	566 / 84.60%
Female gender	109 / 19.22%	458 / 84.60%
Mild psoriasis	132 / 24.63%	404 / 75.37%
Moderate psoriasis	65 / 13.00%	435 / 87.00%
Severe psoriasis	15 / 7.50%	185 / 92.50%
Comorbidities absent	135 / 18.44%	597 / 81.56%
Comorbidities present	77 / 15.28%	427 / 84.72%
Alcohol consumer	45 / 10.98%	365 / 89.02%
Non acohol consumer	167 / 20.22%	659 / 79.78%
Nonsmoker	171 / 19.06%	726 / 80.94%
Smoker	41 / 12.09%	298 / 87.91%
Pupil/student	45 / 3.64%	137 / 11.08%
Worker	130 / 10.52%	622 / 50.32%
Retired	20 / 1.62%	129 / 10.44%
Social assisted	1 / 0.08%	27 / 2.18%
Job less	16 / 1,29%	109 / 8.82%
Family history absent	150 / 17.22%	721 / 82.78%
First degree relatives with psoriasis	38 / 19.00%	162 / 81.00%
Second degree relatives with psoriasis	15 / 13.04%	100 / 86.96%
Third degree relatives with psoriasis	7 / 19.44%	29 / 80.56%
Fourth degree relatives with psoriasis	2 / 14.29%	12 / 85.71%

Table IV. Number of lesions vs residence, gender, index severity, presence of comorbidities, alchohol, smoking, work status, family history of psoriasis.

Parameter/factor	PASI index-correlation	Number of psoriatic lesions-correlation
Onset age	yes	no
Age at the moment of clinical examination	yes	yes
Gender (male)	yes	no
Residence in rural area	yes	yes
History family of psoriasis	yes	no
Presence of comorbidities	yes	no
Alcohol and smoking	yes	yes
Work status-education	Retired persons-jobless	Workers/pupils-students

Table V. PASI vs number of lesions.

Discussion

We have used a simple and direct method of recording any active psoriasis lesion in ten different body regions, instead of using the PASI score or DLQI appreciations.

The extent of the skin disease at the moment of present examination showed no correlations with: age at the moment of examination, confirming different other studies that have reported no difference in extent of lesions linked to the age at onset [1,2].

Multiple lesions were described in late psoriasis (over 40 years of age), although reports support the hypothesis that late psoriasis is milder than early psoriasis [3] based on PASI evaluation.

It is well accepted that psoriasis predominates in men and mild to severe forms of the disease have been reported in male patients [4]. Present study does not attest any link between gender of the patients enrolled in the study and number of psoriasis lesions.

Alcohol and smoking are two parameters strongly connected to extent of psoriasis due to different causes: stress activity, limited access to dermatological care, poor hygiene status, associated diseases induced by alcohol and smoking, lack of stable income and deprived nutrition.

Although it is well known that severe forms of psoriasis (PASI 10 or higher) are associated with the presence of co-morbidities, present study does show any correlation between the extent of psoriatic lesions and the occurrence of other systemic diseases [5].

In urban areas it is described a higher prevalence, but with mild forms, of psoriasis, while in rural areas severe and untreated forms are commonly seen. Explanations can be found in reduced address ability of people living in villages to a specialized psoriasis center, late diagnosis and long period of time with no treatment, longer exposure to sun due to open air activities, smoking and alcohol intake, different nutrition habits, diminished skin care hygiene measures. These may also clarify the prevalence of patients with multiple lesions of psoriasis in patients living in rural areas.

Work status and education are two major factors taken into account when evaluating a patient with psoriasis: severity index correlates with both; multiple lesions of psoriasis were seen in workers and pupils/students while persons with low income and poor living conditions had no extensive diseases.

Family history of psoriasis, although admitted to explain at least partially the severity of the disease in adults, does not have any impact on number of lesions, accordingly to our study.

Conclusion

The number of psoriasis lesions correlates with:

- age at the moment of clinical examination ($F=8.902$, $p=0.0029$);
- residence in rural area ($\chi^2=8.589$, $p=0.00338$, 95%CI);
- alcohol intake ($\chi^2=16.47$, $p=0.00005$, 95%CI);
- smoking ($\chi^2=8.408$, $p=0.00373$, 95%CI);
- occupation:workers/pupils/students ($\chi^2=14.11$, $p=0.0069$, 95%CI).

REFERENCES

1. Ikäheimo I, Tiilikainen A, Karvonen J, Silvennoinen-Kassinen S. HLA risk haplotype Cw6, DR7, DQA1*0201 and HLA-Cw6 with reference to the clinical picture of psoriasis vulgaris. Arch Dermatol Res. 1996;288:363-5.
2. Inerot A, Enerbäck C, Enlund F, Martinsson T, Samuelsson L, Wahlström J, et al. Collecting a set of psoriasis family material through a patient organisation; clinical characterisation and presence of additional disorders. BMC Dermatol. 2005;5:10.
3. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol. 1985;13:450–6.
4. Hägg D, Eriksson M, Sundström A, Schmitt-Egenolf M. The higher proportion of men with psoriasis treated with biologics may be explained by more severe disease in men. PLoS One. 2013;8:e63619.
5. Altobelli E, Petrocelli R, Maccarone M, Altomare G, Argenziano G, Giannetti A, et al. Risk factors of hypertension, diabetes and obesity in Italian psoriasis patients: a survey on socio-demographic characteristics, smoking habits and alcohol consumption. Eur J Dermatol. 2009;19:252-6.

DOI: 10.7241/ourd.20144.93

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

EVOLUTION OF VIDEO CAPILLAROSCOPY FOR 10 YEARS IN A PATIENT WITH RAYNAUD

Maria Bibiana Leroux, Celina Lashak

Centro de Referencia en Raynaud y Colagenopatías, Rosario, Argentina

Corresponding author: Dr Maria Bibiana Leroux leroux_mb@hotmail.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 374-377 Date of submission: 18.08.2014 / acceptance: 10.09.2014

Abstract
Introduction: The nail fold video capillaroscopy allows the study of micro vascular abnormalities in autoimmune rheumatic diseases.
Aim: Report a case of Raynaud's phenomenon, in which images of video capillaroscopy correlate with disease course.
Case Report: Patient with Raynaud's phenomenon that after ten years of evolution develops pulmonary hypertension. The progression of micro vascular disease in the nail fold and lip mucosa was studied.
Discussion: Scleroderma pattern progresses in successive controls were observed in studies of video capillaroscopy. Pro-angiogenic and anti-angiogenic factors may trigger the formation of micro vascular changes during systemic scleroderma. The same can be correlated with lung involvement.
Conclusion: Images of video capillaroscopy collaborate with the diagnosis and prognosis in the spectrum of Systemic Scleroderma.

Key words: capillaroscopy; Raynaud; systemic scleroderma; pulmonary hypertension; SD pattern

Cite this article:
Leroux MB, Lashak C. Evolution of video capillaroscopy for 10 years in a patient with Raynaud. Our Dermatol Online. 2014; 5(4): 374-377.

Introduction

The nail fold video capillaroscopy allows the study of micro vascular abnormalities in patients with autoimmune rheumatic diseases. Its indication is the gold standard in the differential diagnosis between primary and secondary Raynaud. Recognition of the characteristic pattern scleroderma (SD) allows diagnosis of very early stage of systemic scleroderma and its correlation with systemic involvement. The micro vascular damage is considered an independent predictor and proposed as validation criteria for early systemic scleroderma [1-6].

Aim

Report a case of Raynaud's phenomenon, in which images of video capillaroscopy correlate with disease course.

Case Report

The female patient age 48, referred raynaud for 10 years. She refers pallor and cyanosis of hands after contact with the cold. This symptom was treated with nifedipine 20 mg /d during the winter months. During this time, regular checks are made. In control this year, lung involvement is detected. Typical signs of skin sclerosis in face and hands are not observed. In the personal history relates: absence of tobacco, alcohol, drugs, radiation or occupational exposure, and hypothyroidism in treatment. History of present illness is summarized in Table I. In each of the checks, complete physical examination, hematological laboratory, antinuclear antibodies and auto-specific antibodies, radiology, and spirometry, is performed. In the immune laboratory have not detected anti- centromere, anti- topoisomerase 1 RNP or anti- Jo in successive controls. Pulmonary hypertension could correspond to systemic scleroderma or related disease (Figs 1a - c, 2a - c, 3).

Discussion

Video capilaroscopia images in this patient are progressing over ten years. During this time the patient does not meet the classic diagnostic criteria for systemic sclerosis (1980), nor does it have specific auto antibodies. However, after 10 years starting with raynaud develops pulmonary hypertension. According to the proposed criteria for early diagnosis of systemic scleroderma, this case could be considered pre or early systemic scleroderma scleroderma. Currently the definition of criteria for the diagnosis of this entity remain in debate [7-9].
In the study by video capillaroscopy, the characteristic pathological pattern scleroderma (SD) is recognized. It consists megacapilares, decrease or loss of capillaries, neo vessel formation, altered structure of the bed. You can also observe meandering, curled vessels and few branched capillaries (Tabl. II). SD pattern variants are listed in Table III.

In the first study conducted video capillaroscopy scleroderma early pattern is displayed. The density is relatively preserved, absence of avascular areas or neovascularization (Fig. 1).
In the second study, lower capillary density as above is checked. The presence of neovascularization reveals the vascular injury and repair attempt. This description corresponds to active SD pattern (Figs 1b, 1c).
In the third study, a nail fold telangiectasia is observed. These are formed by vessels which are visible to the naked eye (Fig. 2a). They are due to dilation of the post capillary venules located in the papillary and reticular dermis surface. The appearance of telangiectasias on skin is a common skin sign in systemic scleroderma and its presence is associated with pulmonary arterial hypertension. They are a marker of micro vascular disease spread [10].
In the mucosa of the lower lip has a normal appearance with the naked eye. In our case study of megacapilares and neovascularization are detected (Figs 2b, 2c).
The video capillaroscopy in this area ranks as second choice site, because of its easy access. It has a similar capillary perfusion to the fingers, so the display close to 75% of the vessels is ensured.
The study of Grassi et al notes that video capillaroscopy labial mucosa in patients with systemic scleroderma characteristic exhibited as more generalized disruption of the micro vascular network [11,12].
A full nail fold is also analyzed (Fig. 3). Arrows indicate multiple avascular areas. These are very close to the bizarre vessels due to angiogenesis.

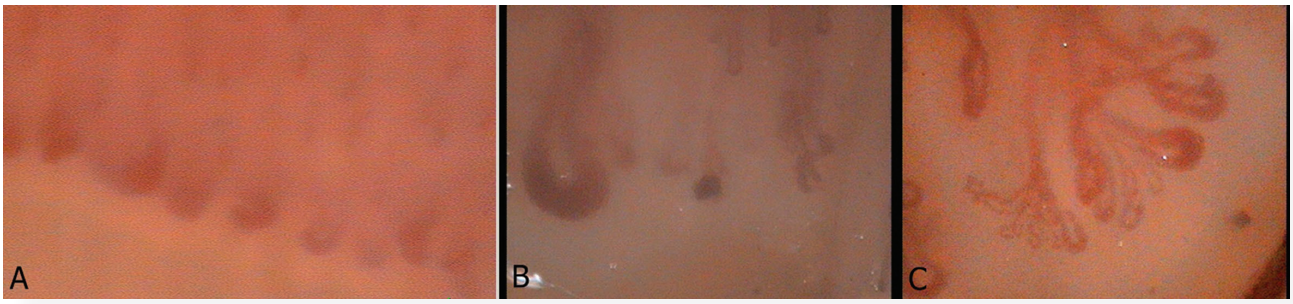


Figure 1. (A). Image video capillaroscopy by 200X in nail fold. 1 study. Very enlarged (mega capilares) capillaries. The largest is marked. Capillary density cap by 7 mm within normal limits. Vision in frosted glass. Scleroderma pattern. (B). Image of video capillaroscopy by 200X in nail fold. Obtained five years ago. One mega capilar shown. Capillary density greatly decreased. Micro hemorrhages. (C). Figure n°3: Image of video capillaroscopy by 200X in nail fold. Obtained five years ago. Neo capillary formation is observed well developed.

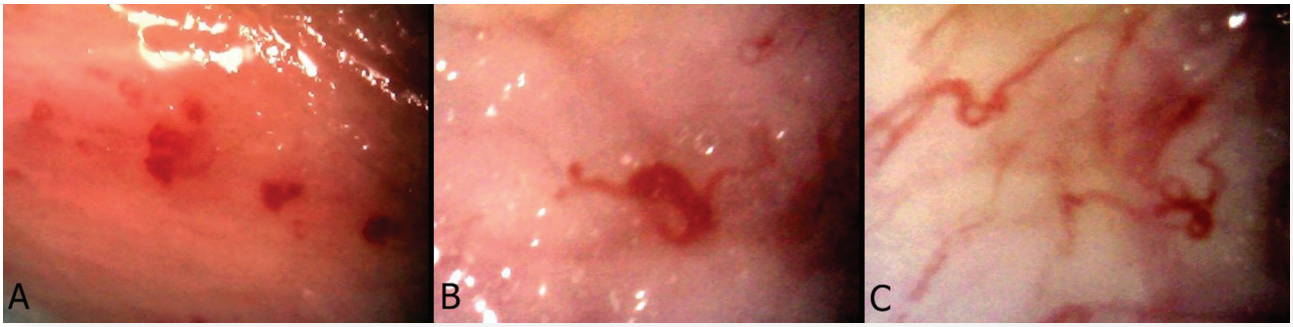


Figure 2. (A). Image video capillaroscopy by 200X in nail fold. Nail fold telangiectasia consist of very enlarged vessels. (B). Image of lower lip mucosa. Mega capilar. (C). Image of lower lip mucosa. Bushy capilar.

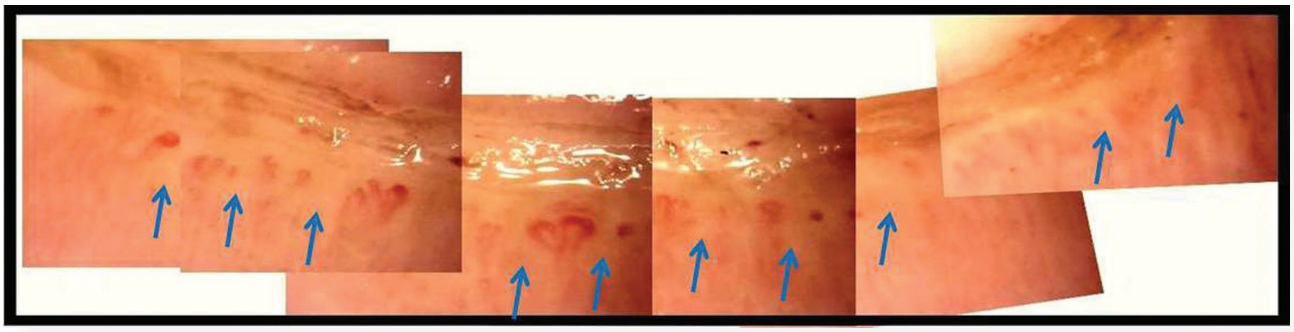


Figure 3. Video capillaroscopy image digitally, full nail fold. Multiple avascular areas, mega capilares, vessels caused by neo angiogenesis and Hemorrhages. Vision in frosted glass. Disorganization of the capillary bed. Pattern SD late.

Evolution	Cutaneous manifestation	Extra cutaneous manifestation	Autoantibodies	Videocapillaroscopy
10 years ago	Raynaud	Not detected	ANA negative	Not performed
8 years ago	Raynaud Periungual erythema Fragility of skin fingertips	Not detected	ANA 1/1280 N	Nail fold SD pattern 1st Study Figure 1a
5 years ago	Same as previous Add hands with persistent edema	Arthralgia	ANA 1/1280 NM	Nail fold SD pattern 2nd Study Figures 1b and 1c
Present day	Same as previoustelangiectasias periungulares Figure 2a	Pulmonary hypertension	ANA 1/1280 N	Nail fold and lip mucose SD pattern 3rd Study Figures 2b, 2c and 3

Table I. Evolution patient.

ANA: antinuclear antibodies

N: nucleolar pattren

M: speckled

SD: scleroderma

Alteration of the microcirculation	Description
Megacapillaries	Very increased in size capillaries to ten times normal.They can coexist with preserved capillaries. They are characteristic of secondary Raynaud and systemic sclerosis.
Vessels caused by neo angiogenesis	Increased in size, heterogeneous, bizarre, bushy capillaries
Tortuous vessels	Capillaries with serpentine arms like that can interbreed or turned on the long axis of the capillary.
Decreased capillary density	Less than 7 cap / mm. It is related to systemic scleroderma syndromes.
Avascular areas	These are caused by capillary loss. It can include one or more dermal papillae. A larger, more severe and are associated with decreased nutrient flow.
Disorder of the vascular bed	Alteration of the polarity of the capillaries.
Hemorrhages	Produced by injury of the capillary wall and consequent outflow of blood to the dermis. Red spots are arranged in rows extending from the capillary into the cuticle.
Exudates	Plasma present in the dermis can be observed in two ways: as a ground glass viewing or tenuous wave shaped figures surrounding the vessel originates.
Vision in frosted glass	Structures are blurred. This is due to the presence of plasma proteins the adjacent dermis.

Table II. Glossary capillaroscopic.

SD Pattern	Characteristics
Early SD	Mega capillaries, few hemorrhages, no apparent capillary loss, bed architecture preserved
Active SD	Mega capillaries and frequent hemorrhages, mild capillary loss , moderate disorganization of the architecture of the bed, formation of new blood vessels in small proportion. Presence of edema. Picture can progress
Late SD	Irregular increase size capillary, hemorrhages, severe capillary loss with extensive avascular areas, disorganization of the capillary bed, bizarre vessels. Picture stable

Table III. SD pattern variants.

SD: scleroderma

In the pathogenesis of systemic sclerosis, endothelial injury and apoptosis are early in the affected skin, prior to the presence of fibrosis events. In early disease, the pro-inflammatory state and increased production of pro -angiogénicos stimulates angiogenesis factors. The presence of hemorrhage, giant capillaries and micro vascular tortuosity changes are formed by uncontrolled angiogenic response. Subsequently, a process where actuated angiostatic factors resulting in reduction in capillary density and extensive areas of avascularity develops. Therefore the imbalance between pro-angiogenic and anti-angiogenic factors would play an active role in the formation of micro vascular alterations [13].

In Systemic scleroderma lower capillary density compared with systemic lupus erythematosus, undifferentiated connective tissue disease and normal controls was demonstrated. In these patients, increased frequency of severe avascularity, megacapilares and micro bleeding was found. The prognostic value of capillaroscopy is manifested in the relationship between the avascularity and organic disease in systemic scleroderma. The presence and severity of pulmonary hypertension in patients are specifically correlated with the reduction in capillary density per millimeter. Recently suggested that the presence of large avascularity is a predictor of mortality in patients with systemic scleroderma [14-21].

The bizarre or bushy capillaries caused by neovascularization are indicators of disease activity. The finding of avascular areas correlates with interstitial lung disease and is more common in patients receiving immunosuppressants, indicating severe disease. The dynamic nature of the process is observed in 16% of patients. The SD pattern is a good indicator of the severity and evolution of the lung [22,23].

Conclusion

Images of video capillaroscopy collaborate with the diagnosis and prognosis of patients in the spectrum of systemic scleroderma.

REFERENCES

1. Roustit M, Cracowski JL. Non-invasive assessment of skin microvascular function in humans: an insight into methods. Microcirculation. 2012;19:47-64.
2. Maricq HR, Valter I. A working classification of scleroderma spectrum disorders: a proposal and the results of testing on a sample of patients. Clin Exp Rheumatol. 2004;22:S5-13.
3. Pistorius MA, Carpentier PH, le groupe de travail « Microcirculation » de la Société française de médecine vasculaire. Minimal work-up for Raynaud syndrome: a consensus report. Microcirculation Working Group of the French Vascular Medicine Society. J Mal Vasc. 2012;37:207-12.
4. Leroux MB, Rinaldi M, Palatnik S, Jorfren M, Fernandez Bussy R. Raynaud primario y secundario a síndromes esclerodermiformes. Comunicación de 97 pacientes estudiados por capilaroscopia periungueal. Arch Argent Dermatol. 2000;50:1519-23.
5. Sulli A, Burroni A, Tuccio M, Pizzorni C, Craviotto C, Ghio M, et al. Nailfold videocapillaroscopy in systemic sclerosis: diagnostic and follow-up parameters and correlation with both specific serum autoantibodies and subsets of skin involvement. Reumatismo. 2004;56:34-45.
6. Avouac J, Fransen J, Walker UA, Riccieri V, Smith V, Muller C, et al. Preliminary criteria for the very early diagnosis of systemic sclerosis: results of a Delphi Consensus Study from EULAR Scleroderma Trials and Research Group. Ann Rheum Dis. 2011;70:476-81.
7. Simeón-Aznar CP, Tolosa-Vilella C, Gabarró-Juliá L. Systemic sclerosis sine scleroderma and limited cutaneous systemic sclerosis: similarities and differences. Clin Exp Rheumatol. 2014;Apr 28
8. Valentini G, Marcoccia A, Cuomo G, Iudici M, Vettori S. The Concept of Early Systemic Sclerosis Following 2013 ACR\EULAR Criteria for the Classification of Systemic Sclerosis. Curr Rheumatol Rev. 2014 Apr 3.
9. Hudson M, Fritzler MJ. Diagnostic criteria of systemic sclerosis. J Autoimmun. 2014;48-49:38-41.
10. Matucci-Cerinic M, Kahaleh B, Wigley M. Review: evidence that systemic sclerosis is a vascular disease. Arthritis Rheum. 2013;65:1953-62.
11. Scardina GA, Pisano T, Carini F, Valenza V, Messina P. Burning Mouth Syndrome: An Evaluation of In Vivo Microcirculation. J Am Dent Assoc. 2008;139;940-6.
12. Grassi W, Core P, Carlino G, Blasetti P, Cervini M. Labial capillary microscopy in systemic sclerosis. Ann Rheum Dis. 1993;52:564-9.
13. Manetti M, Guiducci S, Ibba-Manneschi L, Matucci-Cerenic M. Mechanisms in the loss of capillaries in systemic sclerosis: angiogenesis versus vasculogenesis. J Cell Mol Med. 2010;14:1241-54.
14. Lambova S, Müller-Ladner U. Capillaroscopic findings in systemic sclerosis -- are they associated with disease duration and presence of digital ulcers? Discov Med. 2011;12:413-8.
15. Wildt M, Wuttge DM, Hesselstrand R, Scheja A. Assessment of capillary density in systemic sclerosis with three different capillaroscopic methods. Clin Exp Rheumatol. 2012;30:S50-4.
16. Sulli A, Pizzorni C, Smith V, Zampogna G, Ravera F, Cutolo M. Timing of transition between capillaroscopic patterns in systemic sclerosis. Arthritis Rheum. 2012;64:821-5.
17. Herrick AL, Cutolo M. Clinical implications from capillaroscopic analysis in patients with raynaud's phenomenon and systemic sclerosis. Arthritis Rheum. 2010;62:2595-604.
18. Smith V1, Decuman S, Sulli A, Bonroy C, Piettte Y, Deschepper E, et al. Do worsening scleroderma capillaroscopic patterns predict future severe organ involvement? a pilot study. Ann Rheum Dis. 2012;71:1636-9.
19. Sebastiani M, Manfredi A, Colaci M. Capillaroscopic skin ulcer risk index: a new prognostic tool for digital skin ulcer development in systemic sclerosis patients. Arthritis Rheum. 2009;61:688-94.
20. Corrado A, Carpagnano GE, Gaudio A, Foschino-Barbaro MP, Cantatore FP. Nailfold capillaroscopic findings in systemic sclerosis related lung fibrosis and in idiopathic lung fibrosis. Joint Bone Spine. 2010;77:570-4.
21. Kayser C, Sekiyama JY, Próspero LC, Camargo CZ, Andrade LE. Nailfold capillaroscopy abnormalities as predictors of mortality in patients with systemic sclerosis. Clin Exp Rheumatol. 2013;31:103-8
22. Granier F, Vayssairat M, Priollet P,Housset E. Nailfold capillary microscopy in mixed connective tissue disease. Arthritis Rheum. 1986;29:189-95.
23. de Holanda Mafaldo Diógenes A, Bonfá E, Fuller R, Correia Caleiro MT. Capillaroscopy is a dynamic process in mixed connective tissue disease. Lupus. 2007;16;254–8.

DOI: 10.7241/ourd.20144.94

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

GORLIN'S SYNDROME: ATYPICAL CASE REPORT

Sanjay N. Agrawal, Pranita P. Daware, Yogeshree R. Deshmukh , Subodhkumar Jane

Department of Dermatology, Dr. Panjabrao Deshmukh Memorial Medical College, Amravati-444603, Maharashtra, India

Source of Support: Nil
Competing Interests: None

Corresponding author: Dr Yogeshree R. Deshmukh dr.yogeshree@gmail.com

Our Dermatol Online. 2014; 5(4): 378-380 Date of submission: 07.06.2014 / acceptance: 30.07.2014

Abstract
Gorlin syndrome or basal cell nevus syndrome (BCNS) is a rare autosomal dominant disorder. The condition appears to have complete penetrance and variable expressivity, which makes clinilcal presentation among families variable. All known BCNS carry mutations in PATCHED gene. A 65 years old male patient presented with complaints of characteristic skin lesions on his face, back, palms since early adulthood. The lesions were pigmented nodules with characteristic border. The histopathology showed characteristic features suggestive of Basal Cell Carcinoma (BCC). This case was atypical due to appearance of lesions quite later in life.

Key words: Gorlin's Syndrome; Basal Cell Carcinoma; skin carcinoma

Cite this article:
Agrawal SN, Daware PP, Deshmukh YR, Jane S. Gorlin's syndrome: Atypical case report. Our Dermatol Online. 2014; 5(4): 378-380.

Introduction

The name 'Gorlin' is associated with many genodermatosis like 'Gorlin Sign' in Ehler Danlos syndrome and Goltz-Gorlin syndrome of focal dermal hypoplasia and Gorlin syndrome. Gorlin Syndrome is also known as Basal Cell Nevus Syndrome (BCNS) or Nevoid Basal Cell Carcinoma Syndrome (NBCCS). It is an autosomal dominant genodermatosis characterised mainly by the presence of multiple basal cell carcinoma (BCC), jaw cysts and palmoplantar pits [1-3]. We would like to report an atypical case of Gorlin syndrome presented late in life.

Case Report

A 65 years old male patient presented with complaints of skin lesions on his face, back, palms since early adulthood. These lesions were insidious in onset and gradually increased in size. On dermatological examination six well defined, pigmented, non-tender nodules with raised and pearly border were seen on face (Fig. 1). A single ulcer of 2 x 3 cm with erythematous base and rolled borders was seen on right temporal region (Fig. 2). Multiple pits were present on both palms (Fig. 3). His hairs, nails and mucosa were normal. X-ray chest revealed bifid cervical rib and x-ray skull revealed falx cerebri calcification (Figs 4A and B). Dental examination was normal. On physical examination frontal bossing, kyphosis was present. Ophthalmic examination was normal. Other systemic examination were within normal limits. Routine laboratory investigations were within normal limits. With the characteristic morphology and other associated features, a clinical diagnosis of BCC was made. The biopsy from lesion on back was consistent with BCC.

This case was atypical due to appearance of multiple basal cell carcinoma quite later in life as compared to general appearance of lesions since early childhood or birth.

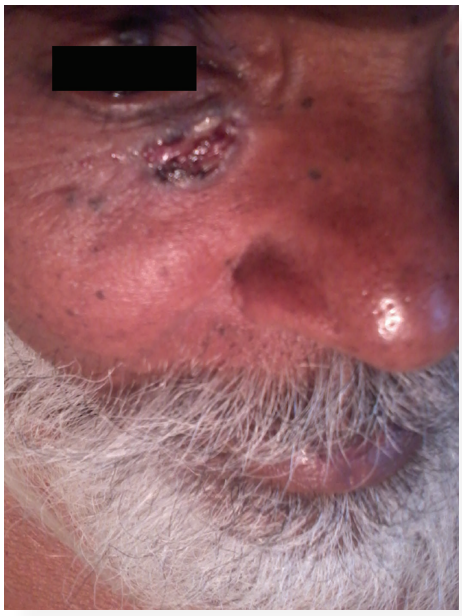


Figure 1. Well defined, pigmented, non-tender nodules with raised and pearly border were seen on face.

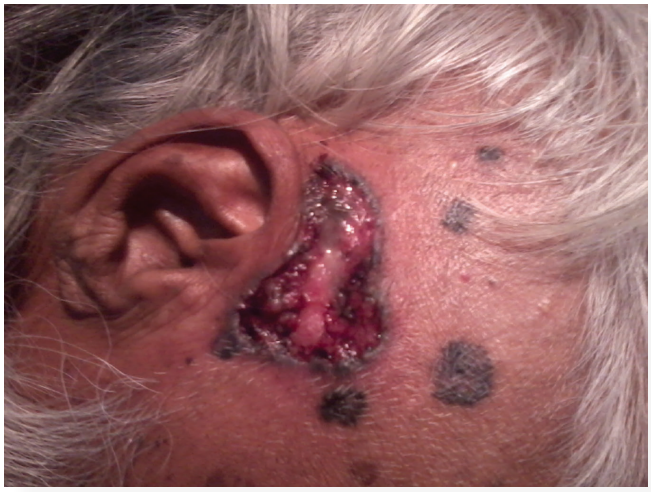


Figure 2. Single ulcer of 2 x 3 cm with erythematous base and rolled borders was seen on right temporal region.

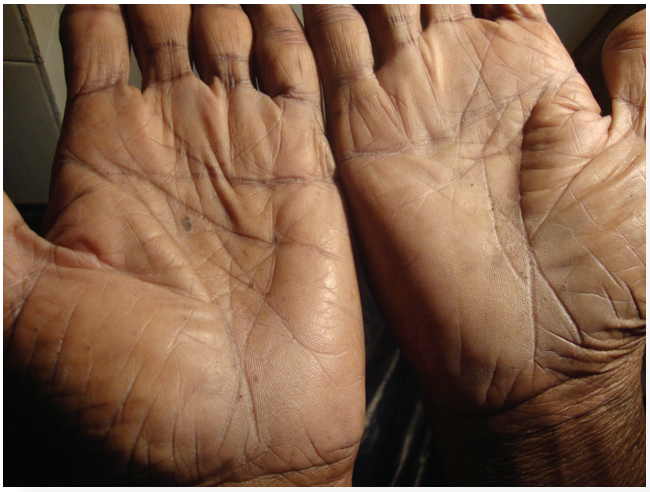


Figure 3. Multiple pits over both palms.

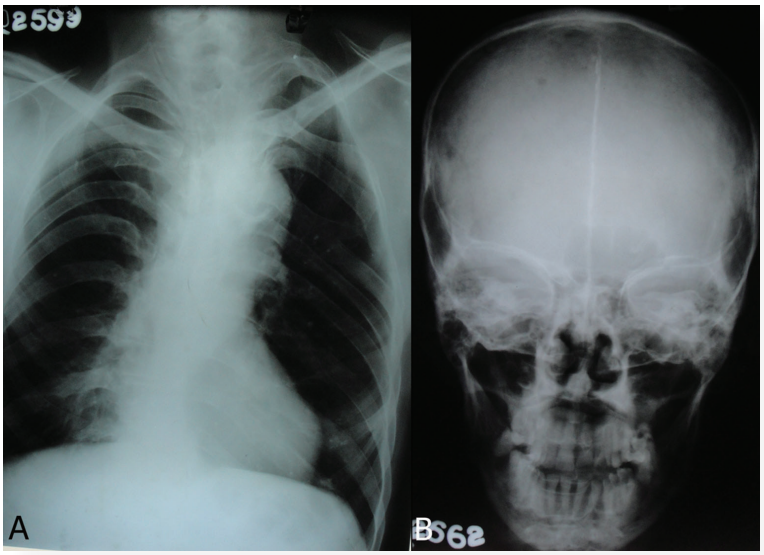


Figure 4 A and B. X-ray chest revealed bifid cervical rib and x-ray skull revealed falx cerebri calcification.

Discussion

Gorlin syndrome or basal cell nevus syndrome (BCNS) is a rare autosomal dominant disorder. Prevalence of BCNS is estimated to be 1 in 60,000 to 1 in 1,20,000 [4]. In different studies, this condition appears to have complete penetrance and variable expressivity, which makes the clinical presentation among families variable. All known BCNS carry mutations in PATCHED gene. The diagnostic criteria for BCNS was put forth by Evans and Collegues and modified by Kimoni in 1997 [4,5,7]. Accordingly, diagnosis of Gorlins syndrome could be established when two major or one major with two minor criteria are present as described below.

Major criteria:

1) BCC before age of 30 or more than 2 BCC.
2) Odontogenic keratocyst before 15 years of age.
3) 3 or more palmar or plantar pits.
4) Falx cerebri calcification.
5) Rib anomaly.
6) First degree relative affected.
7) PTC gene mutation.

Minor criteria:

1) Macrocephaly.
2) Congenital malformations - cleft lip, cleft palate, frontal bossing , hypertelorism.
3) Skeletal deformity – kyphosis, scoliosis.
4) Radiological abnormality – bridging of sella tursica, rib anomaly, Hemivertebra.
5) Ovarian fibroma.
6) Medulloblastoma.

Our patient has four major with two minor criteria which is diagnostic of Gorlin's Syndrome.

The management includes multidisciplinary approach. If the lesions are limited then surgery is indicated. Other treatment modalities include topical imiquimod 5%, laser ablation and strict avoidance of sun exposure. Oral isotretinoin at doses of 0.5-1mg/kg/day may cause regression of lesions of less than 1cm and may prevent new lesions [8]. High doses of retinoids were not effective and were associated with toxicity [4].

Early diagnosis and treatment is important to prevent long term complications of this syndrome that include malignancy, oromaxillofacial deformation and destruction. Aggressive BCC causes death of the patient as a result of tumour invasion to brain or other vital structures and medulloblastoma associated with syndrome causes death during infacy [6]. Genetic counselling also plays a vital role.

This case is atypical due to appearance of lesions quite later in life.

REFERENCES

1. Gorlin RJ, Vickers RA, Kelln E, Williamson JJ. The multiple basal cell naevi syndrome: Analysis of a syndrome consisting of multiple naevoid basal cell carcinoma, jaw skeletal cyst, skeletal anomalies, medulloblastoma, hyper responsiveness to parathormone. Cancer. 1965;18:89-104.
2. Gorlin RJ. The Naevoid basal cell carcinoma syndrome. Medicine (Baltimore). 1987;66:98-113.
3. Fitzpatrick's Dermatology in General Medicine. 7th ed. USA: McGraw-Hill Companies; 2008.p.1042-3.
4. Lo Muzio L. Nevoid basal cell carcinoma syndrome(Gorlin syndrome). Orphanet J Rare Dis. 2008:32-3.
5. Lo Muzio L, Nocini PE, Savoia A, Consolo U, Procaccini M, et al. Nevoid basal cell carcinoma syndrome:Clinical finding in 37 italian affected individuals. Clin Genet. 1999:55:34-40.
6. Gorlin RJ. Basal cell carcinoma syndrome. Medicine. 1997:66:97-113.
7. Muzio LL, Nocini P, Bucci P, Pannone G, Procaccini M. Early diagnosis of Nevoid basal cell carcinoma syndrome. Am Dent Assoc. 1990:130:669-74.
8. Sanchez-Conejo-Mir J, Camacho F. Nevoid basal cell carcinoma syndrome: Combined etretinate and surgical treatment. J Dermatol Surg Oncol. 1989;15:868-71.

DOI: 10.7241/ourd.20144.95

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

KIKUCHI – FUJIMOTO DISEASE. CASE REPORT AND A BRIEF REVIEW OF THE LITERATURE

Manuel Valdebran, Loryart Marte, Nery Charles-Ramirez, Antonio Giraldez, Ángel Taveras, Juan Pablo Guzman, Manuel Cochon, Fernanda Nanita-Estévez

Instituto Dermatológico y Cirugía de Piel "Dr. Huberto Bogaert Díaz", C/Federico Velásquez, esq. Albert Thomas, Santo Domingo, República Dominican

Corresponding author: Dr Manuel Valdebran *investigacion@valdebran.com*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 381-383 Date of submission: 22.06.2014 / acceptance: 13.08.2014

Abstract
Kikuchi Fujimoto disease (KFD) was first described in Japan in 1972 almost simultaneously by Kikuchi and Fujimoto. It is a rare, self-limiting, benign form of histiocytic necrotizing lymphadenitis, which can be mistaken for tuberculosis, lymphoma or systemic lupus erythematosus. Although the pathogenesis of KFD is not fully understood, infectious and autoimmune etiologies have been proposed. It generally presents as cervical lymphadenopathy with associated systemic signs and symptoms. Definitive diagnosis requires histopathological examination of the affected lymph nodes. There are only few cases described in the literature, as far as we are aware we report the first case of KFD in the Dominican Republic.

Key words: Kikuchi Fujimoto disease; Histiocytic necrotizing lymphadenitis; lupus erythematosus, tuberculosis

Cite this article:
Valdebran M, Marte L, Charles-Ramirez N, Giraldez A, Taveras A, Guzman JP, Cochon M, Nanita-Estévez F. Kikuchi – Fujimoto Disease. Case report and a brief review of the literature. Our Dermatol Online. 2014; 5(4): 381-383.

Introduction

Kikuchi – Fujimoto disease (KFD), also called histiocytic necrotizing lymphadenitis, was first reported in 1972 simultaneously by two Japanese authors, Kikuchi and Fujimoto as a "Lymphadenitis characterized by a focal proliferation of reticular cells accompanied by nuclear debris and phagocytosis" and a "cervical subacute necrotizing lymphadenitis" respectively [1,2]. After its initial publication in Japan this entity was described outside the Asian continent for the first time by Pileri and coworkers that reported a series of cases from West Germany, Iran, Italy, South Korea, and Spain [3]. Many similar cases have subsequently been reported and it is now an entity recognized worldwide.

KFD is a benign disorder, predominantly affecting young women. It generally presents as cervical lymphadenopathy but other involved locations have been reported [4]. It is diagnosed by lymph node biopsy with distinctive features that include histiocytic necrotizing lymphadenitis without granulomas or caseous necrosis. Tuberculosis (TB), sarcoidosis, lymphoma and autoimmune diseases should be excluded [5]. Certain authors have reported association of the disease with autoimmune diseases such as systemic lupus erythematosus (SLE) [6-9].

Case Report

A 40 year-old female visited our institution complaining of cervical and axillar nodules for the past 3 months. On examination tender mobile nodules were found on palpation of right axillar region. Past medical history was positive for axillar nodular adenopathies 6 years before with a biopsy performed reporting granulomatous infiltrate with giant cells and caseous necrosis (Fig. 1). Anti-tuberculosis drug regimen was given for 9 months with resolution of the symptoms. 25 years before patient also presented to our institution with a malar rash and a biopsy consistent with chronic discoid lupus showing spontaneous remission thereafter.

An excisional biopsy of the node was performed by the dermatologic surgery department of our institution which showed a lymph node with an architecture partially effaced by a paracortical expansion with wide areas of apoptotic necrosis and diffuse atypical changes (Figs. 2 - 4). Immunohistochemestry analysis were done with positive markers for CD45, CD20, CD3, CD5 and CD10. Serologic analysis reported positive for the presence of antinuclear antibodies (ANA), other tests that included complete blood count, urianalysis, erythrosedimentation rate were reported within normal limits.

Three months later the patient reported the presence of new nodes in her right breast. An ultrasound of soft tissue was performed reporting three ovoid hypoechogenic images with an echogenic hilus suggestive of necrotized lymphadenopathies.

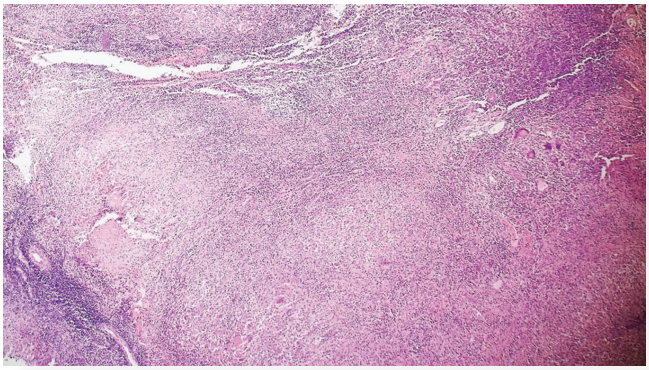


Figure 1. Lymph node with a dense granulomatous infiltrate with foci of caseous necrosis. HE 4X

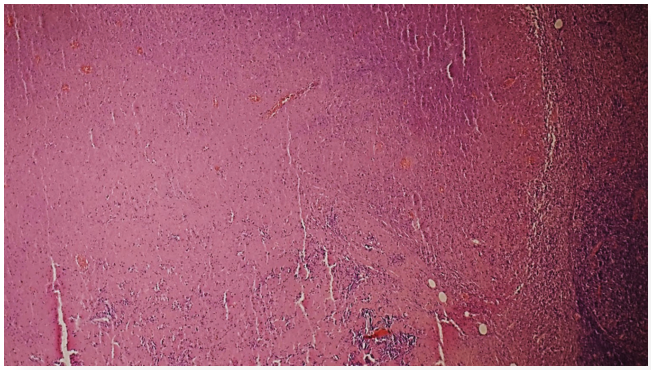


Figure 2. Lymph node with architecture partially effaced by paracortical expansion. HE 4X

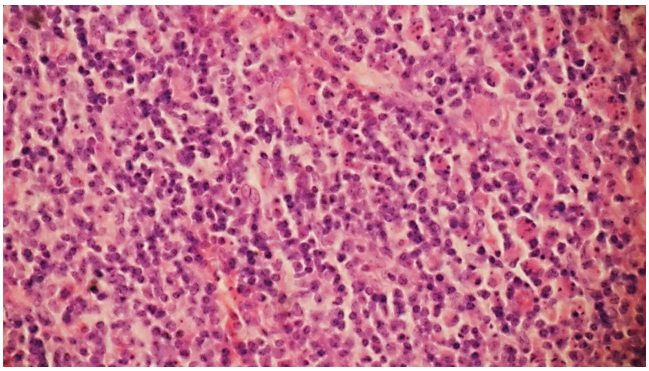


Figure 3. Dense infiltrate constituited by histiocytes, some lymphocytes with augmented nuclei and karyorrhexis. HE 40X

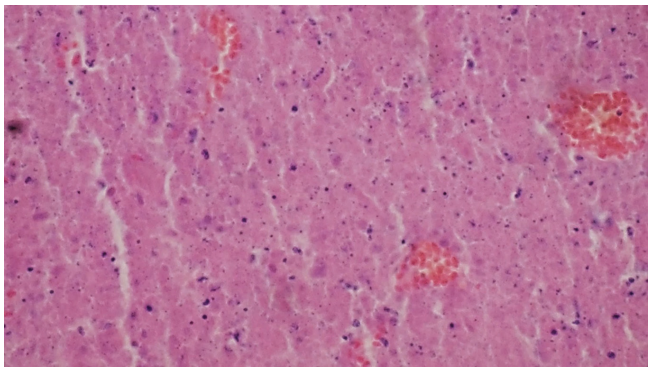


Figure 4. Marked apoptotic necrosis with kariorrhectic debris and dilated and congestive vessels. HE 20X

Discussion

KFD remains an enigmatic condition of unclear etiology with a low prevalence in our geographic area with no reported cases in our country. It is suggested that viral agents, hyperimmune reactions triggered by different antigens and cellular apoptosis are involved in its etiology [10]. Toxoplasma and other bacteria like Yersinia, Bartonella and Brucella have also been implicated as possible triggering agents [11].

The viral hypothesis has been subject of intense research, in fact, it has been emphasized the role of Epstein Barr virus, cytomegalovirus and human herpes virus 6 in eliciting a hyperimmune reaction lead by cytotoxic lymphocytes T towards infected lymphocytes [10,12]. Among the viral antigens listed above, Epstein-Barr virus has been studied most extensively in KFD, but no causal relationship has been demonstrated [13].

Other investigators emphasize the role of immunological mechanisms involved in the pathogenesis of KFD, related with SLE [6-9]. Electron microscopic studies have revealed tubular reticular structures in the cytoplasm of activated lymphocytes and histiocytes in KFD similar of those found in endothelial cells and lymphocytes in patients with SLE [14]. Associations with other autoimmune diseases have been also reported such as Hashimoto's thyroiditis, polymiosytis, mixed connective tissue disease, Still's disease and autoimmune hepatitis [10]. It has been suggested that ANA test should be performed in patients with suspected Kikuchi's syndrome in order to exclude SLE [11].

Clinically the presentation of KFD and TB and SLE may overlap and it may be difficult to segregate them. They may present with fever, upper respiratory sign symptoms, skin rashes, hepatosplenomegaly, weight loss, night sweats, anorexia, diarrhea, vomiting and chest and abdominal pain [15].

Histology and immunohystochemestry studies help to exclude lymphoma. Involved lymph nodes in KFD characteristically demonstrate architecture partially effaced by paracortical expansion composed of circumscribed foci of apoptotic necrosis with abundant karyorrhectic debris and numerous hystiocytes of different types at the edge of necrotic foci [4]. The karyorrhectic foci are formed by different cellular types, predominantly histiocytes and plasmacytoid monocytes but also immunoblasts and small and large lymphocytes. Neutrophils are characteristically absent and plasma cells are either absent or scarce.

Atypia seen in the reactive imunoblastic component is not uncommon and can be mistaken for lymphoma in approximately 30% of patients [4,16].

KFD in the intramammary lymph node is very rare, there has been only one report of involvement in this area [4]. Although not confirmed by biopsy we have ultrasound evidence of necrotic intramammary lymph nodes in our patient. Ultrasonographic features of cervical lymph nodes in KFD have been previously reported. Ying and coworkers described them as hypoechoic, round or oval and tended to have an echogenic hilum and an unsharp border [17]. In our case the breast mass agreed with the findings mentioned above.

In conclusion, we report an unusual case of axillar, intramammary and cervical lymphadenopathy caused by KFD in a patient previously diagnosed with lupus erythematosus and tuberculosis. It is important to differentiate KFD from lymphoma and tuberculosis in an endemic country as ours. Histopathologic findings and immunohystochemical analysis had paramount significance in our case to conclude in a diagnosis.

REFERENCES

1. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytosis. Nippon Ketsueki Gakki Zasshi. 1972;35:379-80.
2. Fujimoto Y, Kozima Y, Yamaguchi K. Cervical subacute necrotizing lymphadenitis: a new clinicopathological entity. Naika. 1972;30:920-7.
3. Pileri S, Kikuchi M, Helbron D, Lennert K. Histiocytic necrotizing lymphadenitis without granulocytic infiltration. Virchows Archives (A) Pathol Anat Histol. 1982;395:257-71.
4. Ohta K, Endo N, Kaizaki Y. Axillary and intramammary lymphadenopathy caused by Kikuchi-Fujimoto disease mimicking malignant lymphoma. Breast Cancer. 2013;20:97-101.
5. Nayak HK, Mohanty PK, Mallick S, Bagchi A. Diagnostic dilemma: Kikuchi's disease or tuberculosis? BMJ Case Rep. 201329;2013.
6. Rao GS, Vohra D, Kuruvilla M. Is Kikuchi-Fujimoto disease a manifestation of systemic lupus erythematosus? Int J Dermatol. 2006;45:454-6.
7. Khanna D, Shrivastava A, Malur PR, Kangle R. Necrotizing lymphadenitis in systemic lupus erythematosus: is it Kikuchi-Fujimoto disease? J Clin Rheumatol. 2010;16:123-4.
8. Gordon JK, Magro C, Lu T, Schneider R, Chiu A, Furman RR, et al. Overlap between systemic lupus erythematosus and Kikuchi Fujimoto disease: a clinical pathology conference held by the Department of Rheumatology at Hospital for Special Surgery. HSS J. 2009;5:169-77.
9. Pace-Asciak P, Black MA, Michel RP, Kost K. Case Series: raising awareness about Kikuchi-Fujimoto disease among otolaryngologists: is it linked to systemic lupus erythematosus? J Otolaryngol Head Neck Surg. 2008;37:782-7.
10. Cellikten A, Metin M, Sayar A, Buyukpinarbasili N, Pekcolaklar A, Citak N, et al. Kikuchi-Fujimoto Disease Presenting with Supraclavicular Lymphadenopathy: A Case Report. Okmeydani Tip Dergisi. 2013;29:44-6.
11. Patra A, Bhattacharya SK. SLE Developing in a Follow-Up Patient of Kikuchi's Disease: A Rare Disorder. J Clin Diagn Res. 2013;7:752–3.
12. Viallard JF, Parrens M, Lazaro E, Caubet O, Pellegrin JL. Subacute necrotizing lymphadenitis or Kikuchi-Fujimoto disease. Presse Med. 2007;36:1683-93.
13. Hutchinson CB, Wang E. Kikuchi-Fujimoto disease. Arch Pathol Lab Med. 2010;134:289-93.
14. Inamura M, Ueno H, Matsuura A, Kamiya H, Suzuki T, Kikuchi K, et al. An ultrastructural study of subacute necrotizing lymphadenitis. Am J Pathol. 1982;107:292-99.
15. Nayak HK, Mohanty PK, Mallick S, Bagchi A. Diagnostic dilemma: Kikuchi's disease or tuberculosis? BMJ Case Rep. 201329;2013.
16. Shafiq S. Cervical lymphadenopathy in a young female: A case report. Int J Med Res Health Sci. 2013;2:666- 8.
17. Ying M, Ahuja AT, Yuen HY. Grey-scale and power Doppler sonography of unusual cervical lymphadenopathy. Ultrasound Med Biol. 2004;30:449-54.

DOI: 10.7241/ourd.20144.96

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

NIMESULIDE INDUCED STEVENS JOHNSON SYNDROME (SJS); MANAGED SUCCESSFULLY WITH COMBINED APPROACH OF STEROIDS, INTRAVENOUS IMMUNOGLOBULIN AND PLACENTREX GEL: A CASE REPORT

Rakesh Tilak Raj[1], Baljinder Kaur[2], Krishan Kumar Lochan[2], Rakesh Kumar Bahl[1]

[1]*Department of Dermatology, Venereology and Leprosy, Government Medical College, Patiala (Punjab), India*
[2]*Department of Paediatrics, Government Medical College and Hospital, Patiala (Punjab), India*

Source of Support: Nil
Competing Interests: None

Corresponding author: Dr Rakesh Tilak Raj *rakeshtraj2012@gmail.com*

Our Dermatol Online. 2014; 5(4): 384-387 Date of submission: 09.07.2014 / acceptance: 13.09.2014

Abstract
There is a high mortality rate in Stevens Johnson Syndrome (SJS) and it ranges between 5%-15%. At present, there is no definite consensus regarding treatment in SJS although the effectiveness of intravenous immunoglobulin's (IVIg) and immunosuppressive like cyclosporine have generated new hopes in the lives of these patients. But the options of combination therapy of steroids, IVIg and Placentrex gel have not been fully exercised in SJS. Henceforth, we report a case of Nimesulide induced SJS; managed successfully with a combined approach without any recurrence during a 12 months follow-up.

Key words: Severe Cutaneous adverse drug reactions (SCAR); Placentrex; Corticosteroids; Immunoglobulin's; SCORTEN Index; Naranjo's ADR probability Scale

Cite this article:
Raj RT, Kaur B, Lochan KK, Bahl RK. Nimesulide induced Stevens Johnson syndrome (SJS); managed successfully with combined approach of steroids, intravenous immunoglobulin and placentrex gel: A case report. Our Dermatol Online. 2014; 5(4): 384-387.

What is known?
· SJS is a fatal, life threatening condition of drug therapy.
· Standardized guidelines regarding treatment are lacking.
· Steroids have a controversial role?
· Different institutions from different countries are adopting different treatment regimens.

Introduction

Stevens-Johnson syndrome (SJS) is a rare and life threatening form of severe cutaneous adverse drug reaction (SCAR) having an unpredictable lethal course in 5-15 % of the cases [1]. The pathogenesis of SJS is unclear and there is no universally accepted definition, but the presence of mucosal involvement and percentage of total body surface area (TBSA) affected can help in classification. Limited skin detachment i.e. epidermolysis (<10% of TBSA) favors SJS whereas widespread involvement (>30%) points towards (TEN) toxic epidermal necrolysis while intermediate cases labeled as SJS/TEN overlap according to Bastuji-Garin et al. [2]. Various etiological factors have been proposed regarding SJS but drugs are the most common cause. Levi et al. confirmed that four groups of drugs were highly suspectable to cause SJS in children < 15 years of age: sulfonamide, phenobarbitone, carbamazepine and lamotrigine [3]. The incidence of SJS in western literature was reported between 1.2-6% cases per million per year and women were more frequently affected than men [4].

In the absence of appropriate literature about the management of SJS in children and there being no established therapeutic guidelines for its management, various treatment modalities such as corticosteroids, thalidomide, pentoxifylline, plasmaphereis, cyclophosphamide, Granulocyte colony stimulating factor (GCS-F), Tissue necrosing factor -alpha (TNF- α) and cyclosporine have been tried [5]. This case report highlights, nimesulide induced SJS in a child who was successfully managed with a combined approach of steroid, IVIg and topical Placentrex gel with no recurrences even after thorough follow-up of one year.

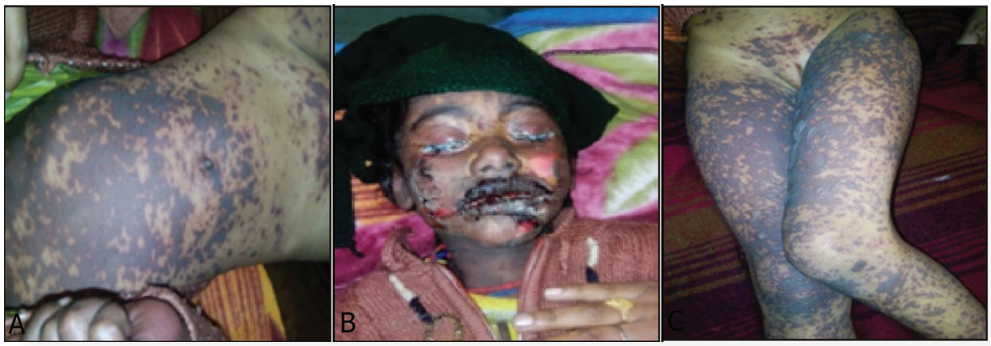
Case Report

A 12 year old girl presented to emergency department of our hospital with the complaints of fever and rash which were intermittent in nature for six days. Those were neither associated with rigor or chills nor with diurnal variations. Patient's mother administered 100mg of oral nimesulide on the advice of private practitioner and after six hours of drug intake, the child started complaining of irritation in her eyes and erythematous rashes over the face. Next morning, the patient's mother noticed swelling of the face and found that the rashes had become atypical, purpuric macular rash which further progressed to involve the neck, chest, back, abdomen, thighs, legs, palms and soles within 24 hours and involved >90% of the body surface area. Oral and genital mucosa was simultaneously affected. These rashes progressed in six days to become vesicular and then bullous purpuric confluents lesions with separation of epidermis over the sites of back, abdomen, thighs and legs (Figs 1A - C). There was no history of any naso-bronchial allergy, diarrhea, upper respiratory tract infection and her past history was also noncontributory regarding any other drug allergy. On examination, she looked ill, febrile and toxic. Her vitals were stable except for tachycardia (pulse>150/min). er oral lesions revealed hemorrhagic crusted lips with difficulty in opening her mouth along with ocular examination showing bilateral congested conjunctiva with matted eyelashes having mucopurulent discharge. Genital examination showed multiple erosions over her vulva with difficulty in micturation. Nikolskys sign was positive and her higher mental functions and other systemic examinations were normal.

Laboratory work up was as under

Complete blood count (CBC) showed Hb-9.4 gm/dl,TLC-10000; DLC (N-78, L-12, E-8, M-2, B-0) and Platelet count- 280,000/ cmm^3. There was mild derangement in liver function tests with SGOT -89 IU/L, SGPT-65 IU/L, RBS 252 mg%, Urine sugar was 4+, 70-80 Red blood cell/high power field. The coagulation profile, Chest X-ray, renal function test, Alkaline Phosphate, Bilirubin, erythrocyte sedimentation rate (ESR), anti-nuclear antibody (ANA), serum electrolytes, serum amylase were within normal limits. Histopathology of skin was denied by the parents of the child. Tzanck smears; skin, blood, urine, fungal and wound culture were negative. Serological studies for herpes, Epstein Barr Virus (EBV), and Cytomegalo Virus (CMV) were negative.

On the basis of history of drug ingestion and clinical features supported by laboratory findings; the case was diagnosed as a Nimesulide induced SJS. Patient was admitted to the intensive care unit (ICU) and all earlier medication was immediately stopped. She was evaluated by SCROTEN index at the time of admission to predict the mortality for the child, that was 3 (pulse rate >120/min, body surface involvement >30%, blood glucose levels as >14 mmol/L) which corresponded to an expected mortality of >35.8%. This case was managed with multidisciplinary approach. Fluid requirements were calculated like burns unit. She received systemic dexamethasone (4-8 mg per day) for first three days which was tapered off gradually and on 3rd day intravenous immunoglobulin's @0.6g/kg/day (dose used was 12g per day) was administered and it continued for four days (total dose used was 48gm). The third generation cephalosporin was added to prevent any super-added infection during the course of disease. Oral and ocular lesions were managed by topical steroids locally. Epidermal wounds were treated on the pattern of burn patients with placentrex gel topically. 10U of plain insulin was administered to control blood glucose levels. On seventh day, patient opened her eyes and her eyelid adhesions were broken by eye surgeon. On 14th day, her lesions regressed, she improved and recovered uneventfully. She was discharged after a stay of 28 days in the hospital with her laboratory reports returning to normal. Regular post SJS follow-ups at the interval of two weeks were normal showing erythema on palms and soles along with hyper and hypo-pigmentation over the involved sites (Figs 2A - C). Oral re-challenge test with Nimesulide was not done on ethical grounds as the potential risk of death outweighs therapeutic benefit. There were no side effects to IVIg, steroid and placentrex gel combination in our patient at the time of discharge with a clear instruction to avoid the culprit drug and after twelve months of follow-up, millia formation were seen on lateral aspects of neck (Fig. 3) along with the persistence of hypo/ hyper pigmentation of the involved sites. No adverse effect related to IVIg was observed in our patient.



Figures 1A - C. Patient at the time of emergency showing atypical purpuric and bullous target lesions on abdomen, thighs, legs, face. neck and lips. There was haemorraghic crusting of the lips and mucopurulent discharge from her eyes.

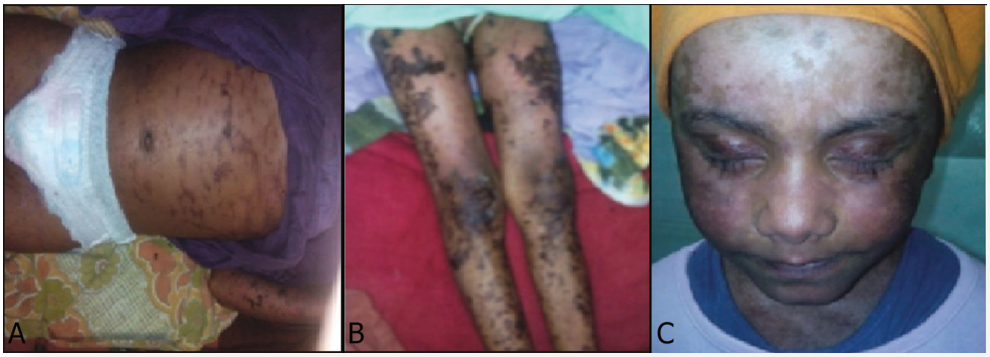


Figure 2A - C. Patient showing hyperpigmentation during recovery phase after the combined approach.

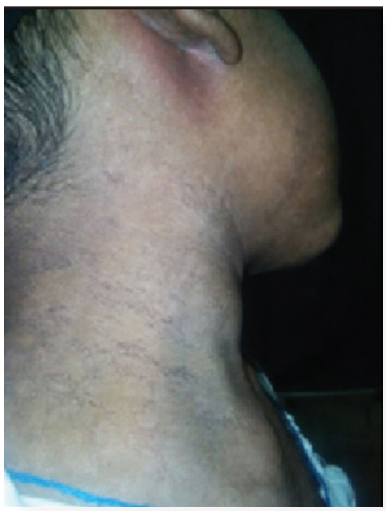


Figure 3. Patient having millia formation over her neck after 6 months of her follow up.

Discussion

The aetiopathogenesis of Stevens Johnson syndrome (SJS) is still unknown and drugs are commonly documented agents involved in its etiology [2]. In India, Nimesulide is easily available as an over the counter drug (OTC). Nimesulide, a selective cyclo-oxygenase inhibitor (COX-2) have been associated with fatal adverse effects due to nimesulide induced hepatotoxicity i.e. 0.1% case per one million cases treated [6] and nimesulide induced SJS has been rarely reported in the literature. Indian government restricted its use in 2011 for paediatric purposes in the age group of less than 12 years [7]. Immunological mechanisms involved in the causation of SJS are by inducing apoptosis of keratinocytes by the releasing cytokines such as IL-6, TNF- α and CD95 system through death receptors (CD 95RL/FasL, CD 95R/Fas). These receptors are a group of glycoproteins within keratinocytes which binds with Fas ligand (Fas-L) initiating apoptosis through caspases leading to DNA disassembly and cell death [8]. Diagnosis of SJS mainly relies on clinico-pathological features and its treatment consists of prompt diagnosis, discontinuation of suspected drug, appropriate symptomatic medication, fluid replacement and meticulous wound care. At present, there is no uniform strategy for managing SJS and administration of corticosteroids is considered controversial [9]. Tripathi et al. considered corticosteroids in the management of SJS in 67 patients and found them effective if given early in the disease and gradually tapered off within 72 hrs from the appearance of epidermal lesions [10]. The Rationale for the use of steroids in TEN/SJS is their role in modulation of cytotoxic T-lymphocytes releasing perforin and granzyme B in the destruction of the epithelium as they also inhibit interferon gamma mediated apoptosis[11]. IVIg is a safe and useful method of treatment in children by blocking Fas antibodies in vitro and preventing apoptosis by the formation of Fas -Fas ligand compounds [12]. The effective drug dosages of IVIg range from 0.2 to 2g/kg/day [13,14].

In this context, combination therapy seems an attractive option as they have a synergistic action targeting different pathways of apoptosis active in TEN/SJS [15]. Placentrex is a biogenic stimulator for humoral and cell mediated immunity that prevents relapse of the disease and increases body resistance. Topical human placentrex in this case has been used for its wound healing and immune-modulatory properties by suppressing interleukin-8 (an inflammatory mediator) by glucocorticoid components present in the Placentrex. [16] The aqueous extract of human placenta used as wound healer is a peptide of 7.4 kDa, its size and partial amino acid sequence indicates its similarity to human fibronectin type III. Fibronectin are adhesive mosaic glycoproteins that maintain normal cell morphology, cell migration, homeostasis, thrombosis and wound healing [17].

In this case, the diagnosis of nimesulide induced SJS was based on history, clinical examination and laboratory findings since the parents of the child denied the consent for histopathological examination. To evaluate prognosis in this case, we used SCROTEN disease severity index [18] to predict the mortality of >35.8%. Naranjo's adverse drug reaction probability scale [19] was used to assess the causal relationship between the drug consumed by the patient and the adverse effect she developed later on. The Naranjo's score in this case was 8 suggesting a probable temporal relationship with the drug as no other drug was taken concurrently. We use systemic corticosteroids early in the course (within 72 hours) of the disease to halt possible tissue damage from cytotoxic T-lymphocytes releasing perforin and granzyme B in the destruction of the epithelium to suppress the immune response and then added IVIg to stop Fas-mediated keratinocytes apoptosis. Placentrex was used as a biogenic stimulator for epidermal lesions to increase cell mediated immunity locally thus, acting as a wound healer.

Therefore, this case report lends support to the view that IVIg is safe and effective in Nimesulide induced SJS in children and addition of low dose steroids with topical Placentrex gel resulted in enhanced healing and better survival indicating combined approach to be superior to monotherapy. However, further multicentric, randomized controlled trials are required to validate these findings.

What is new?
· Combined approach with steroid, IVIg and Placentrex may be an answer to management of SJS.
· Use of Placentrex gel in place of topical steroids or topical antibiotics is more effective in healing of epidermal lesions.

Acknowledgement

We gratefully acknowledge the efforts of postgraduate students of paediatrics department for providing round the clock care, monitoring and coordinating with other departments which helped in saving the precious life of this patient.

REFERENCES

1. Ghislain PD,Roujeau JC. Treatment of severe drug reactions: Stevens Johnson Syndrome, toxic epidermal necrolysis and hypersensitivity syndrome. Dermatol Online J. 2002;8:5.
2. Bastuji-Garin S, Rzany, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical Classification of cases of toxic epidermal necrolysis, Steven-Johnson syndrome and Erythema multiforme. Arch Dermatol. 1993;129:92-6.
3. Levi N, Bastuji- Garin S, Mockenhaupt M, Roujeau JC, Flahault A, Kelly JP, et al. Medication at risk factors for Stevens Johnson syndrome and toxic epidermal necrolysis in children: a pooled analysis. Pediatrics. 2009:123:297-304.
4. Roujeau JC1, Kelly JP, Naldi L, Rzany B, Stern RS, Anderson T, et al. Medication use and the risk of Stevens Johnson Syndrome or toxic epidermal necrolysis. N Engl J Med. 1995;333:1600-7.
5. Allanore LV, Housz Oro SI, Chosidow O, Wolkenstein P. French referral centre management of Steven Johnson syndrome/ toxic epidermal necrosis.Review article. Dermatol Sinica. 2013;31:191-5.
6. Chatterjee S, Pal J, Biswas N. Nimesulide induced hepatitis and toxic epidermal necrolysis. J Postgrad Med. 2008;54:150-1.
7. Jaykare S, Mothghare V, Pise H. Nimesulide induced Steven Johnson Syndrome: A Case report. Indian J Med Case Report. 2012;1:1-3.
8. Wehrli P, Viard I, Bullani R, Tschopp J, French LE. Death receptors in cutaneous biology and disease.Review. J Invest Dermatol. 2000;115:141-8.
9. Depew CL. Toxic epidermal necrolysis. Crit care Nurs. Clin North Am. 1991;3:255-67.
10. Tripathi A1, Ditto AM, Grammer LC, Greenberger PA, McGrath KG, Zeiss CR, et al. Corticosteroid therapy in an additional 13 cases of stevens Johnson syndrome: a total series of 67 cases. Allergy Asthma Proc. 2002;21:101-5.
11. Pereira FA, Mudgil AV, Rosmarin DM. Toxic epidermal necrolysis. J Am Acad Dermatol. 2007;56:181-200.
12. Viard I, Wehrli P, Bullani R, Schneider P, Holler N, Salomaon D, et al. Inhibition of toxic epidermo-necrolysis by blockage of CD95 with human intravenous immunoglobulin's. Science. 1998;282:490-3.
13. Dahl MV, Bridges AG. Intravenous immunoglobulin fighting antibodies with antibodies. J Am Acad Dermatol. 2001;45:775-83.
14. Stella M, Cassano P, Ballero D, Clemente A, Giorio G. Toxic epidermal necrolysis treated with intravenous high dose immunoglobulin: our experience. Dermatology. 2001;203:45-9.
15. Jagadeesan S, Sobhana kumari K, Sadanandan SM, Ravindran S, Divakaran MV, Skaria L, et al. Low dose intravenous immunoglobulins and steroids in toxic epidermo necrolysis. A prospective comparative open-labelled study of 38 cases. Indian J Dermatol Venereol Leprol. 2013;79:506-11.
16. Rosen T, Krikun G, Ma Y, Wang EY, Lockwood CJ, Guller S. Chronic antagonism of nuclear factor- kappa B activity in cytoblasts by dexamethsone: a potential mechanism for anti-inflammatory action of glucocorticoids in human placenta. J Clin Endocrinol Metab. 1998; 83:3647-52.
17. Chakraborty PD, Bhattacharya D. Isolation of fibronectin type III like peptide from human placental extract used as wound healer. J Chromotogr B Analyt Technol Biomed Life Sci. 2005;818:67-73.
18. Bastuji-Garin S, Fouchard N, Bertocchi M, Roujeau JC, Wolkenstein P. SCORTEN: a severity-of-illness score for toxic epidermal necrosis. J Invest Dermatol. 2000;115:149-53.
19. Naranjo CA, Busto U, Sellers BM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239-45.

DOI: 10.7241/ourd.20144.97

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

BECKER'S NEVUS AND IPSILATERAL ACANTHOSIS NIGRICANS

Vijay Zawar[1], Tarang Goyal[2], Sneha Kamra[3]

[1]*Department of Dermatology, Godavari foundation medical College, DUPMC, Maharashtra, India*
[2]*Department of DVL, Muzaffarnagar Medical College & Hospital, Uttar Pradesh, India*
[3]*Consultant Dermatologist, Bhopal, Madhya Pradesh, India*

Corresponding author: Prof. Tarang Goyal tarang_derma@yahoo.co.in

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 388-390 Date of submission: 29.06.2014 / acceptance: 04.09.2014

Abstract
There is paucity in world literature regarding the simultaneous occurrence of Becker's nevus and ipsilateral acanthosis nigricans in the same individual. There is only case reported previously in world literature. We speculate that our case may further strengthen the view of probable, more than a chance, association of these two entities and suggest need for further exploration of the role of androgen receptors in such cases.

Key words: Beckers nevus; ipsilateral acanthosis nigricans; hypoplasia of breast

Cite this article:
Zawar V, Goyal T, Kamra S. Becker's nevus and ipsilateral acanthosis nigricans. Our Dermatol Online. 2014; 5(4): 388-390.

Introduction

The case of ipsilateral Beckers nevus and acanthosis nigricans is presented here for the extreme rarity of a distinct morphological presentation of two different pigmentary disorders in the same patient. Various theories have been proposed for the simultaneous co-existance of the same with hormone dependant theory being the most plausible explanation.

Case Report

A 15-years-old healthy boy presented with asymptomatic gradually progressing brownish-black pigmentation on left side of anterior chest since last 4 years. On examination, a well-defined, large hyperpigmented macule with irregular borders starting from the midline on the left side involving mammary area, extending superiorly upto left infra-clavicular area and anterior left shoulder and also seen involving the antero-medial side of left arm. There was slight extension even on the right parasternal area. There was coarse hypertrichosis in the sternal area as well as acneiform lesions present within the pigmented area (Fig. 1). This clinically was clearly a Becker's nevus. On more careful examination, he interestingly, had an ipsilateral smooth velvety irregular hyperkeratotic plaque with skin tags in the left axillary region. The right side of axilla was normal. The hair in left axilla were much enlarged, pigmented and coarser than the ones in the right axilla. The pigmented lesion in left axilla was clinically suggestive of acanthosis nigricans (Fig. 2). Additional findings noted on clinical examination were hypoplasia of only areola of ipsilateral breast, with scoliosis in the lumbar region and interestingly, a marginal elongation and slight overcurvature of the nail of his left index finger (Fig. 3). He was a right handed person. There was no evidence of acanthosis nigricans in other areas as right axilla, neck, groins, periumbilical areas or forehead. He was investigated by a physician for detailed endocrinal evaluation and also by an orthopedician for bony abnormalities, which were said to be insignificant from investigational and treatment point of view. His complete blood count, blood sugar levels, urinalysis, glycosylated haemoglobin level, glucose tolerance test and plasma insulin levels were all normal. His thyroid status was normal. No hormonal abnormalities were clinically suspected and investigated. His X-ray chest and abdomino-pelvic ultrasound were normal. X-ray Spine revealed slight scoliosis in the thoraco-lumbar region. There was no evidence of internal malignancy. Skin biopsy from pigmented area on chest showed mild acanthosis and hyperkeratosis with regular elongation of rete ridges in epidermis with hyperpigmentation in the basal layer confirming BN (Fig. 4).

In axillary area, hyperkeratosis, papillomatosis and acanthosis were seen with increased pigmentation in the basal layer seen, confirming AN. Thus, a clinical diagnosis of Becker's nevus with acanthosis nigricans was confirmed. We councelled the patient regarding BN and prescribed topical Tretinoin cream 0.1% for AN.

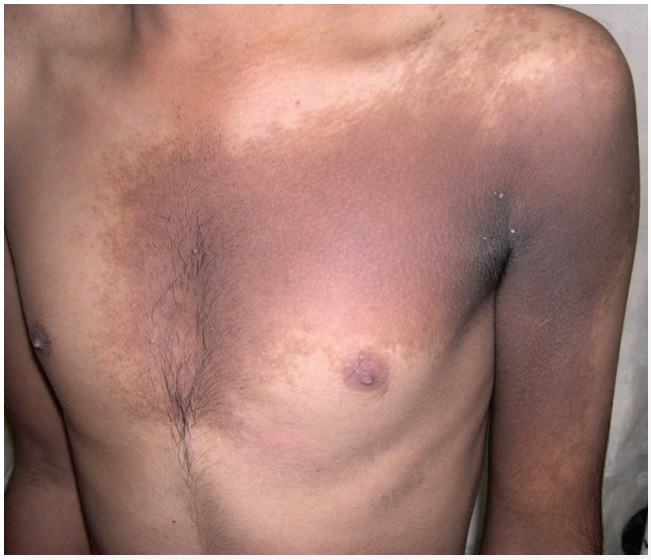


Figure 1. A well defined hyperpigmented macular lesion of Becker's nevus in left mammary area extending on to the anterior shoulder and arm with hypertrichosis and acneiform lesions.

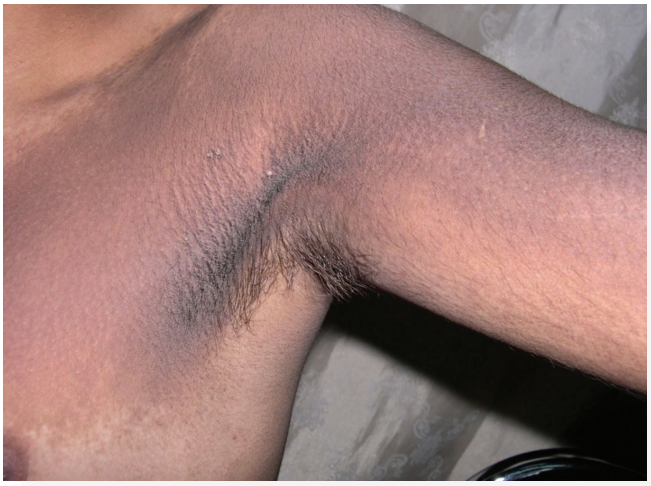


Figure 2. Ipsilateral papillomatous hyperkeratotic plaque in the left axilla with skin tags suggestive of acanthosis nignricans.

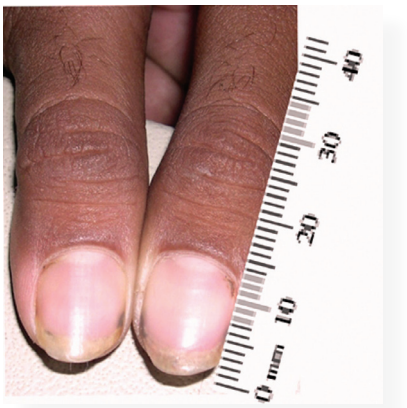


Figure 3. Increased longitudinal curvature and length of left index finger nail.

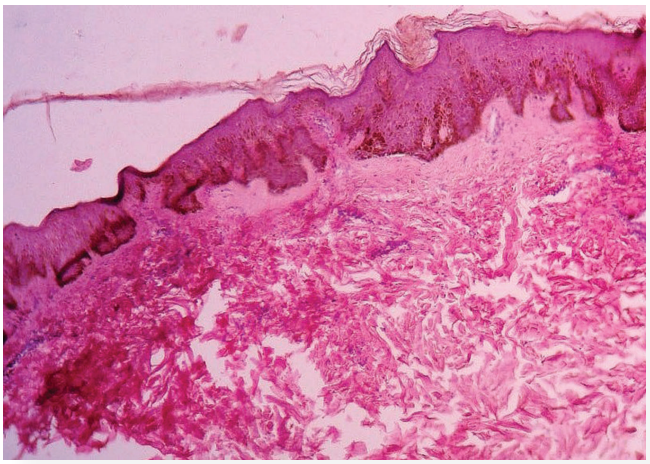


Figure 4. Histopathology showing acanthosis, elongation of rete ridges and hyperpigmentation in basal layer confirming Becker's nevus. H&E (10x10)

Discussion

Becker naevus (BN) was first described by Becker in 1949, as two cases where hypertrichosis and hyperpigmentation occurred on upper back unilaterally [1].Subsequently, term Becker Naevus syndrome [2] was proposed to encompass several developmental anomalies which were found to be associated with BN. Also they made this entity independent from the more generalised term of Hairy Epidermal nevus syndrome [3]. BN is an irregular well defined macular area, which is frequently associated with hypertrichosis and acneiform lesions. The overall incidence being 0.5% in males [4], it is usually more prominent around puberty. It has been postulated to be an ectodermal and mesodermal hamartoma, with increased epidermal (melanocyte), dermal (smooth muscle), and appendageal (hair follicle) components [5]. Some of the associated abnormalities reported are breast hypoplasia, aplasia of underlying pectoralis major, scoliosis, ipsilateral limb shortening, ipsilateral foot enlargement, spina bifida,supernummary nipples, short limbs and segmental odontomaxillary dysplasia. Congenital adrenal hyperplasia, polythelia and accessory scrotum have also been reported [2-6].

Acathosis nigricans (AN) typically presents as symmetric, brown black, velvety, hypertrophic, verrucous, papillomatous plaques most commonly involving the intertriginous sites including axillae, groins, sides of neck. Of the 8 types of AN, unilateral nevoid form is perhaps the rarest form reported [7].

Both sporadic and familial occurrences have been described for AN and it is to be demonstrating a para-dominant inheritance [7,8]. Unilateral Acanthosis nigricans is an extremely rare form of AN that manifests at any age at or before puberty and has a morphologic pattern similar to other forms of AN. It is generally not associated with syndromes, endrocrinopathies, drugs, or malignancies and is said to be inherited as an irregularly autosomal dominant trait that may first become evident at birth, in childhood, or during puberty and extends for a certain period and then either remains stationary or starts regressing [8]. It has a unilateral distribution and the histopathology is similar to the other AN. The differential diagnoses of nevoid AN include confluent and reticulate papillomatosis, Dowling Degos disease, melanocytic nevus and Becker's nevus itself. AN is more hyperpigmented and has raised velvety appaearance than a Becker's nevus.

The regional association between mammary hypoplasia and BN led to the hypothesis of a hormone-dependent disorder. Based on this, increase of the number of androgen-receptors in the affected areas was proved, which explained the appearing of lesions in puberty and alterations such as hypertrichosis and acneiform eruptions restricted to the affected regions. Androgenic sensitivity could also explain the peripubertal manifestation of classic Becker melanosis as well as the association with hypoplasia of the breast and areola in both males and females as this could antagonize estrogenic effects on breast development [9-13].

In our case, ipsilateral association of AN without any family history of Diabetes or AN in a case of BN with acneiform lesions within the nevoid zone, skin tags and hypretrichosis of terminal hairs with darkening compel us to speculate and need to explore underlying androgen sensitivity.

There is paucity in world literature regarding the simultaneous occurrence of these two disorders in the same individual. The only case reported previously being reported by Buck et al and described in detail later by Hulsmans et al [14], where both disorders, BN and AN, had been viewed to be androgen receptors mediated disorders. We were not able to perform androgen receptor studies due to constraint in resources and thus cannot comment on the relation of androgen receptors in our case. However, we speculate that our case may further strengthen the view of probable, more than a chance, association of BN with AN and suggest need for further exploration of the role of androgen receptors in such cases.

The case is presented here for the extreme rarity of a distinct morphological presentation of two different pigmentary disorders in the same patient.

REFERENCES

1. Becker SW. Concurrent melanosis and hypertrichosis in distribution of nevus unis lateris. Arch Dermatol. 1949;60:155-60.
2. Happle R, Koopman RJ. Becker nevus syndrome. Am J Med Genet. 1997;68:357-61.
3. Happle R. Epidermal nevus syndromes. Semin Dermatol.1995;14:111-21.
4. Tymen R, Forestier JF, Boutet B, Colomb D. [Late Becker's nevus. One hundred cases (author's transl)]. Ann Dermatol Venereol. 1981;108:41-6.
5. Chapel TA, Tavafoghi V, Mehregan A, Gagliardi C. Becker's melanosis: An organoid hamartoma. Cutis. 1981;21:405-15.
6. Danarti R, König A, Salhi A, Bittar M, Happle R. Becker's nevus syndrome revisited. J Am Acad Dermatol. 2004;51:965.
7. Schwartz RA. Acanthosis nigricans. J Am Acad Dermatol. 1994;31:1-19; quiz 20–22.
8. Miller JH, Rapini RP, editor Elston D. Acanthosis Nigricans at the URL: http://emedicine.medscape.com/article/1102488, accessed 16th Feb, 2014
9. Grande Sarpa H, Harris R, Hansen CD, Callis Duffin KP, Florell SR, Hadley ML. Androgen receptor expression patterns in Becker's nevi: an immunohistochemical study. J Am Acad Dermatol. 2008;59:834-8.
10. Kim YJ, Han JH, Kang HY, Lee ES, Kim YC. Androgen receptor overexpression in Becker nevus: histopathologic and immunohistochemical analysis. J Cutan Pathol. 2008;35:1121-6.
11. Hoon Jung J, Chan Kim Y, Joon Park H, Woo Cinn Y. Becker's nevus with ipsilateral breast hypoplasia: improvement with spironolactone. J Dermatol. 2003;30:154-6.
12. Formigón M, Alsina MM, Mascaró JM, Rivera F. Becker's nevus and ipsilateral breast hypoplasia--androgen-receptor study in two patients. Arch Dermatol. 1992;128:992-3.
13. Person JR, Longcope Ch. Becker's nevus: an andmgen-mediated hyperptasia with increased androgen receptors. J Am Acad Dermatol. 1984;10:235-8.
14. Hulsman RF, Hulsman FJ. Concomitant Becker's naevus and acanthosis nigricans. Br J Dermatol. 1989;120:716-7.

DOI: 10.7241/ourd.20144.98

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

A COMPLEX IMMUNE RESPONSE IN HALO NEVI CORRELATES WITH IMMUNE REACTIVITY ON INFILTRATED MELANOCYTES, ADJACENT HAIR FOLLICLES AND BLOOD VESSELS

Ana Maria Abreu Velez[1], Vickie M. Brown[2], Michael S. Howard[1]

[1]*Georgia Dermatopathology Associates, Atlanta, Georgia, USA*
[2]*Family Dermatology, Milledgeville, Georgia, USA*

Corresponding author: Ana Maria Abreu Velez, M.D., Ph.D., *abreuvelez@yahoo.com*

Source of Support:
Georgia Dermatopathology Associates, Atlanta, Georgia, USA
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 391-394 Date of submission: 29.07.2014 / acceptance: 10.09.2014

Abstract
Introduction: A clinical "halo nevus" is a benign melanocytic-neoplasm, often exhibiting spontaneous involution. A characteristic clinical feature is depigmentation of the surrounding skin, and a centripetal progression of the tumor regression phenomenon. Case Report: An 18 year old male consulted the dermatologist for changes in color of an asymptomatic mole.
Materials and Methods: A clinical evaluation was performed, and skin biopsies were obtained for hematoxylin and eosin (H&E) review, and for immunohistochemical (IHC) studies including CD3, CD4, CD8, CD20, CD68, CD99, myeloid/histiocyte antigen, S-100, PNL2 and SOX-10.
Results: A neoplastic process was identified on H&E examination, located along the dermal/epidermal junction and within the dermis. The neoplasm was composed of nests, cords and strands of benign melanocytes, with infiltrating lymphocytes. IHC staining demonstrated a strong pattern of positivity with all of the IHC antibodies within, infiltrating and surrounding the primary neoplastic process. In addition, evidence of the primary tumor immune response was noted around surrounding blood vessels and hair follicles, and on adjacent epidermal melanocytes.
Conclusions: In the present study, we demonstrate by histopathologic and immunologic evidence that lymphocytes are primarily responsible for halo nevus tumor regression. Moreover, the immune response involves not only CD8 positive T lymphocytes, but a larger spectrum of B and T lineage lymphocytes. Thus, the immunologic foundations of halo nevus regression are likely of greater complexity than previously determined.

Key words: Halo nevus; CD4; CD8; CD20; CD68; myeloid/histiocyte antigen

Abbreviations and acronyms: Bullous pemphigoid (BP), immunohistochemistry (IHC), direct and indirect immunofluorescence (DIF, IIF), hematoxylin and eosin (H&E).

Cite this article:
Abreu Velez AM, Brown VM, Howard MS. A complex immune response in halo nevi correlates with immune reactivity on infiltrated melanocytes, adjacent hair follicles and blood vessels. Our Dermatol Online. 2014; 5(4): 391-394.

Introduction

A clinical halo nevus, also known as leukoderma acquisitum centrifugum, perinevoid vitiligo and Sutton's nevus is a melanocytic nevus surrounded by a depigmented ring or "halo" [1-5]. The formation of the halo is thought to occur when certain CD8 positive T lymphocytes appear in a lichenoid band below the nevus and destroy the melanocytes. The precise triggers of the CD8 positive lymphocytic attack are undetermined [1-5]. Halo nevi are considered primarily of cosmetic significance; thus, often no treatment is required [1-5]. Although halo nevi seem to be harmless, it is important to monitor these lesions regularly to detect changes in their appearances [1-5]. The current medical literature suggests that if there is a change in appearance, or the halo nevus becomes painful, itchy, or infected, a physician should be consulted [1-5].

Case Report

A 18-year-old male visited the dermatologist, presenting with a 2-week history of a whitening nevus on the back without any other symptoms. Skin biopsies for hematoxylin and eosin (H & E) examination and for immunohistochemical (IHC) studies were performed.

Material and Methods

Our IHC staining was read as positive or negative, in the presence of both negative and positive controls for each marker tested. The readings were performed by an immunodermatologist and were based on the stain positivity of the tumor on 200 and 400X magnification, as previously described [6-8]. The following antibodies were tested: CD3, CD4, CD8, CD20, CD68, CD99, S100, PNL2 (melanocyte specific antigen), myeloid/histiocyte antigen and SOX-10 (a neural crest transcription factor). Staining was performed as previously described [6-8].

Results

Microscopic Description

Review of the hematoxylin and eosin tissue sections demonstrated a melanocytic neoplastic process located along the dermal/epidermal junction and within the dermis. The neoplasm was composed of nests, cords and strands of benign melanocytes. Dermal melanocytic mitotic figures are rare. A band-like, lichenoid infiltrate of lymphocytes and histiocytes was present immediately subjacent to the lesion, and also infiltrating some of the lesional melanocytes (Fig. 1). No dysplastic histologic features are appreciated. The lesion appeared free of the specimen margins in the sections examined.

IHC staining

A strong infiltrate of CD3 and CD8 positive cells was present in a lichenoid pattern subjacent to and infiltrating the lesional melanocytes; in addition, these markers were noted around selected adjacent dermal blood vessels and around perilesional junctional melanocytes. The CD3 and CD8 positive cell populations had similar patterns and intensity of positivity (Figs 2, 3). CD4 positive cells were also observed, in a similar pattern as the CD3 and CD8 positive cells, but with decreased numbers of positive cells per square millimeter of tissue. CD20 positive cells were appreciated, in a similar pattern as the above patterns; however, these cells were noted in greatly decreased numbers relative to CD3, CD4 and CD8. CD68 positive cells were noted infiltrating lesional melanocytes. S100 positive staining was noted on melanocytes, and on Langerhans antigen presenting cells. PNL2 and SOX-10 positive staining was noted on melanocytes. We also noted CD99 positive cells in similar locations as the T cells. Specifically, CD99 staining was noted around the primary melanocytic nevus and on hair follicular units, both in the isthmus and around hair follicle bulb melanocyte. Myeloid/histoid antigen staining was positive around the primary nevus, and on adjacent hair follicle isthmus areas.

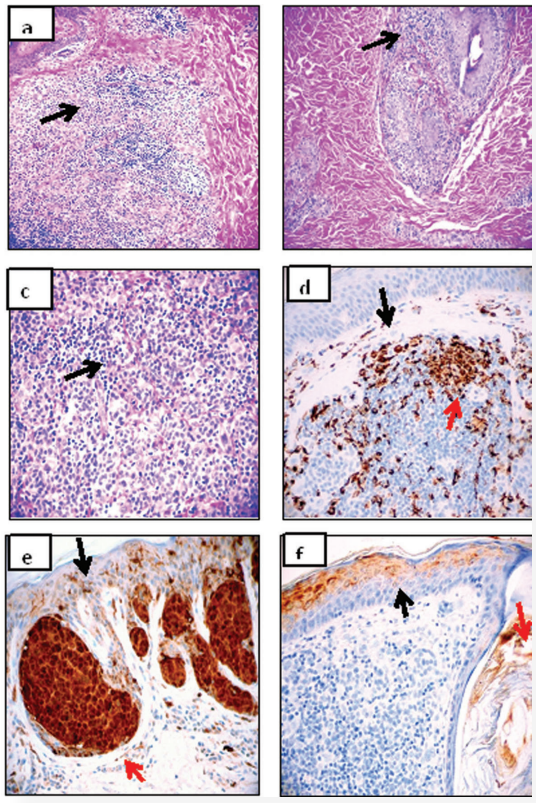


Figure 1. a, H&E stain showing a mixed population of melanocytes, lymphocytes and histiocytes in the halo nevus (black arrow) (40x). **b.** A detail showing that the lymphocytes and histiocytes approach an adjacent hair follicular unit (black arrow)(200x). **c.** Similar to **a**, but at higher magnification (black arrow)(400x). **d.** IHC stain showing CD68 positive cells both in the dermis below the halo nevus (black arrow), and within the halo (red arrow)(brown staining, 200x). **e.** IHC, demonstrating positive S-100 staining in the halo nevus melanocytes (red arrow) and above the nevus, scattered in the epidermis(black arrow)(brown staining) (200x). **f.** IHC stain, showing positivity with myeloid/histoid antigen antibody above the halo nevus in the epidermis (diffuse brown staining; black arrow) and in the hair isthmus (red arrow)(200x).

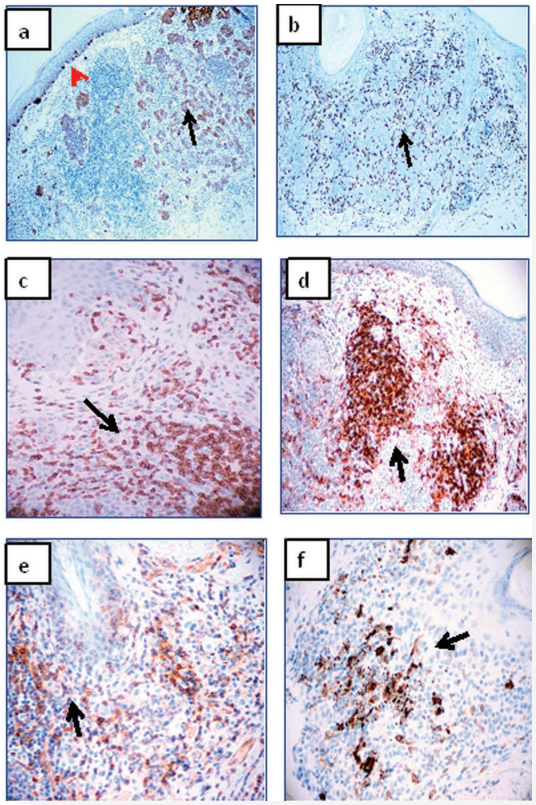


Figure 2. a, Positive IHC staining with PNL2 (black arrow; brown staining). The red arrow highlights staining at the basement membrane zone (100x). **b**. Positive IHC staining with CD68(black arrow; brown staining)(200x). **c.** Positive IHC staining with CD3 (black arrow; brown staining)(200x). **d.** Positive IHC staining with CD4 (black arrow; brown staining) (200x). **e.** Positive IHC staining with CD99 (black arrow; brown staining) (200x). **f.** Positive IHC staining with CD20 (black arrow; brown staining)(200x).

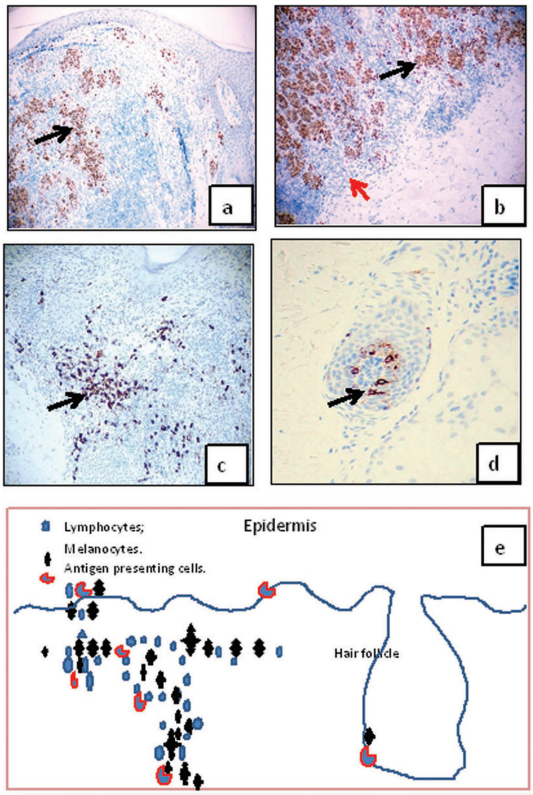


Figure 3. a. Positive IHC staining with SOX-10 on halo nevus melanocytes (brown staining, black arrow) (40x). **b.** Same SOX-10 IHC staining at the lower edge of the halo nevus, showing the nevus cells(black arrow) infiltrating lymphocytes around the edge (red arrow)(200x). **c.** Positive IHC staining with CD20 (brown staining; black arrow). Note these B lymphocytes are not as numerous as the T lymphocytes, but present in similar areas within the infiltrate (100x). **d.** Positive PNL2 IHC staining of melanocytes within a hair follicle bulb, adjacent to the halo nevus (black arrow, brown staining)(400x). **e.** A cartoon diagram, summarizing portions of our data and detailing how T lymphocytes and antigen presenting dendritic cells could surround melanocytes within the halo nevus and within adjacent hair follicles.

Discussion

The halo nevus immune response has been previously regarded as an autoimmune process, mediated primarily by CD8 positive T lymphocytes. Specifically, the CD8 positive T cells are thought to mediate a progressive destruction of nevus cells. Halo nevi may be associated with other autoimmune disorders such as vitiligo, Hashimoto's thyroiditis, alopecia areata, celiac disease and atopic dermatitis. It has been previously noted that halo nevi are often detected after intense sun exposure, and especially after sunburns [3,9]. Minimal information is present win the medical literature regarding specifics of the immune response in halo nevi. On review, we found less than 5 citations specifically confirming the CD8 lymphocytic immune response. One report cited the presence of IgM in lesional skin [10]. Although no direct demonstration of melanocyte destruction has been observed by specific immune effector cells found within the halo, the 1) abundance of antigen-presenting cells in the regressing nevus and 2) presence of T lymphocytes at the site of depigmentation suggest that these cells also participate in the halo immune response. In our case, we were able to further confirm the presence of CD68 positive and myeloid histoid antigen positive cells in and around the halo nevus. In conjunction with these T lymphocyte, Langerhans cell and non-Langerhans histiocyte populations, substantial evidence points to the involvement of CD8 positive T lymphocytes as end line effectors in the destruction of halo nevus melanocytes [1-4]. The specific triggers of the autoimmune breakdown of tolerance that triggers the migration and the presumed activation of these CD8 positive lymphocytes in the nevus (in the apparent absence of disease) are unknown. Selected authors have performed electron microscopic studies, and reported findings of lymphocyte, monocyte, and plasma cell infiltration of halo nevi followed by vacuolar cytolysis. These findings support the concept of a sustained autoimmune reaction in regressing halo nevi [5].

We observed multiple positive antigen presenting cell markers; these markers were present not only around and between the melanocytes of the halo nevus, but also in proximity to adjacent hair follicular units. These immune response details are, to our knowledge, previously undocumented. We also noted that CD99 (also known as MIC2 or single-chain type-1 glycoprotein) marked positively within the halo nevus cells. CD99 (a glycosylated transmembrane protein expressed on all leukocytes and most strongly on thymocytes) is believed to augment both T cell adhesion and apoptosis of T cells.

Because we present a single case, we suggest that the immune response in halo nevi is likely not as simple as a solitary, cytotoxic effect of CD8 positive T lymphocytes on melanocytes. Moreover, we suggest that the other positive markers(and correlating cells) noted in our study do not represent simple epiphenomena. We suggest that these additional cells may not be responsible for the direct destruction of the nevus melanocytes. Further studies are required to confirm and clarify the precise roles of these cells in the overall halo nevus immune response.

REFERENCES

1.Nazzaro G, Rovaris M. The men or women behind nevi: Richard Sutton. JAMA Dermatol. 2014;150:302.

2.Steffen C, Thomas D. The man behind the eponyms: Richard L. Sutton: periadenitis mucosa necrotica recurrens (Sutton's ulcer) and leukoderma acquisitum centrifugum-Sutton's (halo) nevus. Am J Dermatopathol. 2003;25:349-54.

3. Zeff RA, Freitag A, Grin CM, Grant-Kels JM. The immune response in halo nevi. J Am Acad Dermatol. 1997;37:620-24.

4. Pustisek N, Sikanić-Dugić N, Hirsl-Hećej V, Domljan ML. „Halo nevi" and UV radiation. Coll Antropol. 2010;34 Suppl 2:295-7.

5. Jacobs JB, Edelstein LM, Snyder LM, Fortier N. Ultrastructural evidence for destruction in the halo nevus. Cancer Res. 1975;35:352-7.

6. Abreu Velez AM, Howard MS, Pereyo NY, Delman KA, Mihm MC, Rizzo M. Lymphohistiocytic CD45/CD8 immune response in a case of malignant melanoma, with possible cannibalism. North Am J Med Sci. 2012;4:507-9.

7. Abreu Velez AM, Googe PB, Howard MS. Immunohistochemistry versus immunofluoresence in the diagnosis of autoimmune blistering diseases. Our Dermatol Online. 2013;4(Suppl.3):627-30.

8. Abreu Velez AM, Howard MS. Immune reactivity in psoriatic Munro-Saboureau microabscesses, stratum corneum and blood vessels. North Am J Med Sci. 2012;4:257-65.

9. Becker MD, Marcks KM, Trevaskis AE, Heffernan AG, Puchner G. Halo nevus of Sutton. Plast Reconstr Surg. 1966;37:413-5.

10. Tokura Y, Yamanaka K, Wakita H, Kurokawa S, Horiguchi D, Usui A, et al. Halo congenital nevus undergoing spontaneous regression. Involvement of T-cell immunity in involution and presence of circulating anti-nevus cell IgM antibodies. Arch Dermatol. 1994;130:1036-41.

11. Rocchi A, Manara MC, Sciandra M, Zambelli D, Nardi F, Nicoletti G, et al. CD99 inhibits neural differentiation of human Ewing sarcoma cells and thereby contributes to oncogenesis. J Clin Invest. 2010;3:668–80.

DOI: 10.7241/ourd.20144.99

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

XERODERMA PIGMENTOSUM: A BANE IN DEVELOPING COUNTRY - BRIEF REPORT

Hari Kishan Kumar Yadalla, Syeda Juwariya

Department of Dermatology, Raja Rajeswari Medical College & Hospital, Kambipura, Mysore Road, Bangalore, India

Source of Support: Nil
Competing Interests: None

Corresponding author: Assoc. Prof. Hari Kishan Kumar Yadalla *drkishanyadalla@rediffmail.com*

Our Dermatol Online. 2014; 5(4): 395-397 Date of submission: 02.08.2014 / acceptance: 13.09.2014

Abstract
Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder characterized by photosensitivity, cutaneous pigmentary changes, premature skin ageing, and the development of various cutaneous and internal malignancies at an early age. We present this case of a 10 year-old girl in a developing country like India, with significant corneal scarring and multiple cutaneous skin lesions in sun-exposed areas. Developmental delay had been present since 3 months of age, with these clinical features it was consistent with Xeroderma Pigmentosum. We highlight the difficulties encountered due to the lack of diagnostic and treatment modalities for this child, and offer a brief review of XP, including emerging treatments.

Key words: Xeroderma Pigmentosum; Developing countries; Cutaneous lesions

Cite this article:
Yadalla HKK, Juwariya S. Xeroderma Pigmentosum: A Bane in developing country - Brief report. Our Dermatol Online. 2014; 5(4): 395-397.

Introduction

Xeroderma pigmentosum is a rare, genetically heterogeneous, autosomal recessive disorder characterized by photosensitivity, cutaneous pigmentary changes, premature skin ageing, and the development of various cutaneous and internal malignancies at an early age. The basic defect underlying the clinical manifestations is a nucleotide excision repair (NER) defect leading to a defective repair of DNA damaged by ultra violet (UV) radiation [1]. XP is characterized by clinical and cellular hypersensitivity to UV radiation manifesting as intolerance of skin and eyes to light. The skin lesions are comprised of freckles on limbs and face with a dry skin covered with a mixture of mottled, hypopigmented and hyperpigmented, atrophic rounded
and oval macules, giving the entire skin a checkered appearance associated with a generalized actinic keratoses, manifesting on black skin as palpable, rough, blackish spots covered with adherent scales [2,4]. These skin lesions cover both the sun exposed and covered areas. The skin later develops cutaneous malignancies. Ocular changes include photophobia, ocular pigmentary changes, conjunctivitis, corneal keratitis, ulcers, blindness, and malignancies. The diagnosis of XP can be established with studies performed in specialized laboratories. These studies include cellular hypersensitivity to UV radiation and chromosomal breakage studies, complementation studies, and gene sequencing to identify the specific gene complementation group [1-4]. The patient, in our case report, presented with characteristic atrophic, freckled and lentigo skin changes, subnormal intelligence with developmental delay and blurred vision along with the highlighting aspect of delay in medical diagnosis and appropriate treatment.

Case Report

A 10 year-old girl presented to our out-patient department with parental concern regarding progressive skin and ocular lesions. The history was unusual, since the age of 3 months the patient had suffered with persistent developmental delay as well as the appearance of multiple pigmented papular lesions on her face, neck, and forearms. Over time these lesions had enlarged and become progressively more numerous and raised, although were confined to sun-exposed areas. In the last year her mother had noted gradually enlarging corneal lesions bilaterally.
Following normal vaginal delivery at home with no prenatal care, and the development had been limited with low intelligence. Although a generally happy and smiling child. She has 1 normal sibling, and there was no family history or other past medical history of note. The mother denied any consanguinity in the patient's recent lineage.
On examination the patient was smiling and playful, and appeared well-nourished.

There were also numerous hyperpigmented lentigos and freckles with xerosis limited to sun-exposed sites. Few Hyperkeratotic lesions were present on the cheeks and nose with some induration suggestive of actinic keratosis. Marked corneal scarring was evident bilaterally. She had diffuse hyperpigmented lentigos and freckles mixed with hypopigmented macules over the extremeties. (Figs 1 - 2). There was no evidence of anaemia or overt signs of vitamin deficiencies such as rickets, and the mother and siblings appeared well nourished.

Physical examination of the heart, lungs and abdomen was unremarkable. Given the cutaneous, neuro-developmental delay and ocular features a presumptive diagnosis of Xeroderma Pigmentosum was made. A skin biopsy was performed from the cutaneous lesions. Histopathology of skin showed hyperkeratosis and focal thinning of stratum malphigi with atrophy of some of the rete ridges and elongation of others. Dermis is unremarkable. No evidence of malignancy seen (Figs 3 - 4). The clinical features and that of histopathology were those of photosensitive dermatoses suggestive of Xeroderma Pigmentosum.

The patient was referred to ophthalmology and paediatric specialists for further care and was adviced cutaneous photoprotection with judicious use of sunscreens. The patient and parents were educated about the disease and the importance of skin care and was advised for regular follow-up every six months and to report any new skin lesions appearing suspicious.

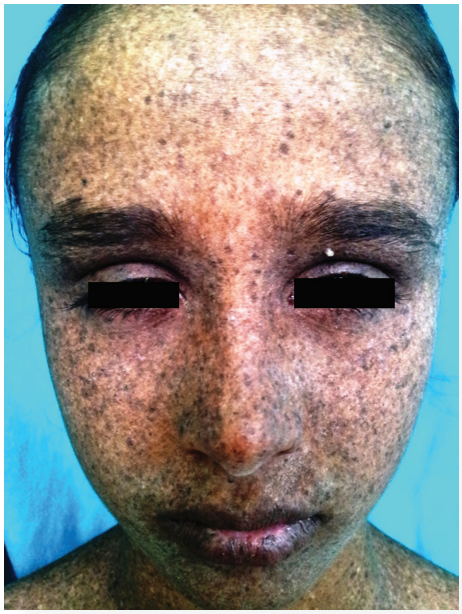


Figure 1. Frontal image of face, showing numerous hyper-pigmented lentigos and freckles with xerosis of the face with diffuse hyperkeratotic lesions. Marked corneal scarring and congestion is evident.

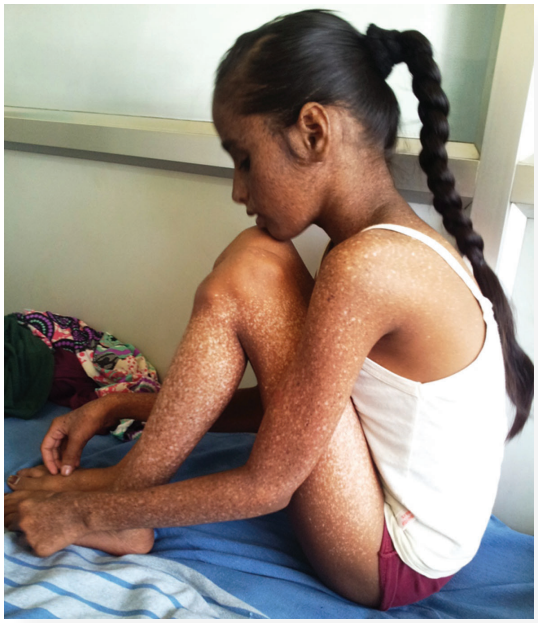


Figure 2. Side view of the child showing diffuse hyperpigmented lentigos and freckles with a mixture of hypopigmented macules over the extremities.

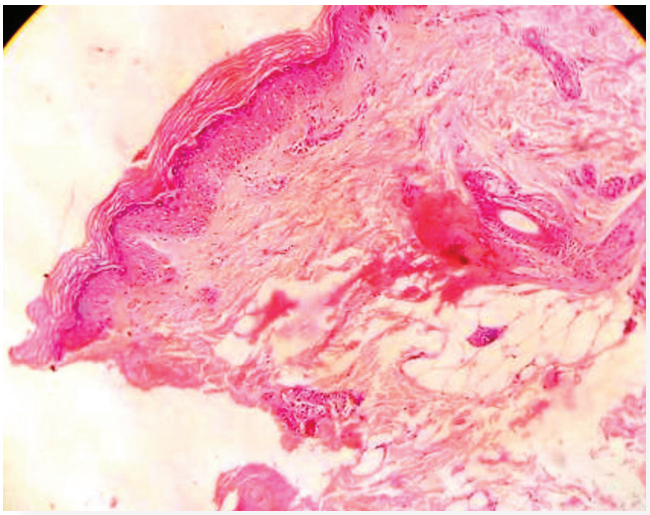


Figure 3. Histopathology of skin under scanner view showing epidermal hyperkeratosis with atrophy of some of the rete ridges and elongation of others. (H&E, 10x)

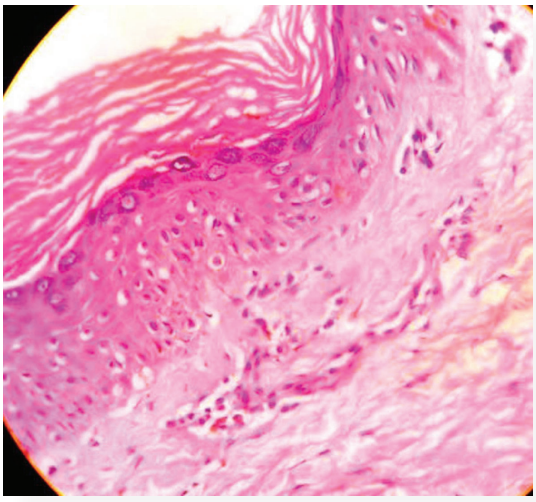


Figure 4. Histopathology of skin under high power view shows hyperkeratosis and focal thinning of stratum malphigi with atrophy of some of the rete ridges and elongation of others. Dermis is unremarkable. No evidence of malignancy seen. (H&E, 40x)

Discussion

Xeroderma Pigmentosum (XP) is a rare genetic disorder that occurs worldwide in all races and ethnic groups. First described by Hebra and Kaposi in 1874, the disorder is characterised by marked photosensitivity and premature onset of all major types of skin cancer [1].

From an early age patients are sensitive to even minimal sun exposure developing erythema, vesicles and oedema. By the age of two years solar lentigos, xerosis and pigmentation occur. Later in childhood dysplastic and neoplastic lesions occur with the development of actinic keratosis, keratocanthoma, basal cell carcinoma, squamous cell carcinoma and malignant melanoma [1]. In one study the median age for development of malignant melanoma was 8 years of age [2]. Ocular complications are nearly as common as skin lesions with keratitis progressing to corneal opacification, loss of eyelashes, ectropion, entropion and benign and malignant lesions of the cornea and eyelids. Neurological complications occur in approximately 30% of cases and can be severe with developmental delay [1,5].

XP is usually inherited in an autosomal recessive manner with phenotypically normal heterozygotes. There are at least seven different subtypes (complementation groups A-G) as well as XP variants. Various rare forms occur in combination with other disorders such as Cockayne's Syndrome [1]. 80% of patients have classical XP where there is a defect in the initiation of DNA nucleotide excision repair after UV induced damage. In XP variant the defect is found in post-replication or daughter-strand repair [4].

The diagnosis of XP is considered when a young patient presents with marked photosensitivity, xerosis and multiple pigmented lesions. Phototesting may be performed showing reduced minimal erythema dose in the 290 to 340 nm range [3]. Although phototesting is widely available in the developed world it is neither sensitive or specific for XP. The diagnostic test of choice is time consuming, highly specialised and expensive: cultured fibroblasts are extracted from a skin biopsy, fused with fibroblasts from known XP lines and exposed to UV irradiation. If the subsequent DNA repair is defective, the XP complementation group may be identified from the fused XP line used. Recent developments include the cloning of all XP genes, so the complementation group can also be determined by using recombinant retroviral vectors [1,2,4].

The treatment of XP is challenging because it is a multi-organ and multi-system disease, and because usually by the time of diagnosis, significant tissue damage has already occurred [1,4]. Malignant tumours may already have developed by the third or fourth year of life [1]. Early diagnosis and immediate implementation of rigorous sun-protection measures may prolong the lives of persons with XP. About two thirds of unmanaged subjects die before the age of 20 years [1,4], but in climates with intense sunlight exposure, children with XP who do not implement sun-protection measures and have limited access to modern medical care, have a life expectancy of about 10 years [6].

Persons with XP must avoid exposure to any sources of UV light including sunlight, fluorescent, halogen and mercury-vapour lights [5], and must wear protective clothing and UV-absorbing eye glasses, and must use high protection factor sunscreens [1]. XP associated cutaneous, ocular and oral lesions and dis-orders should be treated as in any other person. Topical application of 5-fluorouracil or imiquimod is appropriate for premalignant and surgical excision for malignant neoplasms of the skin, tongue, eyelids, conjunctiva and cornea. Methyl cellulose or quinodine-containing eye drops, and bland ointment at night, constitute correct eye-care [7,8]. It must be remembered that persons with XP who are properly protected from sun-light may suffer consequential vitamin D deficiency, and they should routinely take vitamin D supplements [2]. Treatment modalities for XP include Isotretinoin prophylaxis, avoidance of light exposure, surgical excision of pre malignant and malignant tumors, resurfacing with skin grafts, dermabrasion, radiation therapy, and Mohs micrographic surgery [9,10]. Experimental treatments with topical DNA repair enzymes and oral retinoids are showing promise for the future [11,12].

There are particular challenges when a child with XP grows up in a tropical environment as illustrated in this case. The geographical and cultural bars to medical facilities led to a significant delay in diagnosis for this patient. This has resulted in years of photodamage resulting in the patients striking appearance with cutaneous and ocular damage and undoubted limited lifespan. Culturally the patient would have spent most of the day outdoors in the equatorial high UV exposure environment. Even if a medical opinion was sought earlier in life we must consider the lack of specialists and the high cost of the specialized diagnostic tests needed.

REFERENCES

1. Harper JI. Genetics and genodermatoses. In: Champion RH, Burton JL, Burns DA, et al. eds. Rook, Wilkenson, Ebling Text-book of Dermatology. 6th edition. Oxford: Blackwell Science Ltd 1998, pp. 357-436.
2. Kraemer KH, Lee MM, Scotto J. Xeroderma Pigmentosum: cutaneous, ocular and neurological abnormalities in 830 published cases. Arch Dermatol. 1987;123:241-50.
3. Ramsay CA, Giannelli F. The erythemal action spectrum and deoxyribonucleic acid repair synthesis in xeroderma pigmentosum. Br J Dermatol. 1975;92:49-56.
4. Rünger TM, DiGiovanna JJ, Kraemer KH. Hereditary disorders of genome instability and DNA repair. In:Wolff K, Gold-smith LA, Katz SI, et al. Fitzpatrick's dermatology in general medicine. 7th edition. New York: McGraw Hill Co 2008, pp.1311-25.
5. Halpern J, Hopping B, Brostoff JM. Photosensitivity, corneal scaring and developmental delay: Xeroderma pigmentosum in a tropical country. Cases J. 2008;1:254.
6. Cleaver JE, Revet I. Clinical implications of the basic defects in Cockayne syndrome and xeroderma pigmentosum and the DNA lesions responsible for cancer, neurodegeneration and aging. Mech Ageing Develop. 2008;129:492-7.
7. Mahindra P, DiGiovanna JJ, Tamura D, Brahim JS, Hornyak TJ, Stern JB, et al. Skin cancers, blindness, and anterior tongue mass in African brothers. J Am Acad Dermatol. 2008;59:881-6.
8. Goyal JL, Rao VA, Srinivasan R, Agrawal K. Oculocutaneous manifestations in xeroderma pigmentosa. Br J Ophthalmol. 1994;78:295-7.
9. Agrawal K, Veliath AJ, Mishra S, Panda KN. Xeroderma Pigmentosum: Resurfacing Versus Dermabrasion, Br J Plast Surg. 1992;45:311-4.
10. Leal-Khouri S, Hruza GJ, Hruza LL, Martin AG. Management of a Young Patient with Xeroderma Pigmentosum. Pediatr Dermatol. 1994;11:72-5.
11. Kraemer KH, DiGiovanna JJ, Moshell AN, Tarone RE, Peck GL. Prevention of skin cancer in xeroderma Pigmentosum with the use of oral isotretinoin. N Engl J Med. 1988;319:1633-7.
12. Yarosh D, Klein J, O'Connor A, Hawk J, Rafal E, Wolf P. Effects of topically applied T4 endonuclease V in liposomes on skin cancer in xeroderma pigmentosum: a randomised study. Xeroderma pigmentosum study group. Lancet. 2001;357:926-9.

DOI: 10.7241/ourd.20144.100

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

EXOGENOUS OCHRONOSIS MASQUERADING REFRACTORY MELASMA

Swati Sharma[1], Raghavendra Rao[2]

[1]Department of Pathology, Kasturba Medical College, Manipal, Karnataka, India
[2]Department of Dermatology, Kasturba Medical College, Manipal, Karnataka, India

Corresponding author: Ass.Prof. Swati Sharma swatisharma79@yahoo.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 398-400 Date of submission: 15.06.2014 / acceptance: 08.08.2014

Abstract
Exogenous ochronosis is an infrequent dermatosis characterized by dark blue hyperpigmentation. It may be caused largely by hydroquinone, a fenolic compound which is used in the treatment of melasma and other skin hyperpigmentation. The exact etiopathology is still not understood and the results of various treatments offered are unsatisfactory. We present a case of exogenous ochronosis which resembled melasma but clinicopathologic evaluation led to the correct diagnosis. We also emphasize the need to restrict the indiscriminate use of hydroquinone containing compounds without medical prescription.

Key words: ochronosis; hydroquinone; alkaptanuria

Cite this article:
Sharma S, Rao R. Exogenous ochronosis masquerading refractory melasma. Our Dermatol Online. 2014; 5(4):398-400.

Introduction

The term 'ochronosis' was first described by Virchow [1] in 1866 as a brownish-yellow pigment that gets deposited in the connective tissue of various organs. Ochronosis can be endogenous or exogenous in origin. Endogenous ochronosis also called as alkaptonuria is caused by deficiency of the enzyme homogentisic acid oxidase which causes deposition of ochronotic pigments [2]. In contrast, exogenous ochronosis presents as gray-brown or blue-black macules, hyperchromic, pinpoint papules in photo-exposed regions in a symmetrical pattern. It can occur secondary to the topical application of hydroquinone, phenol, resorcinol, or even by oral administration of antimalarials [3].

Case Report

A 47 year old female complaints of black pigmentation over bilateral cheeks for last 6 years which has aggravated for the past 2 years. Symptoms started with redness and gradually progressed to black pigmentation and it gets worsened by sun exposure. Patient has been applying a skin lightening cream over the cheeks for last 7 years on her own without consulting any doctor. For the present symptoms local doctor prescribed topical steroids but her condition did not improve. There was no history of itching, arthralgia, alteration in the colour of urine, hyperpigmentation of sclera, axillae or genitalia. She was started on antidepressants recently. On examination hyperpigmented macules with peripheral erythema was noted at malar area on both the cheeks (Fig. 1). Clinical differentials included pseudo ochronosis, refractory melasma and topical steroid induced telangiectasia. Skin biopsy of the lesion on histopathology revealed acanthotic epidermis overlying dermis showing accumulation of yellow brown pigment causing homogenization and swelling of collagen fibres (Figs 2, 3). A diagnosis of pseudo-ochronosis was given. Patient has been started on sunscreen cream, hydroquinone free and steroid free depigmentating ointments. She is on regular follow up.

Discussion

Exogenous ochronosis was first related by Pick [4] in 1906. Beddard and Plunter [5] described it in a patient using phenol for an ulcer treatment in 1912. However, ochronosis secondary to the use of hydroquinone in topical bleaching agents was first described by Finlay in 1975 [6].

The exact incidence of exogenous ochronosis is unknown due to inability to recognize symptoms at an early stage and inappropriate and indiscriminate use of these topical agents by the patients. It was thought that use of high concentrations of hydroquinone above 4% for a long period of time is responsible for development of exogenous ochronosis. However, recent reports of exogenous ochronosis even in patients using hydroquinone in low concentrations (2%) and for periods as short as 3 months are been described [2,3]

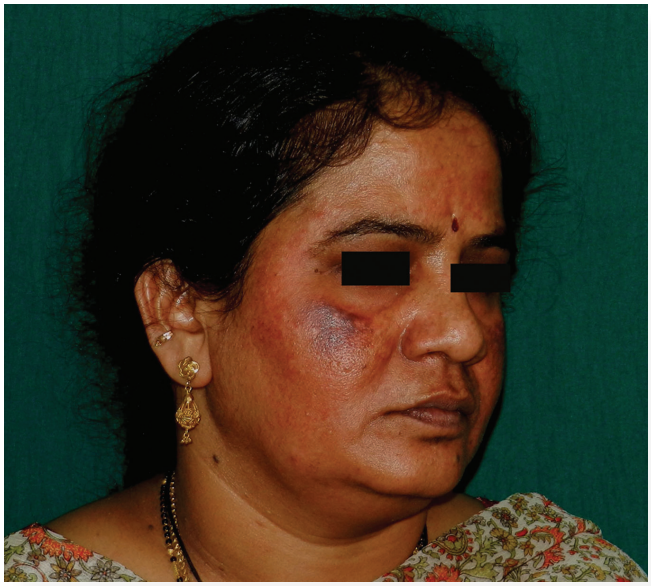


Figure 1. Erythematous plaque on left malar area.

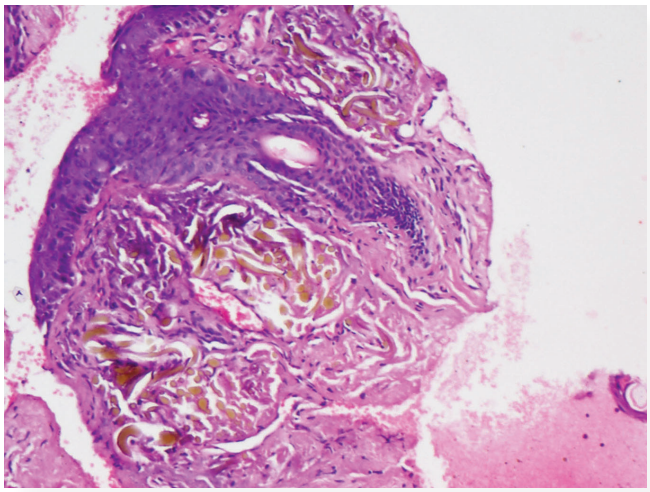


Figure 2. Accumulation of yellow-brown pigment in the dermis. H&E X100

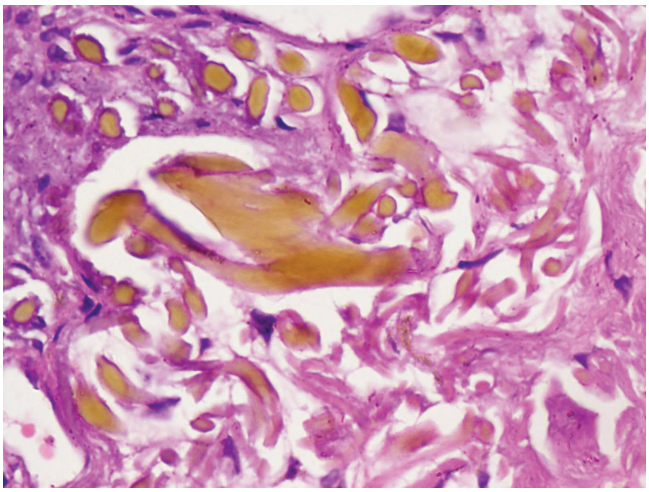


Figure 3. Homogenization and swelling of collagen fibres. H&E X400

The other predisposing factors mentioned in literature include Fitzpatrick's System high phototype, lack of sun protection, skin irritation and vigorous friction [7]. Out of the various theories described the most accepted one is Penneys [8] who attributed the hyperpigmentation due to the inhibition of the enzyme homogentisic acid oxidase by hydroquinone. This leads to the accumulation of homogentisic acid which further polymerizes to form 'ochre' pigment in the dermis. According to Dogliotte and Leibowitz [9] exogenous ochronosis has three clinical stages, first as initial erythema and mild pigmentary change; second hyperpigmentation, black colloid milia, and atrophy; and third as development of papulonodules [3].

Hydroquinone has been used for treating hypermelanosis, senile lentigo, pigmented areas of vitiligo and melasma. It acts by inhibiting production of melanin. Its chronic use causes depigmentation confetti type, exogenous ochronosis, dermatitis, squamous cell carcinoma on the exogenous ochronosis site, reduction of the healing capacity of the skin, pigmentation of sclera and nails and even cataract [2].

Important clinical differential is melasma which can be confirmed on histopathologic examination. Histopathology of ochronosis is characterized by yellow brown, banana-shaped pigment fibers in the dermis in its early stages. As it progresses to the third papulonodular stage, the ochronotic fibers degenerate and form a colloid milium. Some lesions may form sarcoid-like granulomas surrounding the ochronotic fibers [3]. In contrast, melasma shows a significant increase in the amount of melanin in all epidermal layers which can be confirmed in Masson-Fontanna stain.

Pigment incontinence, presence of melanophages and solar elastosis can be seen in both the lesions. Exogenous ochronosis is usually superimposed on the skin affected by melasma. Most importantly there are no ochre fibers in melasma, which is the characteristic finding in ochronosis [10]. Reports of electron microscopy and dermatoscopy differentiation of the two are also well documented [2].

Exogenous ochronosis is refractory to treatment and results are not uniform with the use of topical agents like retinoic acid, azelaic acid, kojic acid; dermabrasion; cryotherapy; laser with CO2, ruby laser Q; sunscreens and corticosteroids. Since the treatment is not easy, hence prevention is very important and suggested. The use of lower concentrations of hydroquinone under medical supervision, sun protection and early diagnosis of symptoms clinically are recommended [2,3,7].

Discussion

Exogenous ochronosis is a rare, cosmetically disfiguring lesion. It usually occurs as a potential side effect of topical use of hydroquinone, which is employed clinically to treat melasma or most of the times self prescribed by the patient as seen in our case. Since this is difficult to treat, it needs early diagnosis and immediate discontinuation of the hydroquinone. One should ensure not to increase its concentration in an attempt to clear the hyperpigmentation. The prescription of hydroquinone for any patient should be accompanied by information of this possible side-effect and also the indiscriminate use of hydroquinone containing compounds without medical prescription should be restricted.

REFERENCES

1. Virchow R. Ein Fall von allegemeiner ochronose der knorpel aud knorpelahnlichen theile. Virchows Arch (Pathol Anat). 1866;37.
2. Ribas J, Schettini APM, Cavalcante MSM. Exogenous ochronosis induced by hydroquinone: report of four cases. An Bras Dermatol. 2010;85:699-703.
3. Mishra SN, Dhurat RS, Deshpande DJ, Nayak CS. Diagnostic utility of dermatoscopy in hydroquinone-inducedexogenous ochronosis. Int J Dermatol. 2013;52:413–17.
4. Pick L. Uber die ochronosis klin. Wochenschr. 1906;43:478-80.
5. Beddard AP, Plumtre CM. A further note on ochronosis associated with carboluria. Q J Med. 1912;5:505-7.
6. Findlay GH, Morrison JG, Simson IW. Exogenous ochronosis and pigmented colloid milium from hydroquinone bleaching creams. Br J Dermatol. 1975;93:613-22.
7. Martins VMR, Sousa ARD, Portela NC, Tigre CAF, Gonçalves LMS, Castro Filho RJL. Exogenous ochronosis: case report and literature review. An Bras Dermatol. 2012;87:633-6.
8. Penneys NS. Ochronosis-like pigmentation from bleaching creams. Arch Dermatol. 1985;121:1239–40.
9. Dogliotti M, Leibowitz M. Granulomatous ochronosis-a cosmetic-induced skin disorder in blacks. S Afr Med J. 1979;56:757-60.
10. Charlin R, Barcaui CB, Kac BK, Soares DB, Rabello-Fonseca R, Azulay-Abulafia L. Hydroquinone-induced exogenous ochronosis: a report of four cases and usefulness of dermoscopy. Int J Dermatol. 2008;47:19–23.

DOI: 10.7241/ourd.20144.101

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

TYPE D LYMPHOMATOID PAPULOSIS: AN UNCOMMON VARIANT. A CASE REPORT AND REVIEW OF THE LITERATURE

Gladys Alejandra Paguaga, Orlando Rodas Pernillo[2], Helga María Sarti[3]

[1]*Graduate of Instituto de Dermatología y Cirugía de Piel, INDERMA, Guatemala, Guatemala*
[2]*Departamento de Patología del Hospital Roosevelt, Patmed, Guatemala, Guatemala*
[3]*Dermatopathology Department, Instituto de Dermatología y Cirugía de Piel, INDERMA, Guatemala, Guatemala*

Corresponding author: Dr Gladys Alejandra Paguaga gladyspaguaga@hotmail.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 401-407 Date of submission: 06.08.2014 / acceptance: 17.09.2014

Abstract
Lymphomatoid papulosis (LyP) is an indolent form of primary cutaneous T-cell lymphoma, currently classified together with primary cutaneous anaplastic large T-cell lymphoma within the spectrum of CD30-positive lymphoproliferative disorders. It is characterized by presenting as a clinically benign but histopathological malignant disease. Clinical features consist in recurrent waxing and waning red papules. Histopathologically, there are 4 variants recognized, Type A or Hystiocitic type, being the most frecuent of all, Type B or Mycosis fungoides-like, Type C or Anaplastic large-cell lymphoma-like and Type D, the most recently described and uncommon variant with features similar to Cutaneous Aggressive CD8-Positive Cytotoxic T-Cell Lymphoma. We present a case of a 22-year-old female with multiple papules and nodules in trunk and limbs that after histopathological and immunochemical examination was compatible with Type D LyP. It is important to report this case, as a perfect example of an uncommon variant of LyP, with emphasis in its typical clinical, histopathological and inmunohistochemical findings and review of the literature.

Key words: type D lymphomatoid papulosis; CD30-positive lymphoproliferative disorder; CD8-positive lymphoproliferative disorder

Cite this article:
Paguaga GA, Pernillo OR, Sarti HM. Type D Lymphomatoid Papulosis: An uncommon Variant. A case report and review of the literature. Our Dermatol Online. 2014; 5(4): 401-407.

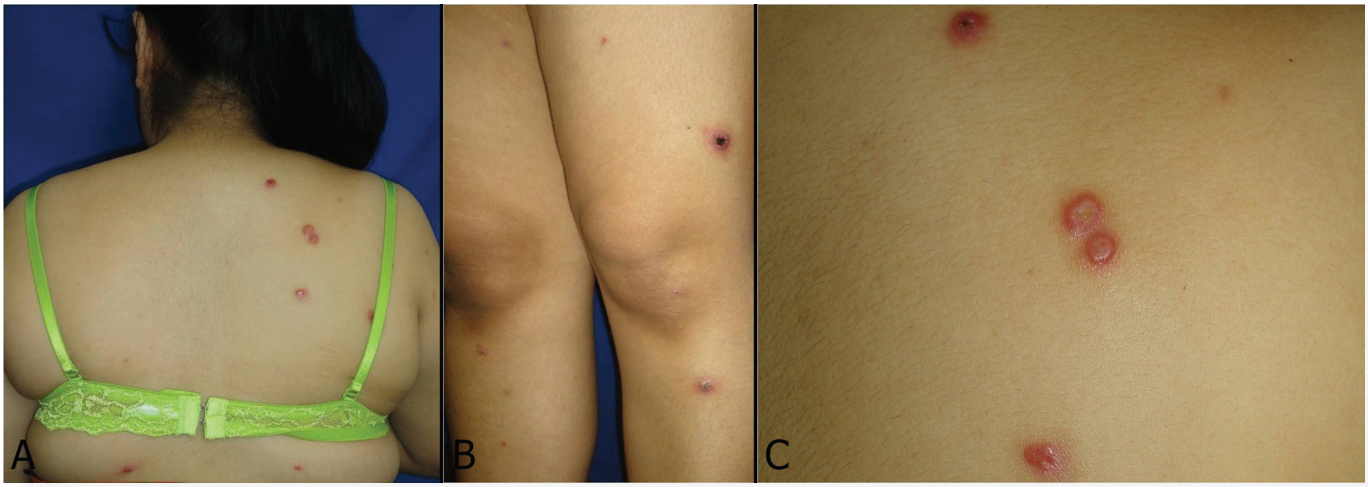
Introduction

Lymphomatoid papulosis (LyP) is considered a cutaneous lymphoid dyscrasia because it manifests a paradoxically indolent clinical course despite cytomorphologic, phenotypic, and molecular features overlapping those of lymphoma. Nevertheless, LyP is recognized as a neoplastic process lying at the benign end of the spectrum of CD30+ lymphoproliferative diseases [1]. Clinically it is defined as a rhythmic paradoxical chronic, recurrent, self-healing eruption of erythematous papules and small nodules, characterized by a waxing and waning course and by histopathologic features of cutaneous T-cell lymphoma [2,3]. Four histologic subtypes of LyP are well recognized: (1) type A, characterized by a mixed infiltrate containing large atypical CD30+ cells admixed with small lymphocytes, histiocytes, neutrophils, and/or eosinophils; (2) type B, with a mycosis fungoides (MF)–like histologic picture; (3) type C, characterized by a more monotonous population of large CD30+ cells, similar to those seen in anaplastic large T-cell lymphoma and (4) type D, the most recently described variant, simulating an aggressive epidermotropic CD8-positive T-cell lymphoma. Unlike a true aggressive epidermotropic CD8-positive T-cell lymphoma type D LyP have a similar clinical presentation and an indolent course as the other variants [4].

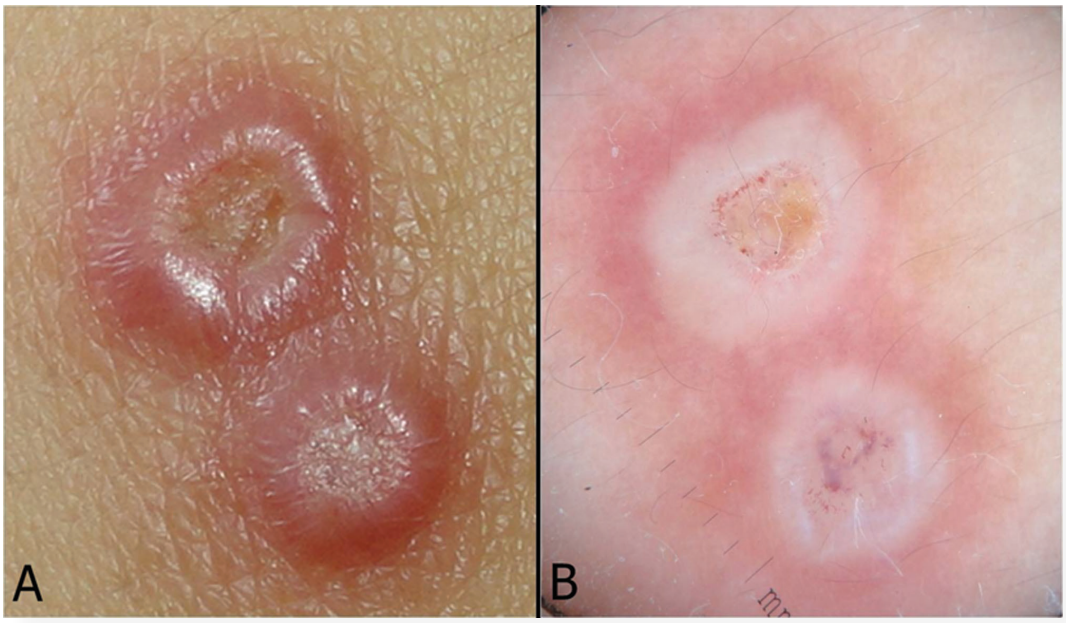
We describe a case of a 22-year old female patient with the newly described type D LyP who presented typical clinical aspects of LyP but unusual histopathologic and inmunohistochemical features with predominant epidermothropism showing CD8 expression on the immunophenotyping study, a phenotype not seen in the three other common variants.

Case Report

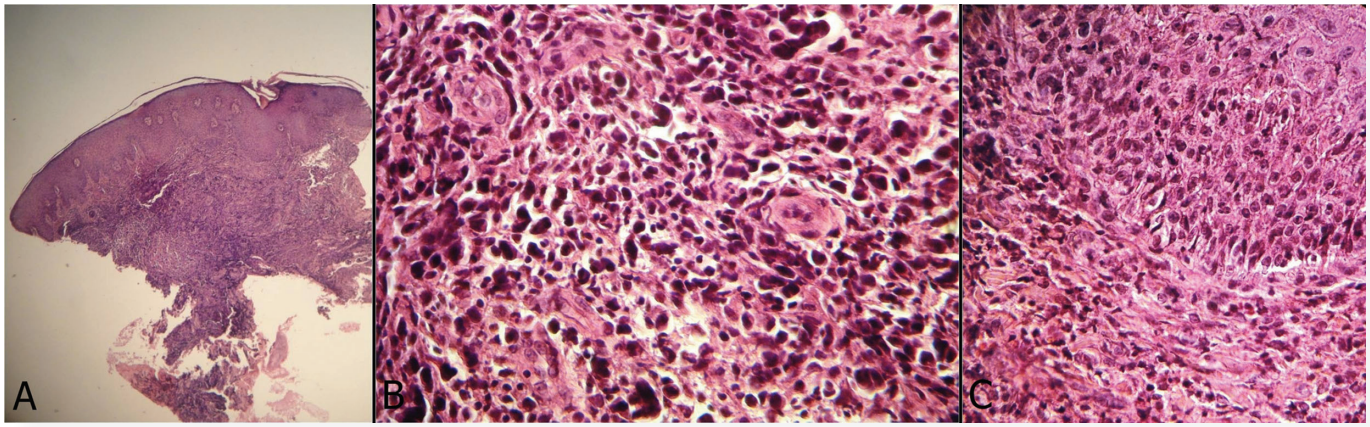
A 22-year-old otherwise healthy female presented with history of multiple self-healing red lesions in trunk and extremities for one month duration. These lesions were associated with mild pruritus. Systemic symptoms were not present. At physical examination we found a polymorphic dermatosis with multiple red papules and nodules, ranging from 0.5 to 2 cm. Some lesions presented central ulceration and others necrotic or serous crusts (Figs 1a - c). The dermatoscopical examination demonstrated thrombosed vessels and serous crusts (Figs 2a - b). Histological examination of a punch biopsy revealed an interesting picture of LyP. The epidermis showed acanthosis and epidermotropism with exocytosis of small lymphocytes. The dermis presented a lymphoid infiltrate in a perivascular and diffuse pattern with cells showing scant cytoplasma and small nuclei with fine cromatine and no atypia. In deep dermis we founded groups of atypical pleomorphic cells with large hypercromatic nuclei arranged in clusters. A few number of atypical mitosis were also seen (Figs 3a - c). A complete inmuhistochemical panel revealed that the malignant infiltrate in deep dermis composed of atypical pleomorphic cells was strongly positive for CD30 (Fig 3d) and partially positive for CD45, but negative for CD3, CD20, anaplastic lymphoma kinase (ALK), epithelial membrane antigen (EMA) and citokeratin. Interestingly, the small T-cells with epidermotropism were strongly positive for CD8 (Fig. 3e) and negative for CD4 and CD3. A complete blood count, urinalysis, HIV, prothrombin and partial thromboplastin time were all within normal limits. With the overall workup of the case we finally concluded that the patient have a newly described type of LyP, known as type D.



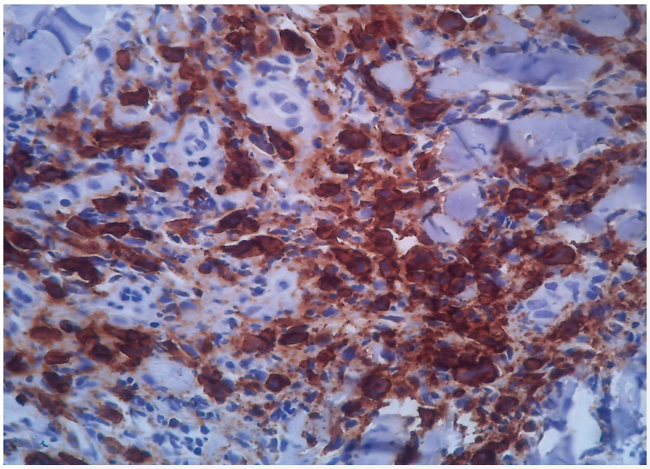
Figures 1A - C. Multiple erythematous papules and nodules in trunk and limbs some ulcerated with necrotic eschar or crust.



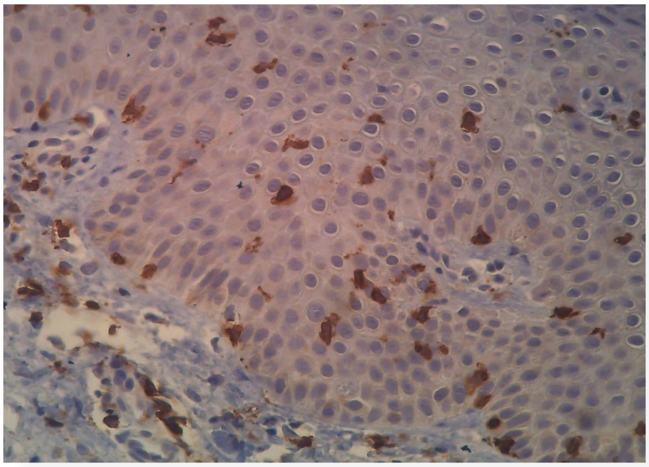
Figures 2A and B. Dermatoscopical features.



Figures 3. (A). Panoramic view. H&E, 4x. (B). Large atypical pleomorphic cells with hyperchromatic nuclei. H&E 40x. (C). Small uniform lymphoid cells wih epidermothropism. H&E 40x



Figures 3D. CD30-positive large atypical pleomorphic cells with hyperchromatic nuclei. 40x



Figures 3E. CD8-positive small uniform lymphoid cells wih epidermothropism. 40x

Discussion

The term lymphomatoid papulosis originally was used by Macaulay in 1968 to describe „a self-healing rhythmical paradoxical eruption, histologically malignant but clinically benign" [5-7]. Before introduction of the term lymphomatoid papulosis, several cases of continuing self-healing eruptions were diagnosed by some authors as a variety of Mucha-Habermann Disease [6]. Even a few decades ago controversy still surrounded this condition. However, the classification system for cutaneous lymphomas has evolved rapidly, and, during consensus meetings in 2003-2004, the World Health Organization—European Organization for Research and Treatment of Cancer (WHO-EORTC) classification grouped lymphomatoid papulosis among the indolent cutaneous T-cell lymphomas within the spectrum of CD30-positive lymphoproliferative disorders. The rationale for classifying lymphomatoid papulosis as a cutaneous lymphoma is its association with other malignant lymphoproliferative disorders; however, even today some experts hesitate to classify this chronic skin disease as a true malignancy because of its spontaneous resolution and benign clinical course considering it as a pseudolymphomatous inflammatory process [1,7,8]. It was not until recently that there were just three histological variants of LyP known (A, B and C). In 2010, Saggini et al described 9 cases of a newly variant simulating an aggressive epidermotropic CD8-positive T-cell lymphoma that became to be known as type D LyP [2,4].

Epidemiology. The CD30+ cutaneous lymphoproliferative disorders account for approximately 25% of cutaneous T-cell lymphoma cases. The prevalence of lymphomatoid papulosis is estimated to be 1.2-1.9 cases per million population [9]. Although LyP occur at all ages, the peak incidence is between the fourth and fifth decades of life, with a median age of 45 years. It has a slightly predominance in males 1.5:1, even though some few studies have reported a female predominance. Black persons may be less affected by LyP than other racial groups [10-13]. LyP rarely presents in childhood, but when it does it present with age of onset of 12 years. The most common histopathologic subtype described for adult and pediatric-onset is type A LyP [8].

Etiology and pathogenesis. Even though in the past, LyP was considered a pseudolymphomatous disorder, nowadays genetic rearrangement studies have demonstrated that it is clearly an authentic cutaneous lymphoma of low grade malignancy, which together with primary cutaneous anaplastic large cell lymphoma (PCALCL) and borderline CD30-positive lesions is included as a part of a spectrum of CD30-positive cutaneous lymphoproliferative disorders.

Borderline CD30 lesions represent cases where histologic features are LyP-like, but clinically behave as lymphoma or cases where histologic features are consistent with PCALCL, but clinically behave as LyP [13,14].

The CD30 antigen is a type I transmembrane glycoprotein with an extracellular domain homologous to tumor necrosis factor and nerve growth factor receptor family members. CD30 is commonly expressed on activated B and T cells [12]. In addition to the CD30+ lymphoproliferative diseases, malignant lymphomas such as Hodgkin disease (HD), node-based systemic anaplastic large cell lymphoma (ALCL), and mycosis fungoides (MF) with large cell transformation may express the CD30 antigen [9,13].

The etiology of LyP remains uncertain [14,15]. Some investigators hypothesized that a retrovirus related to Human T lymphotropic virus-1 may be responsible for the activation and clonal expansion of the LyP cells. Such a virus can be suspected because of the usual adult onset of the disease, cutaneous lesions, and the presence of large, atypical T cells resembling the transformed cells of adult T-cell leukemia/lymphoma. Further research is needed to prove this hypothesis [12]. In the other hand, CD30 signaling is known to have an effect on the growth and survival of lymphoid cells, and one hypothesis is that genetic instability and accumulated genetic defects may have a role in the development of lymphomatoid papulosis and the progression to associated neoplasms [9].

Clinical findings. It presents as a recurrent polymorphic cutaneous eruption characterized by generalized self-healing (within a period of 20 days to 2 months) erythematous asymptomatic to mildly pruritic crops of waxing and waning papules and nodules that are at different developmental stages and progress in recurrent episodes. Some lesions ulcerate and develop a necrotic eschar or crust. Their size varies, but usually do not exceed 2cm [7-10,14-16]. They can be a few or a thousand of them, being in mayority of cases scattered and symmetrically distributed affecting principally trunk and proximal limbs. Mucosal membranes are usually not affected, but there are cases of involvement oral and vulvar mucosa. Unless accompanied by systemic lymphoma, most patients have no constitutional symptoms. Unusual presentations described include localized forms being more frequently seen in children and young adults, pustulous variants, LyP variants affecting the mucosal membranes and hidroa-vacciniforme-like variants [9,11,14,16,17-20]. Lesions heals spontaneously within 2-8 weeks, leaving a hypopigmented or hyperpigmented, depressed, oval, and varioliform scar, especially if the previous lesion was an ulcero-necrotic nodule [9,11,14,21].

Evolving lesions have been described under dermoscopy. The initial papular lesion shows a vascular pattern of tortuous vessels radiating from the center. A white structureless area is seen around the vessels. More mature lesions, hyperkeratotic papules, looked similar except the vascular pattern in the center of the lesion is darker. As the lesions progress to necrotic ulcerations, the vascular pattern is only seen at the periphery, while the center of the lesions presents brownish-gray areas. The final, or cicatricial phase, is similar except no vessel pattern is seen [9].

Histopathological findings. The tipical lesions of LyP present as a wedge infiltrate with a varied number of large atypical cells that can be solitary or clustered [1,11].

Since 2010, there are 4 histological types of LyP well described [2,4,11]. The most common histopathologic subtype of LyP is Type A or hystiocitic type, it represents the prototypic subtype of LyP originally described by Macaulay. It is characterized by a mixed infiltrate containing large, atypical, CD30-positive lymphocytes with bizarre-shaped nuclei, resembling Reed-Sternberg cells from Hodgkin's lymphoma presented in a wedge-shaped distribution throughout the dermis mixed with various numbers of inflammatory cells (small lymphocytes histiocytes, neutrophils and/or eosinophils) and no epidermothropism. Type B or Mycosis Fungoides (MF)-like is less common and is characterized by small, atypical, CD30 lymphocytic cells with hyperchromatic cerebriform nuclei (resembling the lymphocytes known as Sézary cells found in mycosis fungoides) that are distributed in a bandlike pattern, with concomitant epidermotropism (similar to that seen in patch/plaque stage of mycosis fungoides). In addition, type B is probably the most ambiguous histopathologic variant of LyP, as besides the similarities to MF and lack of large anaplastic cells, which are the features that distinguish it from the conventional (type A) variant of LyP, in many cases reported in the past, neoplastic cells lacked CD30 expression too, thus being a source of conceptual confusion and of diagnostic problems. Type C or Anaplastic large-cell lymphoma-like is rarer and consists of a monotonous population of large, atypical, CD30-positive cells diffusely infiltrating the dermis, with fewer associated inflammatory cells than those seen in other types. Type D, simulating an aggressive epidermotropic CD8-positive T-cell lymphoma is characterized by uniform small to medium-sized, CD8-positive lymphocytic cells with pagetoid reticulosis-like epidermothropism and large, atypical, pleomorphic CD30-positive cells distributed in clusters throughout the dermis. Other important features are absence of eosinophils and neutrophils and common vasculitic changes possibly reflective of the concomitant cytokine milieu [1-4,11,22-25].

Inmunohistochemical findings. LyP is characterized immunohistochemically by the presence of large atypical neoplastic cells that present phenotype of activated T- helper cells that express typically CD4+, CD30+ and CD25+. Half of the cases, regardless of the subtype are CD56+. Even though this marker is associated to a poor prognosis in others lymphoproliferative disorders, this is not the case in LyP. Cytotoxic molecules that do not imply a different clinical behavior as Granzime B and Perforin may also be found. In the case of type D LyP, the hallmark feature is the presence of small T-cells with epidermothropism that express CD4+ in addition to the CD30+ neoplastic cells [3,11,26].

Differential diagnosis. LyP should be differentiated first from other conditions that present atypical large cell infiltrate. In the past it was considered that the presence of the CD30 antigen was exclusive of some lymphomas, but nowadays CD30+ has being confirmed in various benign cutaneous conditions. The differential diagnosis of LyP type A from cutaneous CD30-positive anaplastic large cell lymphoma (ALCL) and Hodgkin Disease (HD) can be difficult on both clinical and morphologic grounds. Lymphomatoid papulosis, cutaneous CD30-positive ALCL, and HD belong to the spectrum of primary cutaneous CD30+ lymphoproliferative disorders,and some cases may have similar clinical presentation and histopathologic findings; however, the presence of self-healing papules and nodules is more characteristic of LyP.

In LyP type A the size of the papules and nodules usually does not exceed 2cm, whereas in primary cutaneous CD30-positive ALCL and HD the tumors are usually larger than 2cm and persistent. Morphologically, the anaplastic large cells and RS-like cells that characterized LyP type A may resemble the neoplastic cells that are present in CD30-positive ALCL and HD. The differential diagnosis of LyP from CD30-positive ALCL is based on the number of large, anaplastic, and Reed Sternberg-like cells. In CD30-positive ALCL the atypical cells represent the majority of the cellular infiltrate, whereas in LyP type A the infiltrate contains mostly small, mature lymphocytes and only occasional large, atypical cells. Immunophenotypically, the large, atypical cells of LyP and CD30-positive ALCL have an identical profile: they are positive for CD30 and CD45 and are negative for CD15. The differential diagnosis of LyP type A from HD is based almost exclusively on the immunophenotypic findings: in contrast to LyP, the RS cells of HD are negative for CD45 and positive for CD15 [15,26]. The cases negative for CD30 (LyP type B) should be distinguished from the papular variant of mycosis fungoides. Type C LyP could be difficult to distinguished from anaplastic large cell lymphoma (ALCL), because many times they exhibit clinical, histological and immunochemical overlap [11,24,26]. The differential diagnosis of Type D LyP includes primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (CTCL), mycosis fungoide, pityriasis lichenoides et varioliformis acuta (PLEVA) and pagetoid reticulosis. The cornerstone for distinguishing between these disease entities is the clinic-pathologic correlation. Ultimately, it is the indolent waxing and waning clinical behavior characteristic of LyP that permits this critical distinction to be made.

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (CTCL) unlike LyP is characterized by the rapid onset of patches, plaques, nodules, and tumors frequently exhibiting necrosis and ulceration. The clinical course is aggressive with a median survival of 32 months. Extracutaneous spread to unusual sites including the testes, lung, and central nervous system is a frequent feature. Histologically, it shows characteristically striking epidermotropism of atypical lymphocytes with a CD8+ cytotoxic phenotype, hence bearing many similarities to our case. Most importantly, CD30 is usually negative. A papular variant of MF has been described recently; however, prominent (pagetoid reticulosis-like) epidermotropism is not a feature of this variant of MF, and lesions are stable without the typical spontaneous resolution observed in LyP. In addition, neoplastic lymphocytes in papular MF have always been reported as being CD4+, CD8-, and CD30-. A more difficult differential diagnosis is with PLEVA, as this disorder shares some clinical and histopathologic features with LyP, and most reported cases had a CD8+phenotype. In addition, monoclonal rearrangement of the TCR genes has been observed in a variable proportion (10% to 100%) of cases of PLEVA studied in the past. Finally, cases reported as ‘‘clonal CD30+ PLEVA’’ have further contributed to the existing confusion in this field of dermatology and dermatopathology.

It is quite plausible that at least some among the cases reported in the past as conventional or febrile ulcero-necrotic PLEVA with ‘‘atypical’’ and/or CD30+ lymphocytes may in fact be better classified as the peculiar variant of LyP that we described in this article. In contrast, epidermotropism with a pagetoid reticulosis-like pattern is not a typical feature of PLEVA, and presence of medium sized, atypical, pleomorphic lymphocytes should be considered as virtually ruling out this diagnosis. Another differentiating feature is the absence of necrotic keratinocytes in LyP, in contrast to the apoptotic cells commonly found in PLEVA.

Pagetoid Reticulosis PR (Woringer–Kolopp disease) was also considered based on the histologic findings. It is regarded as a variant of MF in the current classifications. The clinical setting is rather different from LyP, manifesting as solitary or localized scaly or hyperkeratotic plaques with slow growth and indolent behavior, typically involving the extremities. Histologically, it is characterized by striking epidermotropism by atypical pagetoid cells, and the phenotype is frequently CD8+. Unlike LyP, the infiltrate tends to be more superficial and not wedge shaped, and tumor cells tend to be almost exclusively confined to the epidermis. Interestingly, CD30 positivity has also been increasingly reported in PR, and so confident distinction from this variant of LyP based on the immunophenotype alone is not reliable and ultimately depends on clinicopathologic correlation [1-4].

Clinical Course and Prognosis. Patients with LyP have a chronic, indolent, self-healing, recurrent and relapsing clinical course regardless of treatment modalities [9,11]. Spontaneous regression of LyP is seen almost universally and recurrence in crops establish a chronicity that generally last for years, even though most of patients with LyP remain in good health. No clinical or pathological features can predict increased risk for developing malignancy and although it is not an aggressive malignant process, patients with LyP have an increased risk for developing a nonlymphoid tumour or more commonly a lymphoma (10-20%) including mycosis fungoides, Hodgkin’s disease, and cutaneous and systemic CD30+ large-cell lymphoma and 10% of these are associated with extracutaneous involvement [3,9,21,22,27-30].

The prognosis of LyP is characterized by disease-specific 5-year survival rates around 100%. Especially in Type D LyP, this is clearly different from the aggressive clinical course and poor prognosis of other lymphomas that are included in the differential diagnosis of this new variant, particularly the aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma [4].

Treatment. The treatment options proposed are varied, however none of them have proven to be completely effective, causing relapses soon after treatment is suspended. While some authors proposed aggressive therapies based on the increased risk of developing another lymphoproliferative disorder, others disagree based in the concept that treatment modalities wont modified the natural history of LyP [11,31].

Treatment should be individualized. It goes from simple observation to the use of drugs when this is required [22]. Cases with few lesions that resolve without scars do not require active treatment [31]. Patients with LyP need to be educated about their disease. They should be told of its benign clinical nature and that it is not lymphoma. On the other hand, they need to realize that their disease can evolve into lymphoma and that the exact risk is still unknown.

It is very important to inform about the possible changes that might indicate malignancy: persistence of nodules, increased size of lesions, B symptoms, and lymph node enlargement. After a history and physical examination, patients should have the following baseline investigations: complete blood cell count, liver function tests, a roentgenogram of the chest, and a computed tomographic scan of the abdomen.

A bone marrow examination is indicated if the complete blood cell count is abnormal. These investigations can serve as baseline in the event of change and negative results can help reassure the often concerned patient that there is no evidence of lymphoma. Because there is an acumulative risk of transformation into lymphoma these patients need to be examined regularly. At least, an annual examination is indicated, or more frequently depending on the severity of the disease and the type of treatment chosen [32]. Overall is difficult to assess efficacy of the different treatment options because LyP is a self-healing disorder and even though there is no curative treatment, the use of topical steroids, systemic steroids, PUVA, retinoids and methotrexate may induce temporary remissions. The used of low dose oral methotrexate (15-20 mg per week) alone or with PUVA have been reported to induce the best results, causing long remissions after low dose treatments. It has proven safe and effective even in severe cases in which it is well tolerated. A few reports also have found that topical carmustine, topical nitrogen mustard, topical MTX, topical imiquimod cream, intralesional interferon, low-dose cyclophosphamide, chlorambucil, excimer laser therapy, photodynamic therapy, antibiotics as tetracycline, antiviral as acyclovir and dapsone help disease suppression. Surgical excision in cases with few lesions is also reported. Polychemotherapy is not indicated. Overall, treatment in each case should be individualized and risk/benefit ratio of these therapies should be carefully assessed [9,10,14,21,31,33].

Conclision

The diagnosis of LyP can be quite challenging due to the specific histologic features of the disease making misdiagnosing more likely. Moreover, unusual variants like Type D LyP may pose a significant diagnostic problem, especially if immunochemical examination is not available. In this article we describe a case of a newly LyP variant know as Type D in a 22-year old female. We emphasized the importance of the overall workup made; with clinical, dermatoscopical, histological and immunochemical features that support the diagnosis. Since its original description in 2010 until now this recently described variant has rarely been reported so we hope that with our case we can help others get to know this uncommon variant. As others type D LyP cases our patient presented typical clinical aspects of LyP but with unusual histopathologic and inmunohistochemical features, with predominant epidermothropism with CD8 expression on the immunophenotyping study, a phenotype not seen in the other three more common variants. These findings resembled primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, a lymphoma that is characterized by an aggressive course with very poor prognosis. With that said, we believe that recognition of this variant allows correct classification of these cases, since the differentiation of LyP from other lymphoproliferative disorders is crucial for proper management of the patients.

REFERENCES

1. Magro C, Crowson N, Morrison C, Merati K, Porcu P, Wright E. CD8+ lymphomatoid papulosis and its differential diagnosis. Am J Clin Pathol. 2006;125:490-501.

2. Saggini A, Gulia A, Argenyi Z, Fink-Puches R, Lissia A, Magaña M, et al. A variant of lymphomatoid papulosis simulating primary cutaneous aggressive epidermotropic CD8+ cytotoxic t-cell lymphoma. Description of 9 cases. Am J Surg Pathol. 2010;34:1168–75.

3. Sim J, Kim Y. CD8+ lymphomatoid papulosis. Ann Dermatol. 2011;23:104-7.

4. Cardoso J, Duhra P, Thway Yi, Calonje E. Lymphomatoid papulosis type D: A newly described variant easily confused with cutaneous aggressive CD8-positive cytotoxic t-cell lymphoma. Am J Dermatopathol. 2012;34:762–5.

5. Macaulay W. Lymphomatoid papulosisA continuing self-healing eruption, clinically benign—histologically malignant. Arch Dermatol. 1968;97:23-30.

6. Macaulay W. Lymphomatoid papulosis. Int J Dermatol. 1978;17:204-12.

7. Souza A, Azhary R, Camilleri M, Wada D, Appert D, Gibson L. In search of prognostic indicators for lymphomatoid papulosis: A retrospective study of 123 patients. J Am Acad Dermatol. 2012;66:928-37.

8. Souza A, Camilleri M, Wada D, Appert D, Gibson L, Azhary R. Clinical, histopathologic, and immunophenotypic features of lymphomatoid papulosis with CD8 predominance in 14 pediatric patients. J Am Acad Dermatol. 2009;61:993-1000.

9. Zic J. Lymphomatoid papulosis. emedicine.medscape.com; Updated: Jan 24, 2012 http://emedicine.medscape.com/article/10989.54-overview

10. Sanches J, Zavaloni C, Festa Neto C. Lymphoproliferative processes of the skin. Part 2 – Cutaneous T-cell and NK-cell lymphomas. An Bras Dermatol. 2006;81:7-25.

11. Alperovich M. Lymphomatoid papulosis. Dermatol Argent. 2011;17: 354-64.

12. Ishiji T, Takagi Y, Niimura M. Cutaneous lymphomas in Tokyo: analysis of 62 cases in a dermatology clinic. Int J Dermatol. 2001;40:37-40.

13. Liu H, Hoppe R, Kohler S, Harvell J, Reddy S, Kim Y. CD30+ cutaneous lymphoproliferative disorders: The Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. J Am Acad Dermatol. 2003;49:1049-58.

14. Rodríguez Peralto J, Calzado L, Vanaclocha F. En: Herrera Ceballos E, Moreno Carazo A, Requena Caballero L, Rodríguez Peralto J. editores. Dermatología: correlación clínico-patológica. Barcelona: Signament edicions, S.L., 2007;pp:447-50 .

15. Sioutos N, Asvesti C, Sivridis E, Aygerinou G, Tsega A, Zakopoulou N, Zographakis I. Lymphomatoid papulosis type A: clinical, morphologic, and immunophenotypic study. Int J Dermatol. 1997;36:514-7.

16. Hsu Y, Su L, Hsu Y, Tsai T, Hsiao C. Localized lymphomatoid papulosis. J Am Acad Dermatol. 2010;62:353-5.

17. Eminger L, Shinohara M, Kim E, Heymann W. Clinicopathologic challenge: acral lymphomatoid papulosis. Int J Dermatol. 2012;51:531–4.

18. Yancovitz M, Walters R, Kamino H, Brown L. Acral lymphomatoid papulosis. J Am Acad Dermatol. 2010;62:530-1.

19. Chimenti S, Fargnoli M, Pacifico A, Peris K. Mucosal involvement in a patient with lymphomatoid papulosis. J Am Acad Dermatol. 2001;44:339-41.

20. Tabata N, Aiba S, Ichinohazama R, Kikuchi K, Aoyama H, Watanabe M, et al. Hydroa vacciniforme-like lymphomatoid papulosis in a Japanese child: A new subset. J Am Acad Dermatol. 1995;32:378-81.

21. Hurtado J, Bravo F. Papulosis linfomatoide. Dermatol Per. 2000;10:130-2.

22. Lin J, Shiau W, Lu C, Tsai C, Wong W. Chung-Yee Hui R. Lymphomatoid papulosis: a clinical and histopathologic review and follow-up study of 34 cases in Taiwan. Derm Sinica. 2011;29:8-12.
23. Ally M, Robson A. Pagetoid reticulosis in lymphomatoid papulosis type D and mycosis fungoides, mimicking aggressive epidermotropic CD8+ (‘‘Berti’’) lymphoma. J Am Dermatol. 2012;66:AB81.
24. Vonderheid E, Kadin M, Gocke C. Lymphomatoid papulosis followed by pityriasis lichenoides: a common pathogenesis? Am J Dermatopathol. 2011;33:835-40.
25. Wu W, Tsai H. Lymphomatoid papulosis histopathologically simulating angiocentric and cytotoxic t-cell lymphoma. Am J Dermatopathol. 2004;26:133-5.
26. Flann S, Orchard G, Wain M, Russell-Jones R. Three cases of lymphomatoid papulosis with a CD561 immunophenotype. J Am Acad Dermatol. 2006;55:903-6.
27. Louvet S, Martin A, Troussard X, Galateau E, Moreau A, Reman O, et al. Spectrum of CD30 lymphoproliferative diseases from lymphomatoid papulosis to anaplastic large cell lymphoma. Int J Dermatol. 1996;35:842-8.
28. Heald P, Subtil A, Breneman D, Wilson L. Persistent agmination of lymphomatoid papulosis: An equivalent of limited plaque mycosis fungoides type of cutaneous T-cell lymphoma. J Am Acad Dermatol. 2007;57:1005-11.
29. Siddiqui M, Sullivan S, Al-Mofadhi A. Lymphomatoid papulosis and FK 506. Int J Dermatol. 1997,36:198-212.
30. Tokuriki A, Kiyohara T, Ido T, Kumakiri M. A case of lymphomatoid papulosis with extensive limb disease followed by extracutaneous involvement and acquired ichthyosis. Acta Derm Venereol. 2012;92:278–9.
31. Narro R, Lacy R, Hojyo M. Papulosis linfomatoide. Reporte de dos casos tratados con PUVA. Dermatología Rev Mex. 2007;51:158-60.
32. Demierre M, Goldberg L, Kadin M, Koh H. Is it lymphoma or lymphomatoid papulosis? J Am Acad Dennatol. 1997;36:765-72.
33. Bergstrom J, Jaworsky C. Topical methotrexate for lymphomatoid papulosis. J Am Acad Dermatol. 2003;49:937-9.

TYPE D LYMPHOMATOID PAPULOSIS: AN UNCOMMON VARIANT. A CASE REPORT AND REVIEW OF THE LITERATURE

by Gladys Alejandra Paguaga, Orlando Rodas Pernillo, Helga María Sarti

comment:

Ass. Prof. Małgorzata Sokołowska-Wojdyło MD, PhD, MSc

Department of Dermatology, Venereology and Allergology,
Medical University of Gdansk,
Gdansk, Poland
E-mail: mwojd@gumed.edu.pl

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 408 Date of submission: 23.09.2014 / acceptance: 27.09.2014

Cite this article:
Sokołowska-Wojdyło M. Comment: Type D Lymphomatoid Papulosis: An uncommon Variant. A case report and review of the literature. Our Dermatol Online. 2014; 5(4): 408.

The interesting article touches the unfamiliar for most of doctors problem: the existence of skin lymphoproliferative disease which is malignant in histopathology but mild in course: lymphomatoid papulosis (LyP) It presents with papules in the skin of the trunk and the extremities. Those papules can appear scaly and typically develop superficial, central necrosis. They also tend to heal spontaneously (most often in 3-12 weeks). LyP mainly affects adults (the median age at diagnosis is 45 years), with a slight predominance of males but children are also affected [1]. Histologically, what was mentioned by Paguaga et al., LyP is generally divided into the following 4 subtypes:

- type A is characterized by large CD30+ atypical cells intermingled with a prominent inflammatory infiltrate consisting of histiocytes, small lymphocytes, granulocytes and eosinophiles;
- type B is characterized epidermotropism and infiltration with smaller atypical cells with hyperchromatic cerebriform nuclei resembling the atypical lymphocytes in Mycosis fungoides (MF), and of antigen composition of C-ALCL.;
- type C is characterized by sheets of CD30+ anaplastic large lymphocytes;
- type D is characterised by infiltrates similar to those in CD8+ aggressive epidermotropic lymphoma or/and resembling pagetoid reticulosis (CD8+ CD30+, sometimes CD4+, CD56+).

The malignant histopathological features do not correlate with chronic / mild course. That is why the diagnose can not be determined only on the base of them. The clinical symptoms analysis is necessary to avoid the overtreatment because the diagnose of Hodgkin disease, MF or aggressive epidermotropic lymphoma instead LyP. That is why the every case of unusual or rare type of LyP is worth of publication – to remind the dermatologists, oncologists, haematologists and pediatricins that this dermatose exist. The problem is even more difficult because other histopathological subtypes of LyP, not mentioned in the publication of Paguaga et al., were described so far ex. granulomatous and eccrinotropic [2-4]. Those two subtypes can be discussed as subtypes of typ B LyP – analogously to MF and ex. pilotropic, syringotropic subtype. Type D of LyP can even imitate the pagetoid reticulosis type of MF (before known as Woringer-Kolopp type). There is also possibility that, as in Mycosis fungoides – where 31 clinical subtypes were described, there are also other subtypes of LyP, not only those four named A-D [5]. The authors mentioned also other important problem - LyP have an increased risk for developing a nonlymphoid tumour or, more commonly, a lymphoma (10-20%). It can be primary cutaneous lymphoma [6]. That is why there are cases of coexistence of LyP and CD30+ cutaneous or systemic T-cell lymphoma with secondary cutaneous involvement, which should be not misdiagnosed [7]. The authors rightly noted that there are no clinical or pathological features predicting increased risk for developing malignancy. That is why the observation of LyP patients should be very vigilant.

REFERENCES

1. Weaver J, Mahindra AK, Pohlman B, Jin T, Hsi ED. Non-mycosis fungoides cutaneous T-cell lymphoma: reclassification according to the WHO-EORTC classification. J Cutan Pathol. 2010;37:516-24.
2. Jain N, Gutte R, Jadhav P, Khopkar U. Granulomatous and eccrinotropic lymphomatoid papulosis. Indian J Dermatol Venereol Leprol. 2012;78:82-4.
3. Kempf W. CD30+ lymphoproliferative disorders: histopathology, differential diagnosis, new variants, and simulators. J Cutan Pathol. 2006;33 Suppl 1:58-70.
4. Morimura S, Sugaya M, Tamaki Z, Takekoshi T, Sato S. Acta Derm Venereol. 2011;91:712-3.
5. Requena L, González-Guerra E, Angulo J, DeVore AE, Sangueza OP. Anetodermic mycosis fungoides: a new clinicopathological variant of mycosis fungoides. Br J Dermatol. 2008;158:157-62.
6. Min JA, Oh ST, Kim JE, Cho BK, Chung NG, Park HJ. Lymphomatoid papulosis followed by anaplastic large cell lymphoma in a pediatric patient. Ann Dermatol. 2010;22:447-51.
7. Marschalkó M, Eros N, Holló P, Hársing J, Bottlik G, Bátai A, et al. Secondary ALK negative anaplastic large cell lymphoma in a patient with lymphomatoid papulosis of 40 years duration. Am J Dermatopathol. 2010;32:708-12.

DOI: 10.7241/ourd.20144.102

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

A HUGE FIBRO EPITHELIAL POLYP OF THE VULVA WITH MYXOID STROMA IN TUNISIAN NULLIPAROUS WOMAN

Mariem Mohamed[1], Mouna Korbi[1], Rim Hadhri[2], Hayet Akkari[1], Awatef Hajjaji[3], Monia Youssef[1], Montasser Amri[1], Hichem Belhadjali[1], Jameleddine Zili[1]

[1]*Department of Dermatology, Fattouma Bourguiba University Hospital, Monastir, Tunisia*
[2]*Department of Pathology, Fattouma Bourguiba University Hospital, Monastir, Tunisia*
[3]*Department of Obstetrics and Gynecology, Fattouma Bourguiba University Hospital, Monastir, Tunisia*

Source of Support: Nil
Competing Interests: None

Corresponding author: Dr Mariem Mohamed mariemmohamed79@yahoo.fr

Our Dermatol Online. 2014; 5(4): 409-411 Date of submission: 16.08.2014 / acceptance: 20.09.2014

Abstract
Introduction: Fibroepithelial polyps are a type of mesenchymal lesion that typically occurs in women of reproductive age. These lesions can be polypoid or pedunculated and are usually solitary. They are typically asymptomatic and do not grow larger than 5 cm in diameter. However, there are few reported cases of giant fibroepithelial polyps of the vulva. In these cases, tumors cause usually symptoms including bleeding, discharge and general discomfort (with sensation of a mass).
Case Report: Here we report a painful giant fibro epithelial polyp on the left labia majora in a 47-year-old Tunisian nulliparous woman. The mass was pedunculated, firm, 10cm in diameter. It was excised and the histological examination confirmed the diagnosis of fibro epithelial polyp with myxoid stroma and abcesses.
Conclusion: The current case is characterized by huge fibro epithelial polyp of the vulva, rare disorder which may cause symptoms resulting from its size. Abcesses can be added to the main complications of these tumors such as bleeding, discharge and superficial ulceration.

Key words: fibro epithelial polyp; vulva, fibroma; myxoid stroma; abcesses

Cite this article:
Mohamed M, Korbi M, Hadhri R, Akkari H, Hajjaji A, Youssef M, Amri M, Belhadjali H, Zili J. A huge fibro epithelial polyp of the vulva with myxoid stroma in Tunisian nulliparous woman. Our Dermatol Online. 2014; 5(4): 409-411.

Introduction

Different types of tumors of the vulva are reported [1]. Fibromas are the most common benign tumours of the vulva [1]. fibromas are connective-tissue benign tumors that have multiple synonyms (naevus molluscum, acrochordon, templeton skin tag, and fibroepithelial polyp) [2]. Fibro epithelial polyps are a type of mesenchymal lesion that typically occurs in women of reproductive age [3]. These polyps are site-specific and have a predilection for the vulvovaginal region. They are most frequently found in the vagina. Infrequently they occur on the vulva and cervix and rarely are found in extra-genital sites. These polyps are hormone sensitive and most commonly occur in pregnancy. Here we report a case of a FEP on the left labia majora with myxoid stroma and complicated by multiple abcesses.

Case Report

A 47-year-old woman, with no particular medical history, was referred to our department for a painful giant polyp on the left labia majora that was progressively increasing in size over three years. Physical examination revealed a 10x8 cm pedunculated, globular, and firm mass. The proximal edge was connected to the left labia majora by 3x1.5 cm pedicle (Fig. 1). No lymph nodes were palpable in the vulvar and inguinal regions. The mass was excised at the base of the pedicle. The surgical specimen consisted of a pedunculated spherical mass, 10 cm in diameter (Fig. 2). It was well circumscribed but had no definite capsule. Cut surface was homogenous, tan-white, gelatinous, and with abcesses (Fig. 3). On microscopic examination, the mass was entirely coverd by an epidermis.

It was hypocellular with abundant loose connective tissue stroma and focal myxoid area (Fig. 4). No mitosis or cytologic atypia was noted. Areas of dense inflammatory infiltrate of neutrophils forming abcesses were showed (Fig. 5). These findings are consistent with the diagnosis of vulvar fibroepithelial polyp with myxoid stroma and abcesses. One year later, the patient showed no evidence of recurrent disease.

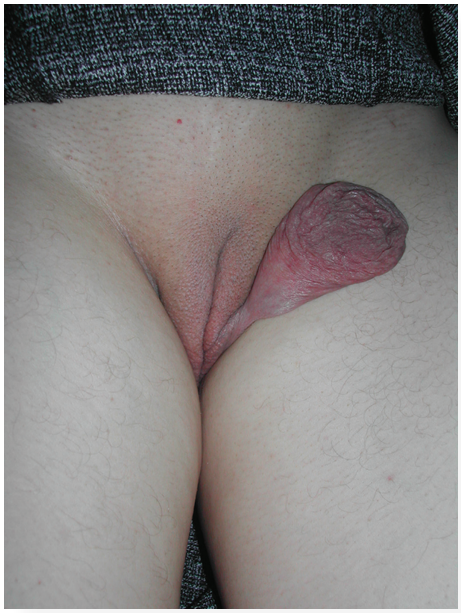


Figure 1. Pedunculated tumor originating from the left labia majora.

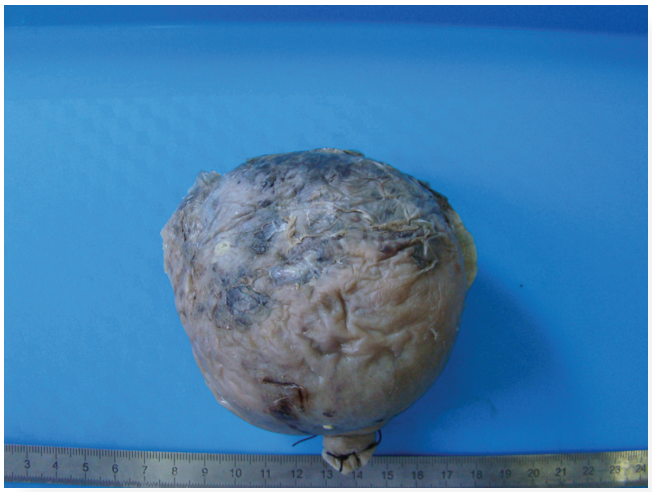


Figure 2. A spherical cutaneous mass, 10cm in diameter.

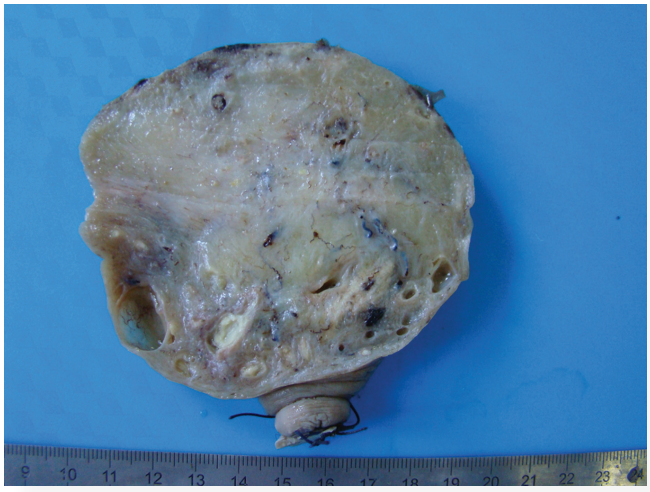


Figure 3. Cut surface of the tumor mass demonstrating a homogenous firm and gelatinous features with abscesses.

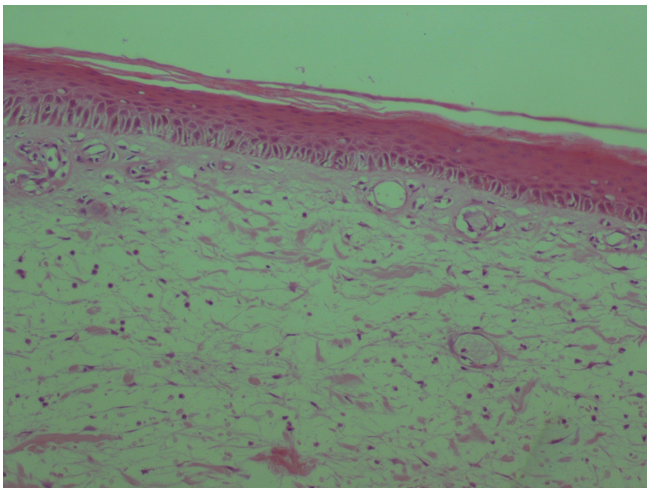


Figure 4. The mass covered by an epidermis and formed by a hypocellular connective tissue with myxoid area. (HEX100)

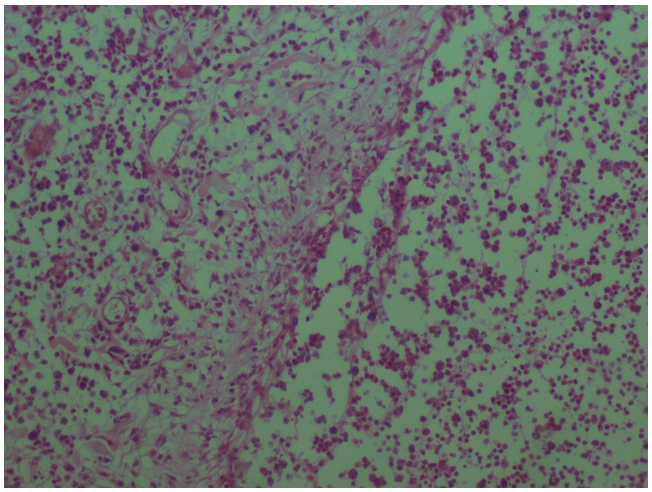


Figure 5. Dense infiltrate of neutrophils with formation of abscesses. (HE X 100)

Discussion

Vulvovaginal polyps are very rare lesions of the female genital tract [4]. It was first reported originally by Norris and Taylor in 1966 as a benign injury [5]. Vulvar FEP is a benign tumour that is predominantly found in women of reproductive age group [3]. However, they have been also reported in infants and in post menopausal women [2,3]. The tumor may arise from either the deep connective tissue of introitus, labia majora, perineal body or round ligament [6]. Usually, these tumors are small [4], but they, rarely, can have an extremely large size [1-4] as the case of our patient. The largest FEP was reported by Chan et al in 201, the tumor weighed 1.112 kg and measured 20.5 x 17 x 5 cm [1]. FEP are usually asymptomatic in the beginning, however they develop symptoms resulting from their size and from their main complication, the superficial ulceration [2]. Symptoms usually include bleeding, discharge and general discomfort with sensation of a mass. They may also cause extreme emotional upheaval, psychological disturbances and social withdrawal [6]. Macroscopically, the polyps can be sessile or pedunculated [2,3]. Differential diagnosis may be lipoma, inguinal hernia, vulvovaginal cyst, vulval elephantiasis and other benign tumors of the vulva [2,6]. Histologically, vulvar fibroepithelial polyps are hypocellular with abundant loose connective tissue stroma and focal myxoid areas [4]. The stromal cells may be reactive with desmin, vimentin, actin, and S-100 [4]. The surgical excision, which was the treatment proposed to our patient, is the first line treatment according to the literature [1-4]. Only 2 recurrences were reported within two years following initial surgical treatment [3,4]. The pathogenesis of FSP is not yet well understood [1]. Some authors suggest a reactive hyperplastic process involving the distinctive subepithelial mesenchyma of the lower female genital tract [7]. Moreover, the potential role of hormonal influence is raised by the fact that FSP rarely occurs before puberty and multiple FSPs are often associated with pregnancy [8]. On the other hand, some diseases associated with FEP have been previously reported such as psoriasis [9] and congenital lymphoedema [10].

In summary, we report a new case of a giant FEP in Tunisian women complicated by abcesses. Further report cases of these rare tumors may allow a more detailed understanding of their morphological and epidemiological characteristics.

REFERENCES

1. Chan MM, Yong TT, Sittampalam K. Giant labial fibroepithelial stromal polyp. Malays J Pathol. 2013;35:91-4.
2. Lopes Filho LL, Lopes IMRS, Ferreira Filho ES, Gonçalves Neto TR, Lopes LRS. Giant soft fibroma located in the vulva: a case report. Surg Cosmet Dermatol. 2012;4:200-2.
3. Madueke-Laveaux OS, Gogoi R, Stoner G. Giant fibroepithelial stromal polyp of the vulva: largest case reported. Ann Surg Innov Res. 2013;7:8.
4. Khalil AM1, Nahhas DE, Shabb NS, Shammas FG, Aswad NK, Usta IM, et al. Vulvar fibroepithelial polyp with myxoid stroma: an unusual presentation. Gynecol Oncol. 1994;53:125-7.
5. Norris HJ, Taylor HB. Polyps of the vagina. The benign injury resembling sarcoma botryoides. Cancer. 1966;19:227-32.
6. Najam R, Chowdhury HH, Awasthi S. A Large Fibroma Polyp of Labia Majora–A Case Report. J Clin Case Rep. 2013;3:297-8.
7. Nucci MR, Young RH, Fletcher CD. Cellular pseudosarcomatous fibroepithelial stromal polyps of the lower female genital tract: an underrecognized lesion often misdiagnosed as sarcoma. Am J Surg Pathol. 2000;24:231-40.
8. Armo M, Agrawal S, Minj M, Babbar K. Recurrent vulval fibroepithelial polyp with pregnancy: a rare presentation. Int J Reprod Contracept Obstet Gynecol. 2013;2:245-7.
9. Dane C, Dane B, Cetin A, Erginbas M, Tatar Z. Association of psoriasis and vulval fi broepithelial polyp: first reported case. Am J Clin Dermatol. 2008;9:333-5.
10. Orosz Z, Lehoczky O, Szoke J, Pulay T. Recurrent giant fi broepithelial stromal polyp of the vulva associated with congenital lymphedema. Gynecol Oncol. 2005;98:168-71.

DOI: 10.7241/ourd.20144.103

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

S-100 POSITIVE MULTICENTRIC RETICULOHISTIOCYTOSIS – REPORT OF A RARE CASE WITH BRIEF REVIEW OF LITERATURE

Manna Valiathan[1], Swati Sharma[1], C. Balachandran[2]

[1]Department of Pathology, Kasturba Medical College, Manipal, Karnataka, India
[2]Department of Dermatology, Kasturba Medical College, Manipal, Karnataka, India

Corresponding author: Ass. Prof. Swati Sharma swatisharma79@yahoo.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 412-415 Date of submission: 05.06.2014 / acceptance: 21.07.2014

Abstract
Background: Multicentric reticulohistiocytosis (MRH) is a rare histiocytic proliferative disorder involving skin, mucosa and joints. Diagnosis is confirmed by histopathological examination.
Case Report: A 45 year old patient presented with non-pruritic papules over the body and multiple joint pains. Histopathologically, the lesion was composed of oncocytic macrophages and multinucleate giant cells with abundant, eosinophilic and granular cytoplasm with ground glass appearance. Immunohistochemical expression for CD-68 and S-100 was seen .
Conclusion: We describe a case of MRH along with brief review of literature with unusual immunohistochemical expression of S-100 protein which is reported negative in majority of previously presented cases, however CD68 positivity confirmed the non-langerhans cell origin.

Key words: Multicentric reticulohistiocytosis; Skin nodules; Arthritis; S-100

Cite this article:
Valiathan M, Sharma S, Balachandran C. S-100 Positive Multicentric Reticulohistiocytosis – report of a rare case with brief review of literature. Our Dermatol Online. 2014; 5(4): 412-415.

Introduction

Multicentric reticulohistiocytosis (MRH) is a rare histiocytic proliferative disorder of unknown etiology usually manifesting as skin nodules and progressive arthritis. Although first described by Caro and Senear [1] in 1952 as "reticulohistiocytic granuloma", the term MRH was first given by Goltz and Laymon [2] in 1954 because of its multifocal origin and systemic involvement. Characterstically, MRH presents with papulo-nodular skin eruptions with a predilection for hands and destructive, deforming, symmetrical polyarthritis [3]. The diagnosis is confirmed histologically by the presence of infiltrative histiocytic multinucleated giant cell with eosinophilic, ground glass cytoplasm [4] which stain positive for Periodic-acid Schiff. Immunohistochemistry (IHC) reveals positivity for markers of monocyte or macrophage origin [5]. There is no consistently effective treatment established [6], however systemic steroids and cytotoxic drugs are tried with variable success. We report this case for its rarity, striking skin lesions and minimal joint involvement and the unusual expression of S-100.

Case Report

A 45 year old man came to the OPD with the complaints of asymptomatic skin-colored, non-pruritic papules over face and body for two and half months. Lesion started over the forehead, progressively increased in number and size to involve the scalp, face, trunk and lower limb. Patient also complained of multiple joint pains involving the knee, shoulder, elbow and hip joint. He was treated with oral steroids and parenteral antibiotics by a local doctor but did not show improvement. Cutaneous examination showed multiple skin colored to reddish, firm papules sized 2-5 mm over the scalp, face, trunk, dorsal aspect of palms and legs (Fig. 1).

Oral cavity showed linear hyperpigmented macules over upper and lower lip. Palms, soles and genitals were spared. There was no joint deformity. Routine biochemical and hematological investigations were normal. ESR was 44mm of Hg at the end of one hr. Histopathology of skin biopsy showed thinned out epidermis overlying a lesion in dermis composed of oncocytic macrophages, few multinucleate giant cells with abundant, eosinophilic, finely granular cytoplasm with ground glass appearance along with diffuse mixed inflammatory infiltrate (Fig. 2).

The oncocytic macrophages were positive for periodic acid-Schiff stain. IHC showed positivity for CD68 and S-100 (Figs 3, 4).

On further evaluation lipid profile, C-reactive protein, rheumatoid factor, ANA profile, chest X-ray, ultrasound abdomen, gastroscopy and bone marrow examination were normal. A diagnosis of MRH was given. Patient was put on Methotrexate, Hydrochloroquin and Folic acid. He responded well to the treatment and the skin lesions regressed. Patient was on regular follow up.

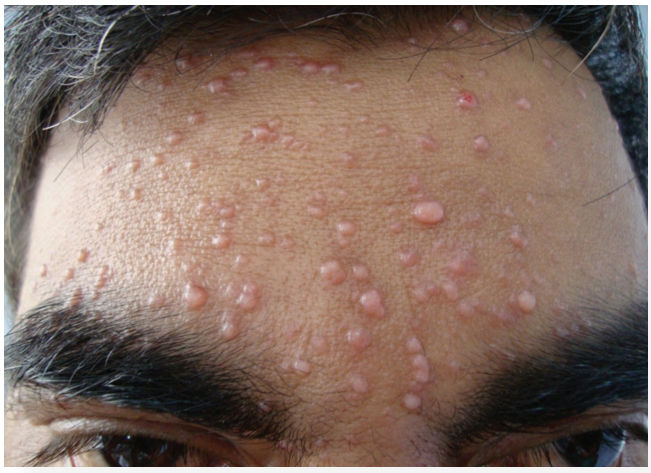


Figure 1. Multiple firm non-pruritic papules over the forehead.

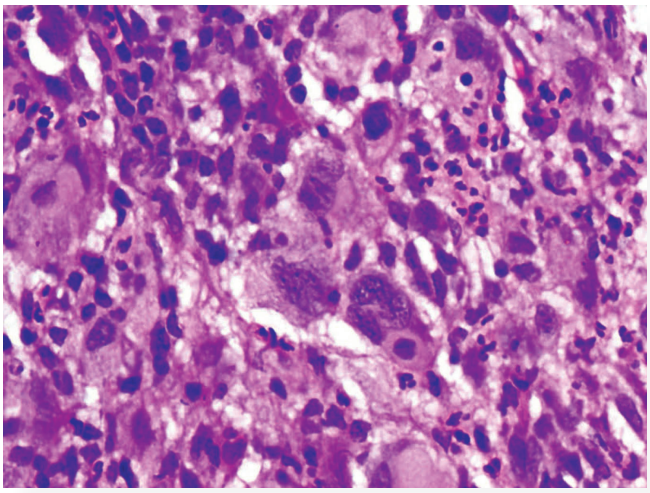


Figure 2. Multinucleate giant cells, oncocytic macrophages, with ground glass appearance. (H&E)

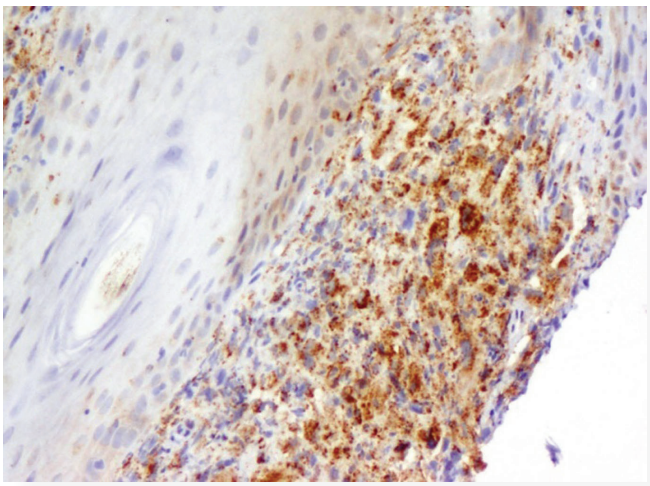


Figure 3. CD-68 positivity establishing non-langerhans cell origin. (x 200)

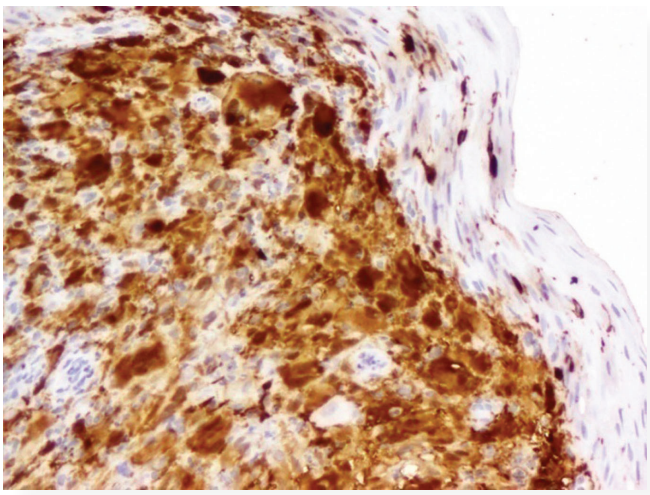


Figure 4. S-100 positivity in oncocytic macrophages. (x 200)

Discussion

Histiocytosis is broadly classified into type I- langerhans cell histiocytosis, type IIa- histiocytes involving cells of dermal dendrocyte lineage, type IIb- histiocytes involving cells other than langerhans cell and dermal dendrocytes, and type III- malignant histiocytic disorders [7].

MRH also known as lipoid dermatoarthritis, lipoid rheumatism and giant cell reticulohistiocytosis is a rare systemic disease of unknown etiology [4,8]. Less than 200 cases have been reported in literature [3]. MRH is proliferative disease, because of its rarity and the absence of any infectious agents, possibility of individual predisposition was considered [9]. MRH has a worldwide distribution with female predominance (60-75 %). It usually begins during the fourth decade of life and presents with polyarthritis (50% of cases), cutaneous lesions (25%) or concurrent arthritis and skin manifestations (25%) [3]. MRH is characterized by proliferation of resident mononuclear phagocytes other than langerhans cells which may be due to the release of monokines, cytokines and other secretory products by unregulated macrophage activation, causing pro-inflammatory actions [8].

Characterstic skin lesions are non-pruritic nodules, commonly seen on the extremities. On the face, these papules may coalesce producing leonine facies. Many small papules along the nail fold create the "coral bead" sign [10]. The polyarthritis may be mild or severe. It may be mutilating, especially on the hands, through destruction of articular cartilage and subarticular bone. The disease tends to wax and wane over years with mutilating arthritis and disfigurement [10].

This case is unique as there was minimal joint involvement. Mucosal surfaces are involved in about 50% cases.

Oropharyngeal, nasal mucosa and tongue are most commonly affected [5]. Our patient showed mucosal involvement. MRH can also involve muscles, tendon sheaths, lymph nodes, bone marrow, eyes, salivary glands, larynx and thyroid6. It is found to be associated with diabetes (6%), hypothyroidism (6%), Sjogren's syndrome, primary biliary cirrhosis, tuberculosis (6%), pregnancy and malignancy in 25% of cases [3,6]. It has been proposed that MRH may be similar to a paraneoplastic syndrome [11] and may be the presenting feature of an undetected malignancy [12]. Our patient showed involvement of skin, mucosa and minimal joint involvement. No underlying disease or malignancy was detected. Radiology of bone lesions in MRH shows bilateral symmetric joint involvement with predeliction for metacarpophalangeal and interphalangeal joints. Bony destruction is disproportionate compared to articular cartilage loss [6]. Osteoporosis and periosteal new bone formation is absent, differentiating it from other inflammatory arthritis [8]. However this case did not show any joint deformity. Diagnosis of MRH is made on histology with the lesion showing presence of numerous multinucleate giant cells and oncocytic macrophages with abundant eosinophilic, finely granular cytoplasm with ground glass appearance. Older lesions show giant cells and fibrosis [10]. The histiocytic multinucleated giant cells contain diastase-resistant, periodic acid Schiff (PAS)–reactive material suggesting a polysaccharide component other than glycogen or acid mucopolysaccharide [13]. IHC of these cells shows a monocyte and macrophage origin and stain positive for CD68, HAM56, Mac387, alpha 1-antitrypsin, CD11b, CD11c, CD14 and CD15. S-100 and CD1a are negative and hence support a non-langerhans cell histiocytic origin [8]. Our case showed positivity for PAS-DR, CD-68 and was interestingly positive for S-100 as well. This is also been described by Miettinen and Fetsch [14] as focal expression in a few cases in a series of 44 biopsies and by few others [15-17]. According to Sidoroff et al. [18] generalized eruptive histiocytoma seems to be an early indeterminate stage of various non-X histiocytic syndromes. Presently it is difficult to assess if S-100 positivity can help in establishing the definitive diagnosis of MRH. However in this patient diagnosis of MRH was based on other pronounced histological and clinical features.

Clinically, differential diagnosis of MRH includes lepromatous leprosy, sarcoidosis, xanthomatosis, histiocytosis X, juvenile and adult xanthogranuloma, generalized eruptive histiocytoma, familial histiocytic dermatoarthritis, and neurofibromatosis. The presence of skin lesions with erosive arthritis differentiates MRH from these diseases. The characterstic histological picture along with IHC helps in confirming the diagnosis. Xanthalesma is associated in one third of patients with MRH and can be confused with familial dyslipidemia, the papulo-nodules can be mistaken for xanthomas, however, lipid profile helps in the differentiation. Lepromatous leprosy presenting with nodular lesions can be differentiated by slit skin smear examination and skin biopsy [8]. Radiologically, MRH can be differentiated from rheumatoid arthritis by the absence of periarticular osteoporosis and early joint space loss. Also rapidly destructive arthritis with joint deformities, characteristic skin lesions and a negative rheumatoid factor helps in differentiation [3]. A case of MRH with positive anticyclic citrullinated antibodies in described by Chauhan A et al. [11]. Our patient was negative for rheumatoid factor and ANA profile was within normal limits.

Although MRH can spontaneously resolve in 5–10 years [11] the natural course of the disease may result in severe destructive arthropathy and disfiguring cutaneous lesions [19]. There is no effective treatment for MRH. Several treatment regimens have been tried but the efficacy is difficult to assess due to disease fluctuations and spontaneous remissions [3]. Systemic steroids, cytotoxic drugs like cyclophosphamide, chlorambucil, methotrexate, etanercept and infliximab, biphosphonates like alendronate and zolidronate are reported to be effective [6]. In our case Methotrexate was given and skin lesions were regressed and the patient responded well.

Conclusion

MRH is a rare histiocytic proliferative disorder of unknown etiology with characteristic clinical features. It may be associated with systemic diseases or underlying malignancy. Diagnosis is confirmed on histopathological examination with characterstic oncocytic macrophages with abundant, eoisinophilic, ground glass cytoplasm staining positive for PAS-DR and CD-68. Some cases are reported to show positivity for S-100 protein. Further studies are required to establish the utility of S-100 positivity in establishing the diagnosis. MRH resolves spontaneously but can result in destructive arthropathy and disfigurement.

REFERENCES

1. Caro MR, Senear FE. Reticulohistiocytoma of the skin. AMA Arch Derm Syphilol. 1952;65:701-13.
2. Goltz RW, Laymon CW. Multicentric reticulohistiocytosis of the skin and synovia: reticulohistiocytoma or ganglioneuroma. AMA Arch Derm Syphilol. 1954;69:717-31.
3. Rezaieyazdi Z, Sandooghi M, Torghabe HM, Derhami A. Multicentric reticulohistiocytosis: A case report. Acta Med Iran. 2005;43:372-76.
4. Wahiduzzaman M, Pubalan M, Elena EMT. Multicentric reticulohistiocytosis resembling dermatocytosis: A report of a case and literature review. Egyptian Dermatol Online J. 2009;5:14.
5. Nassur R. Multicentric Reticulohistiocytosis: The Course of a Rare Disease. Meds 2006.
6. Kaul A, Tolat SN, Belgaumkar V, Mha CB. Multicentric reticulohistiocytosis. Indian J Dermatol Venereol Leprol. 2010;76:404-7.
7. Sharath Kumar BC, Nandini AS, Niveditha SR, Gopal MG, Reeti. Generalized eruptive histiocytosis mimicking leprosy. Indian J Dermatol Venereol Leprol. 2011;77:498-502.
8. Boon BF. Multicentric reticulohistiocytosis in a Malaysian Chinese lady: A case report and review of literature. Dermatol Online J. 2009;15:1.
9. Luz FB, Gasper NK, Gasper AP, Carneiro S, Ramos-e-Silva M. Multicentric reticulohistiocytosis: a proliferation of macrophages with tropism for skin and joints. Skinmed. 2007;6:227-33.
10. Burgdorf WHC, Zelger B. The Histiocytosis. In: Lever's Histopathology of the Skin (Elder DE, Elenitsas R, Johnson Jr. BL, Murphy GF, eds), 9th edn: Lippincott Williams & Wilkins Publications. 2005;681-703.
11. Chauhan A, Mikulik Z, Hackshaw KV. Multicentric reticulohistiocytosis with positive anticyclic citrullinated antibodies. J Nat Med Associat. 2007;99:678-80.
12. Tirumalae R, Raut P, Jayaseelan E, Shet A, Devi S, Kumar KR. Paraneoplastic multicentric reticulohistiocytosis: a clinicopathologic challenge. Indian J Dermatol Venereol Leprol. 2011;77:318-20.

13. Gorman JD, Danning C, Schumacher HR, Klippel JH, Davis JC. Multicentric reticulohistiocytosis: case report with immunohistochemical analysis and literature review. Arthritis Rheumat. 2000;43:930-38.
14. Miettinen M, Fetsch JF. Reticulohistiocytoma (solitary epithelioid histiocytoma): a clinicopathologic and immunohistochemical study of 44 cases. Am J Surg Pathol. 2006;30:521-28.
15. Bialynicki-Birula R, Sebastian-Rusin A, Maj J, Wozniak Z, Baran E, Dziegiel P. Multicentric Reticulohistiocytosis with S100 Protein Positive Staining: A Case Report. Acta Dermatovenerol Croat. 2010;18:35-7.
16. Perrin C, Lacour JP, Michiels JF, Flory P, Ziegler G, Ortonne JP. Multicentric Reticulohistiocytosis: Immunohistological and Ultrastructural Study: A Pathology of Dendritic Cell Lineage. Am J Dermatopathol. 1992;14:418-25.
17. Weber L, Hesse G, Feller A. Multicenter skin tumor of the interdigitating dendritic cell. Hautarzt. 1988;39:28-33.
18. Sidoroff A, Zelger B, Steiner H, Smith N. Indeterminate cell histiocytosis- a clinicopathological entity with features of both X- and non-X histiocytosis. Br J Dermatol. 1996;134:525-32.
19. Trotta F, Castellino G, Lo Monaco A. Multicentric reticulohistiocytosis. Best Pract Res Clin Rheumatol. 2004;18;759-72.

DOI: 10.7241/ourd.20144.104

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

PHOTODISTRIBUTED ACUTE FEBRILE NEUTROPHILIC DERMATOSIS: A CASE REPORT

Kanthilatha Pai[1], Sathish Pai[2], Raghavendra Rao[2], Sricharit Shetty[2]

[1]*Department of Pathology, Kasturba Medical College, Manipal, Manipal University, Karnataka, India*
[1]*Department of Dermatology, Kasturba Medical College, Manipal, Manipal University, Karnataka, India*

Source of Support:
Nil
Competing Interests:
None

Corresponding author: Dr Sathish Pai drsbpai@yahoo.co.in

Our Dermatol Online. 2014; 5(4): 416-418 Date of submission: 26.04.2014 / acceptance: 18.07.2014

Abstract
Photoexposed area involvement in acute febrile neutrophilic dermatosis is uncommon and has rarely been described in literature. We report a case of photodistributed Sweets syndrome in a middle aged lady who responded to symptomatic treatment with NSAID and systemic antibiotic. Sweets syndrome is an uncommon inflammatory disorder characterized by the abrupt appearance of painful, oedematous and erythematous papules and plaques or nodules on the skin. Fever and leukocytosis frequently accompany cutaneous lesions. Our patient presented with fever and abrupt onset of painful erythematous plaques over exposed parts of the body.

Key words: Acute febrile Neutrophilic dermatosis; photodistributed; colchicine

Cite this article:
Pai K, Pai S, Rao R, Shetty S. Photodistributed Acute febrile neutrophilic dermatosis: a case report. Our Dermatol Online. 2014; 5(4): 416-418.

Introduction

Acute febrile neutrophilic dermatosis or Sweet's Syndrome (SS) is characterized by a constellation of clinical symptoms, physical features, and pathologic findings which include fever, neutrophilia, tender erythematous skin lesions and a diffuse infiltrate consisting predominantly of mature neutrophils that are typically located in the upper dermis. Sweet's syndrome presents in three clinical settings: classical (or idiopathic), malignancy-associated, and drug-induced [1]. Approximately 70% of cases are idiopathic and the paraneoplastic form is present in 10-20 of the cases [2]. We present an unusual presentation of a case of Idiopathic or Classical Acute neutrophilic dermatosis in middle aged lady involving photoexposed regions and review the literature.

Case Report

A 45 year old woman presented to the outpatient department with history of painful lesions over the face and extremities accompanied by fever. She gave history of photosensitivity with burning sensation over the forearms. There was no history of sore throat, cough, arthralgia, drug intake or any systemic complaints prior to the present illness. Clinical examination revealed erythematous well defined tender plaques with raised margins over the V area of neck (Fig. 1), malar region (Fig. 2), bilateral palms, and legs, with pseudovesiculation over extensors of forearms and dorsum of hands (Fig. 3). The photo-protected areas were spared. A clinical differential diagnosis of Sweet's syndrome, Hansen's disease with type 2 reaction and erythema multiforme was considered. General examination revealed that she was febrile with a temperature of 102° and mild anemia. s

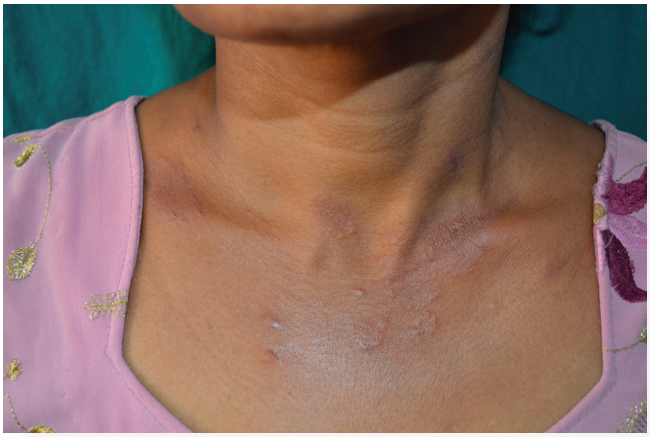


Figure 1. Multiple erythematous plaques and papules on V area of neck.

Figure 2. Erythematous plaque on left malar area.

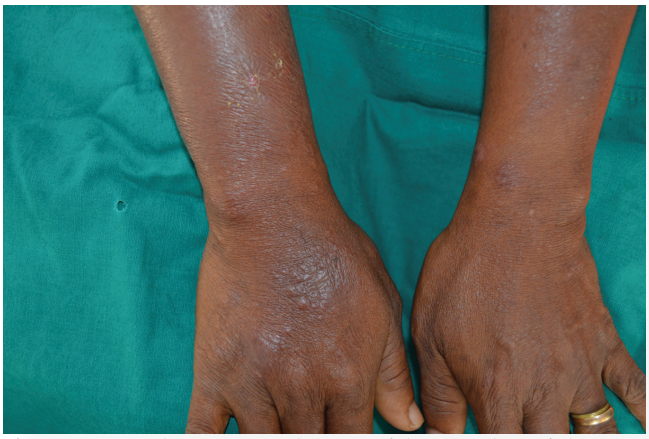


Figure 3. Erythematous plaque with pseudovesicle over dorsum of hand.

The photo-protected areas were spared. A clinical differential diagnosis of Sweet's syndrome, Hansen's disease with type 2 reaction and erythema multiforme was considered. General examination revealed that she was febrile with a temperature of 102° and mild anemia. Investigations revealed a Haemoglobin of 10.6 gm/dl, neutrophilia of 72% and raised ESR of 106mm/1 hour. ASO and ANA tests were negative, but C - reactive protein was positive. A slit skin smear examination was negative for acid fast bacillus. Systemic and radiological examination for underlying cause revealed no abnormalities. A skin biopsy was performed. Microscopic examination of skin biopsy showed marked edema in papillary dermis (Fig. 4) with diffuse interstitial and perivascular infiltration by predominantly neutrophils and blood vessels lined by plump endothelial cells with no evidence of vasculitis (Fig. 5). Patient was treated symptomatically with NSAID,s topical steroids and systemic antibiotics. Parenteral amoxicillin and clavulinic acid in the dose of 1.2 gm three times a day was used intravenously for the initial 3 days and then switched over to oral for a total duration of 7 days. Classical Sweets syndrome is usually associated with underlying infections and our patient had fever, abrupt onset of painful lesions and her ESR was raised with positive C reactive protein hence a course of systemic antibiotic was used. Clobetsol propionate 0.05% cream 30 gm diluted with 70 gms of cream base was used topically twice daily for 7 days and then once daily for 7 days. She improved and the lesions healed with scaling (Fig. 6). As she had dramatic improvement with systemic antibiotic and NSAID's, systemic steroids were not considered. She had a recurrence after 2 weeks and was treated with colchicine 0.5 mg three times a day. She has been on colchicine for about 2 months without any recurrences.

Discussion

Acute neutrophilic dermatosis was first described in 1964 by Robert Douglas Sweet, and has been termed Sweet's syndrome [3]. Classic Sweet's syndrome occurs in middle-aged women after a nonspecific infection of the respiratory or gastrointestinal tract. Raised erythematous plaques with pseudoblistering and occasionally pustules occur on the face, neck, chest, and extremities, accompanied by fever and general malaise. Involvement of the eyes, joints, and oral mucosa as well as internal manifestations of Sweet's syndrome in the lung, liver, kidneys, and central nervous system has been described. The disease is thought to be a hypersensitivity reaction. Approximately one-third of patients with Classical Sweets syndrome experience a recurrence of the dermatosis.

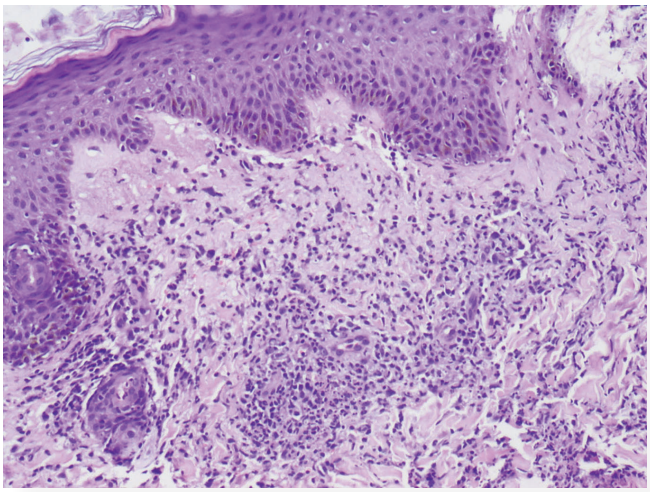


Figure 4. Photomicrograph showing marked edema in papillary dermis.

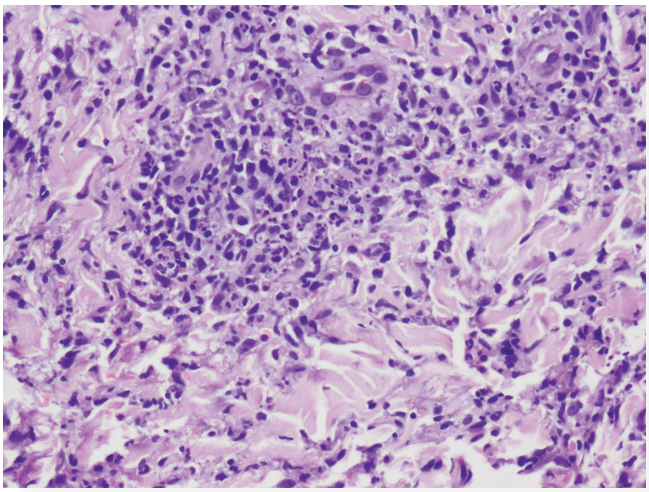


Figure 5. Diffuse infiltration of the dermis by neutrophils with no evidence of vasculitis H & E.

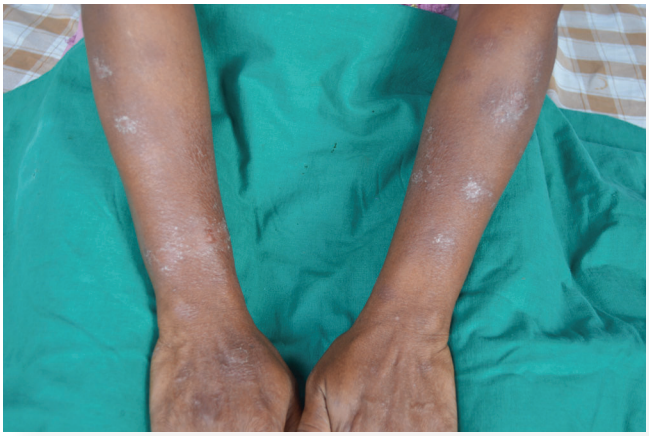


Figure 6. Healing of the lesions with scaling.

The malignancy-associated Sweet's syndrome can occur as a paraneoplastic syndrome in patients with an established cancer or individuals whose Sweet's syndrome-related hematologic dyscrasia or solid tumor was previously undiscovered; the dermatosis can precede, follow, or appear concurrent with the diagnosis of the patient's cancer. Hence, can be the cutaneous harbinger of either an undiagnosed visceral malignancy in a previously cancer-free individual or an unsuspected cancer recurrence in an oncology patient. Drug-induced Sweet's syndrome most commonly occurs in patients who have been treated with granulocyte-colony stimulating factor; however, other medications may also be associated with this form of Sweet's syndrome. The pathogenesis of Sweet's syndrome may be multifactorial and still remains to be definitively established. Clinical and laboratory evidence suggests that cytokines have an etiologic role.

Histologically the hallmark is a diffuse infiltrate consisting predominantly of mature neutrophils typically located in the upper dermis and no evidence of leukocytoclastic vasculitis.

Extracutaneous manifestations in the form of alveolitis, sterile osteomyelitis, renal, hepatic, and central nervous system involvement have also been reported .Although it is not one of the common life-threatening dermatoses, Sweet's syndrome can potentially cause significant pulmonary involvement and respiratory compromise and one needs to be aware of this condition.

Drug induced SS in photo-exposed regions have been described previously [4]. There are occasional case reports describing the worsening of idiopathic Sweet syndrome after sun exposure or photo distribution of lesions [5]. Lesions have also been described at site of previous phototoxic reaction [6]. The pathomechanism could involve either an isomorphic Koebner reaction, classically described in neutrophilic dermatoses, or the direct action of UV-B on neutrophil activation and recruitment in skin through the production of cytokines, such as interleukin 8 or tumor necrosis factor α [7]. Our patient presented with abrupt onset of fever and painful erythematous plaques over extensors of forearms, V area of neck and both malar area. She had a raised ESR, neutrophilia, positive C reactive protein and histopathology showed perivascular neutrophilic infiltration without evidence of vasculitis satisfying 2 major and 2 minor criteria's to arrive at a diagnosis of Sweets syndrome.

Systemic corticosteroids are the therapeutic gold standard for Sweet's syndrome. After initiation of treatment with systemic corticosteroids, there is a prompt response consisting of dramatic improvement of both the dermatosis-related symptoms and skin lesions. Topical application of high potency corticosteroids or intralesional corticosteroids may be efficacious for treating localized lesions. Other first-line oral systemic agents are potassium iodide and colchicine. Second-line oral systemic agents include indomethacin, clofazimine, cyclosporine, and dapsone. The symptoms and lesions of Sweet's syndrome may resolve spontaneously, without any therapeutic intervention; however, recurrence may occur.

Systemic antibacterials against Staphylococcus aureus frequently result in partial improvement of Sweet's syndrome lesions when they are impetiginized or secondarily infected. In some patients with dermatosis-associated bacterial infections, organism-sensitive specific systemic antibacterials have been helpful in the management of their Sweet's syndrome. Although patients with hematologic malignancy-associated Sweet's syndrome often receive cytotoxic chemotherapy agents and antimetabolic drugs for the treatment of their underlying disorder, these agents are seldom used solely for the management of the symptoms and lesions of Sweet's syndrome. Spontaneous resolution is not uncommon in classical SS. Recurrence may occur in one third patients despite appropriate treatment. Our patient responded to a course of systemic antibiotic, topical steroid and non-steroidal anti-inflammatory drug and did not need systemic steroids. The relapse which occurred after 2 weeks was well controlled with colchicine. Knowledge about this entity and its early recognition and prompt treatment is important to prevent devastating outcomes.

REFERENCES

1. Cohen PR, Kurzrock R . Sweet's syndrome: a review of current treatment options. Am J ClinDermatol. 2002;3:117-31.
2. Cohen PR, Kurzrock R. Sweet's syndrome and malignancy. Am J Med. 1987;82:1220-6.
3. Von den Driesch P. Sweet's syndrome (acute febrile neutrophilicdermatosis). J Am Acad Dermatol. 1994;31:535-56.
4. Walker DC, Cohen PR. Trimethoprim-sulfamethoxazole-associated acute febrile neutrophilicdermatosis: Case report and review of drug-induced Sweet's syndrome. J Am Acad Dermatol. 1996;34:918-23.
5. Bessis D, Dereure O, Peyron JL, Augias D, Guilhou JJ. Photoinduced Sweet syndrome. Arch Dermatol. 2001;137:1106-8.
6. Belhadjali H, Marguery MC, Lamant L, Giordano-Labadie F, Bazex J. Photosensitivity in Sweet's syndrome: Two cases that were photoinduced and photoaggravated. Br J Dermatol. 2003;149:675-7.
7. Strickland I, Rhodes LE, Flanagan BF, Friedmann PS. TNF-alpha and IL-8 are upregulated in the epidermis of normal human skin after UVB exposure: Correlation with neutrophil accumulation and E-selectin expression. J Invest Dermatol. 1997;108:763-8.

DOI: 10.7241/ourd.20144.105

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

IMMUNOREACTIVITY TO DERMAL VESSELS IN A PATIENT WITH PYODERMA GANDRENOSUM

Ana Maria Abreu Velez[1], Michael S. Howard[1], Vickie M. Brown[2]

[1]Georgia Dermatopathology Associates, Atlanta, Georgia, USA
[2]Family Dermatology, Milledgeville, Georgia, USA

Corresponding author: Ana Maria Abreu Velez, M.D., Ph.D., abreuvelez@yahoo.com

Source of Support:
Georgia Dermatopathology Associates (AMAV, MSH), USA
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 419-422 Date of submission: 08.08.2014 / acceptance: 19.09.2014

Abstract
Introduction: Pyoderma gangrenosum (PG) represents a lesion with an elusive etiology associated with Crohn's and/or arthritic diseases. A genuine associated vasculitis has not been proven; however, dilation of the dermal blood vessels the presence of neutrophilic and/or lymphocytic infiltrates in selected biopsies suggests that vessels are likely play a role in the pathogenesis of PG.
Materials and Methods: A patient presented with a necrotic pustule or furuncle, evolving into a large necrotic ulcer with violaceous borders and surrounding erythema. A skin biopsy for hematoxylin and eosin (H&E) review and immunohistochemistry (IHC) stains was obtained. A second biopsy for direct immunofluorescence (DIF) was also taken.
Results: H&E review demonstrated an ulcerated epidermis; within the ulcer base were numerous neutrophils, lymphocytes, histiocytes and fibrin. No vasculitis was present. DIF revealed strong deposits of FITC conjugated fibrinogen around superficial and the deep dermal vessels. FITC conjugated Complement/C1q and albumin conjugated were also seen between dermal extracellular matrix fibers. IHC showed that the dermal vessels (venules, arterioles and lymphatics) displayed dilation, and a loss of normal endothelial markers including von Willebrand factor and D2-40/podoplanin.
Conclusions: Our case of PG shows that there seems to be an alteration of several skin structures, including dermal vessels. An alteration of the vascular fibrin-fibrinogen balance was also detected, causing some autoreactivity to fibrinogen and an immune response involving neutrophils and T lymphocytes. Our findings suggest that the etiology of PG is more complex than previously thought.

Key words: Pyoderma gangrenosum; von Willebrand factor; vascular degeneration, autoimmunity; lymphatic vessels; CD99; D2-40

Abbreviations and acronyms: Pyoderma gangrenosum (PG), immunohistochemistry (IHC), direct immunofluorescence (DIF), hematoxylin and eosin (H&E).

Cite this article:
Abreu Velez AM, Brown VM, Howard MS. Immunoreactivity to dermal vessels in a patient with pyoderma gandrenosum. Our Dermatol Online. 2014; 5(4): 419-422..

Introduction

Pyoderma gangrenosum (PG) is an uncommon cause of painful skin ulceration. It may affect any part of the skin; however, it mainly presents on the lower legs, and has an unknown etiology resembling a Class II Schwartzman-like hypersensitivity reaction. PGs usually initially present as a single pustule, progress to solitary or multiple erythematous macules and papules and then to ulcerated, painful nodules or plaques with undermined, dusky borders. Patients are often systemically ill, with associated symptoms such as fever, malaise, arthralgias, and myalgias. Lesional pain may be severe. When lesions heal, the scars are often cribriform. PG is sometimes classified as a neutrophilic dermatosis, and has often been considered a reaction to another internal disease such as Crohn's disease, ulcerative colitis, polyarteritis nodosa or hematologic alterations. PG may affect males and females of any age, but is more common in people over 50 years [1-5]. PG combined with acne and a pyogenic arthritis may represent a rare genetic disorder characterized by its effects on skin and joints (PAPA syndrome).

Case Report

A 58 year old female presented to her dermatologist for evaluation of a pustule or furuncle that was evolving into an ulcer. The patient denied any gastrointestinal, acne or joint problems concomitant with the presentation of the skin lesions. Physical exam revealed a large, necrotic ulcer with violaceous border and surrounding erythema.

On examination, the ulcer was tender. Skin biopsies were obtained for hematoxylin and eosin (H&E) review, immunohistochemistry (IHC) staining and direct immunofluorescence (DIF) studies.

Material and Methods

For DIF, we incubated 4 micron glass slides with our secondary antibodies as previously described [6-9]. We utilized FITC conjugated rabbit anti-total IgG (Dako, Carpinteria, California, USA) at a 1:25 dilution. The samples were run with positive and negative controls. We also utilized FITC conjugated rabbit antisera to human IgG, IgA, IgM, Complement/C1q, Complement/C3, fibrinogen and albumin. Anti-human IgA antiserum (alpha chain) and anti-human IgM antiserum (mu chain) were obtained from Dako. Anti-human IgE antiserum (epsilon chain) was obtained from Vector Laboratories (Burlingame, California, USA). Anti-human IgD FITC-conjugated antibodies were obtained from Southern Biotechnology (Birmingham, Alabama, USA). The slides were counterstained with 4',6-diamidino-2-phenylindole(DAPI) (Pierce, Rockford, Illinois, USA). A mouse anti-collagen IV monoclonal antibody (Invitrogen, Carlsbad, California, USA) was also utilized, with secondary donkey anti-mouse IgG antisera (heavy and light chains) conjugated with Alexa Fluor 555 (Invitrogen).

Immunohistochemistry (IHC)

We performed IHC utilizing multiple monoclonal and polyclonal antibodies, all from Dako (Carpinteria, California, USA). For all our IHC testing, we used a dual endogenous peroxidase blockage, with the addition of an Envision dual link (to assist in chromogen attachment). We applied the chromogen 3,3-diaminobenzidine(DAB), and counterstained with hematoxylin. The samples were run in a Dako Autostainer Universal Staining System. Positive and negative controls were consistently performed. Our studies were specifically performed as previously described [6-9].The following antibodies were utilized: 1) monoclonal mouse anti-human CD99, MIC2 gene products, Ewing's sarcoma marker Clone 12E7, monoclonal mouse anti-human, 2) von Willebrand Factor, Clone F8/86, 3) polyclonal rabbit anti-human myeloperoxidase, monoclonal mouse anti-human neutrophil elastase Clone NP57, 4) polyclonal rabbit anti-human somatostatin, 5) monoclonal mouse anti-human podoplanin, Clone D2-40, 6) monoclonal mouse anti-human CD4, Clone 4B12, 7) monoclonal mouse anti-human CD45, Leucocyte Common Antigen Clones 2B11 + PD7/26, 8) monoclonal mouse anti-human CD8, Clone C8/144B, 9) monoclonal mouse anti-human IMP3 (Clone 69.1), (insulin-like growth factor II mRNA binding protein 3, 10) monoclonal mouse anti-human CD68 Clone EBM11, 11) monoclonal mouse anti-metallothionein Clone E9, 12) monoclonal mouse anti-human tissue inhibitor of metalloproteinases 1 and 13) polyclonal rabbit anti-human alpha-1-antitrypsin.

Resulrs

H&E tissue sections demonstrate an ulcerated epidermis (Fig. 1). Within the ulcer base were numerous neutrophils, lymphocytes and histiocytes; abundant fibrin was also present. Several vessels were dilated (Fig. 3). No vasculitis was noted; a dermal perivascular and interstitia infiltrate of lymphocytes and mononuclear cells was present. Fungal and bacterial stains were negative for organisms.

Direct immunofluorescence (DIF)

DIF displayed the following results: IgG (+, focal deep dermal perivascular); IgG3(-); IgA (++, focal deep dermal perivascular); IgM (+); IgD (-); IgE (-); Complement/C1q (++, focal deep dermal perivascular); complement/C3 (+, focal deep dermal perivascular); complement/C4(-); albumin (++, superficial dermal perivascular) and fibrinogen (++++, superficial and deep dermal perivascular, and around eccrine gland supply vessels). Fibrinogen was the strongest immunoreactant seen around the upper and deep dermal vessels, with Complement/C1q of second strongest intensity (Figs 1 - 4). In Figure 4, using Alexa 555 conjugated anti-human IgG antibody (red staining) we show positive staining of possible damaged vessels, amalgamated with some dermal structures

IHC staining

CD99 staining was very positive on dermal vessels subjacent to and surrounding the ulcer (Fig. 2). Somatostatin was weakly positive, within the dermal extracellular matrix. Our most important finding was the presence of significantly dilated lymphatic vessels via D2-40 staining, especially surrounding and subjacent to the ulcer (Fig. 2) Myeloperoxidase staining was positive, and showed some cellular defragmentation around one edge of the ulcer. Neutrophil elastase, CD4 and CD8 staining were predominantly negative. CD45 staining was positive in only few focal perivascular areas, adjacent to the ulcer. Anti-insulin-like growth factor II/mRNA binding protein 3 staining was negative. Of note, many dermal vessels were involuted and significantly damaged, observed by staining alterations with the von Willebrand antibody (Fig. 3).

Discussion

PG onsets are rapid, often at the site of a minor injury. The lesion may begin as a small pustule, a red bump or a blood-blister, with these lesions subsequently progressing to an ulcer. The ulcer often grows rapidly; the edges are usually purple and very painful and tender. Multiple ulcers may progress at the same time [1-5]. An ulcer may spontaneously improve, and complete healing may take months. It is important to evaluate if concomitant local venous disease is present, because this may play a negative role in the healing process. The clinical pathergy test is frequently positive (a skin prick test causing a papule, pustule or ulcer). Peristomal PG occurs close to abdominal stomas, and comprises about 15% of all cases of PG [1-2]. Most of these patients have inflammatory bowel disease, but peristomal PG may also occur in patients who have had an ileostomy or colostomy for either malignancy or diverticular disease. However, about 50% of those affected by PG demonstrate none of these associated risk factors.

Clinical differential diagnoses of PG lesions include antiphospholipid antibody syndrome, anthrax, Wegener's granulomatosis, atypical mycobacterial infections, Sweet's syndrome, venous or arterial disease, and Behçet's disease [1-5]. A final diagnosis of PG is based on the clinical appearance, and on ruling out histopathologic features of other disorders. There is no specific positive laboratory test for PG. However, it is recommended to swab PG ulcers for superinfecting pathogens. In our case, these studies were negative. It is also recommended to perform a chest radiogram. Angiography

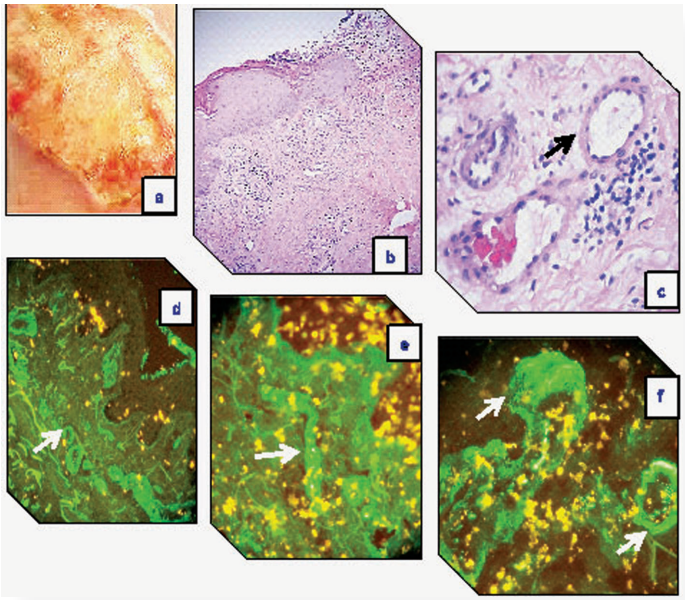


Figure 1. a, Clinical PG photograph, showing the PG ulcer. **b,c.** H&E photos at lower and higher magnification, respectively. In **b,** an ulcerated epidermis with numerous neutrophils, lymphocytes and histiocytes within the ulcer base; fibrin was also present. In **c,** we show several dilated dermal blood vessels. **d-f.** DIF. **d-f.** IgG conjugated with Alexa 555 (yellow staining) and FITC conjugated anti-fibrinogen(white arrows; green staining) on dermal lymphatic vessels.

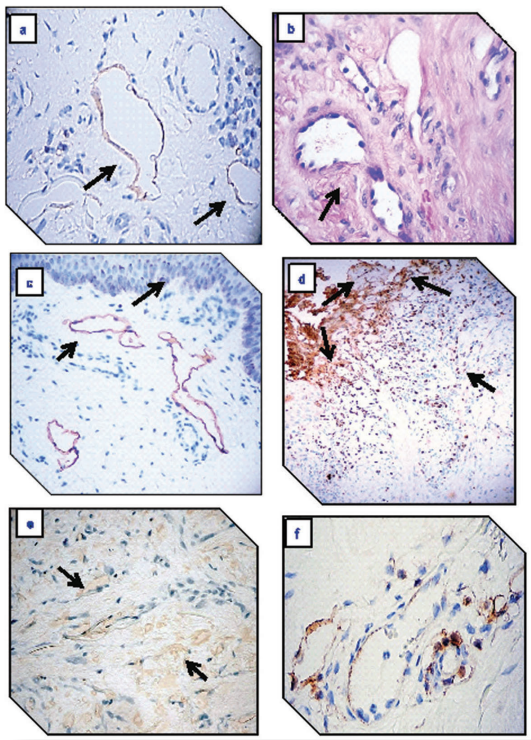


Figure 2. a, c, and **f,** CD99 positive IHC staining on dermal vessel endothelia(brown staining, black arrows). **b.** H & E staining, demonstrating dilated vessels in the dermis (400x) **d.** Positive IHC staining for myeloperoxidase (black arrows; brown staining). **e.** Positive IHC somatostatin staining in small dermal vessels of unknown identity (black arrows; light brown staining color).

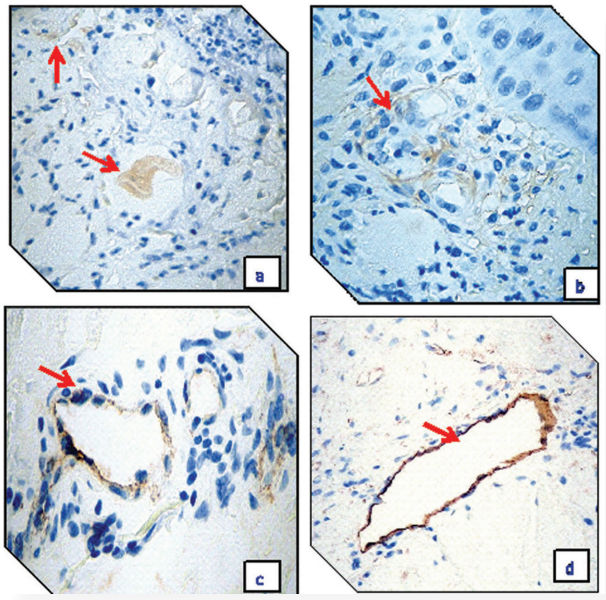


Figure 3. a-c. IHC staining, demonstrating damage to dermal vessels (showing degenerative changes and uneven staining with von Willebrand antibody (red arrows; light brown staining). **d.** Positive IHC staining, demonstrating a large, dilated lymphatic vessel via D2-40 antibody (red arrow; brown staining).

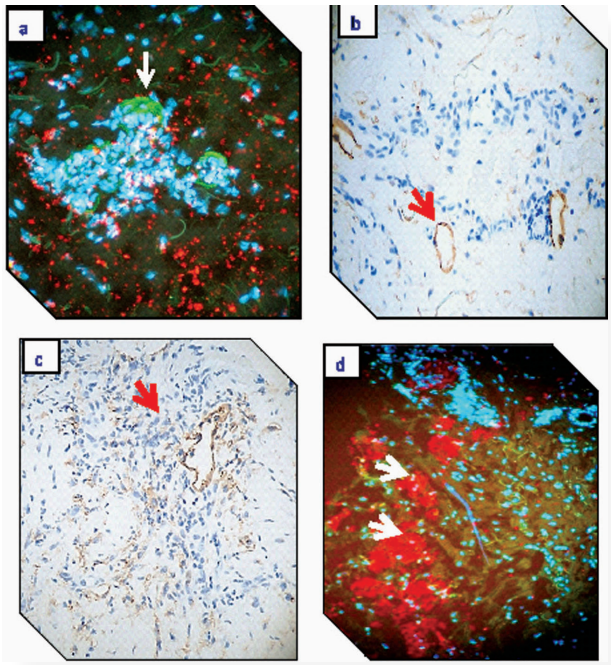


Figure 4. a. DIF, with Alexa 555 conjugated IgG (red staining) shows a tremendous deposition on some dermal structures (scattered red dots), and FITC conjugated fibrinogen (white arrow; green staining). Cell nuclei were counterstained with DAPI (blue). **b.** Positive D2-40 IHC staining documenting dilated dermal lymphatics (red arrow; brown staining) and in **c,** evidence of lymphatic vessel endothelial fragmentation(red arrow; brown staining). **d.** Positive DIF staining with Alexa 555 conjugated IgG (red staining) showing possible damaged vessels amalgamated with unidentified dermal structures (white arrows). Cell nuclei were counterstained with DAPI (blue).

Angiography or Doppler studies may be carried out in patients suspected of having arterial or venous insufficiency, and colonoscopy or other testing may be warranted to exclude associated inflammatory bowel disease in selected patients [1-5].

PG treatment includes the gentle removal of necrotic tissue. Small ulcers may be treated with potent topical steroid creams, intralesional steroid injections, and special dressings including silver sulfadiazine cream, potassium iodide or hydrocolloids. In some instances, oral anti-inflammatory agents such as dapsone or minocycline may help. If tolerated, careful compression bandaging may be helpful for swollen legs. Some severe cases warrant extended, systemic immunosuppressive therapy. The focus of treatment in these patients is long-term immunosuppression, often with high doses of corticosteroids or low doses of cyclosporin [2,3]. Lately, good outcomes have been reported for treatments with anti-tumor necrosis factor α; infliximab has also proven effective in a randomized, controlled clinical trial.

The etiopathology of PG is not clear. Some people believe that neutrophils play a critical role in this disease, because is common to see a neutrophilic dermal inflammatory infiltrate (as we found); however, this finding is not always present. Some patients may have positive ANCAs (antineutrophil cytoplasmic antibodies). In our case, these antibodies were negative. We found many defragmented neutrophils via positive staining for myeloperoxidase at the edges of the ulcer. Most T lymphocytic stains were negative (ie, CD4 and CD8; a few CD45 positive cells were noted). We found altered dermal vessels, and some degeneration of the vessels as demonstrated by altered staining of von Willebrand factor (especially under the ulcer and in close proximity). We also found many dermal vessels in these areas to be dilated, including the lymphatics; and we detected a immune response to these vessels, as demonstrated by positive CD99 staining in many of them. In addition, strong staining with anti-fibrinogen against these vessels was clearly present. The specific etiologic role of this vascular immune response is not known.

Other authors had reported clinical, histologic, and immunofluorescent findings in 68 PG cases. Notably, 78 per cent had associated systemic diseases, with arthritis and inflammatory bowel disease being most common. These authors reported cutaneous histopathologic changes varied with the site of biopsy. Specifically, lymphocytic vasculitis was predominant in the zone of erythema peripheral to the ulcers, while neutrophilic infiltrates and abscess formation were more prominent in central ulcer areas. In most of the cases studied, DIF showed immunoglobulins and complement deposited in and around superficial and deep dermal vessels, as we also observed [10].

Other authors reported the results of biopsies from ulcer edges in 8 PG patients. These biopsies were examined by DIF. Deposits of Complement/C3 were seen in the vessel walls of all samples, and IgM in three and IgA in one. Granular deposits of Complement/C3 were seen at the dermal-epidermal junction in 2 patients. Biopsies from clinically normal skin of 6 of the patients were DIF negative [11]. In agreement with our findings, these authors suggested that deposition of immune complexes in multiple dermal vessel walls may play a role in the pathogenesis of PG [11].

Conclusion

PG presents with multiple clinical appearances, and is easy to misdiagnose. The histopathology of PG is nonspecific; a biopsy is needed to exclude other diagnoses. Given our data, multiple dermal vessels including lymphatics, venules and arterioles seem to play a role in the immunopathology of PG.

REFERENCES

1. Weizman A, Huang B, Berel D, Targan SR, Dubinsky M, Fleshner P, et al. Clinical, Serologic, and Genetic Factors associated with pyoderma gangrenosum and erythema nodosum in inflammatory bowel disease patients. Inflamm Bowel Dis. 2014;20:525-33.
2. Dantzig PI. Letter: Pyoderma gangrenosum. N Engl J Med. 1975;292:47-8.
3. Bernard P, Amici JM, Catanzano G, Cardinaud F, Fayol J, Bonnetblanc JM. Pyoderma gangrenosum and vasculitis. Pathogenic discussion apropos of 3 cases. Ann Dermatol Venereol. 1987;114:1229-34.
4. Su WP, Schroeter AL, Perry HO, Powell FC. Histopathologic and immunopathologic study of pyoderma gangrenosum. J Cutan Pathol. 1986;13:323-30.
5. Brooklyn T, Dunnill G. Diagnosis and treatment of pyoderma gangrenosum. BMJ. 2006;333:181–4.
6. Abreu Velez AM, Howard MS, Grossniklaus HE, Gao W, Hashimoto T. Neural system antigens are recognized by autoantibodies from patients affected by a new variant of endemic pemphigus foliaceus in Colombia. Clin Immunol. 2011;31:356-68.
7. Abreu Velez AM, Smith JG Jr, Howard MS. Neutrophil extracellular traps (NETS), IgD, myeloperoxidase (MPO) and antineutrophil cytoplasmic antibody (ANCA) associated vasculitides. North Am J Med Sci. 2009;1:309-13.
8. Abreu Velez AM, Zhe J, Howard MS, Dudley SC. Cardiac immunoreactivity in patients affected by a new variant of endemic pemphigus foliaceus in El-Bagre, Colombia, South America. J Clin Immunol. 2011;31:985-97.
9. Abreu Velez AM, Yi H, Googe PB Jr, Mihm MC Jr, Howard MS. Autoantibodies to melanocytes and characterization of melanophages in patients affected by a new variant of endemic pemphigus foliaceus. J Cutan Pathol. 2011;38:710-9.
10. Powell FC, Schroeter AL, Perry HO, Su WP. Direct immunofluorescence in pyoderma gangrenosum. Br J Dermatol. 1983;108:287-93.
11. Ullman S, Halberg P, Howitz J.Deposits of complement and immunoglobulins in vessel walls in pyoderma gangrenosum. Acta Derm Venereol. 1982;62:340-1.

DOI: 10.7241/ourd.20144.106

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

SARCOIDOSIS MIMICKING SEBORRHEIC DERMATITIS: ANOTHER CASE OF SHERLOCKIAN DERMATOLOGY

César Bimbi

Member of Dermatological Comittee of State Medical Council of Rio Grande do Sul Brazil, Brazilian Society of Dermatology

Source of Support:
Nil
Competing Interests:
None

Corresponding author: Dr César Bimbi *cbimbi@terra.com.br*

Our Dermatol Online. 2014; 5(4): 423-425 Date of submission: 12.06.2014 / acceptance: 04.08.2014

Abstract
Even tiny despicable skin signs may eventually unveil systemic illnesses enabling a prompt start of medication and better prognosis. Here, we present a case of a 28-year-old female patient who came to the office complaining of a „minor irritation" on the left eyebrow that was a discrete and asymptomatic 5mm infiltrated apple jelly coloured papule that had started 6 months earlier. Biopsy of a second similar lesion discovered on left forearm showed granulomatous features of sarcoidosis.
Under subsequent systemic investigation, the presence of sarcoidosis in other organs was found to be positive as stage II pulmonary sarcoidosis, and also with reticulo-endothelial involvement manifested by enlarged mediastinal lymph nodes.
This case highlights the skin as a mirror to internal multisystemic disease and also the importance of investigating even small and discrete lesions with care and in depth.

Key words: sarcoidosis; differential diagnosis; seborrheic dermatitis

Cite this article:
Bimbi C. Sarcoidosis mimicking seborrheic dermatitis: another case of Sherlockian Dermatology. Our Dermatol Online. 2014; 5(4): 423-425.

Introduction

Sarcoidosis is a systemic disorder that can involve almost any organ system but especially the lungs, lymph nodes, liver, spleen and eyes. Between 20% and 35% of patients with systemic sarcoidosis have various forms of skin involvement [1]. The clinical course of sarcoidosis is progressive with frequent remissions and relapses [2] Granulomatous infiltrates in the skin may present on diverse morphology of which few are specific for the disease. They are not only common but may be the initial presentation of the systemic inflammatory process and provide a visible clue to the diagnosis being also an easily accessible source of tissue for histologic examination [3]. Cutaneous sarcoidosis si considered among the "great imitators" in dermatology [4]. Erythema nodosum is the typical non-specific skin lesion and is often associated with an acute presentation and generally portends a good prognosis. Papules, plaques, nodules, lupus pernio and scar infiltration among others are the specific presentations and mostly tend to be chronic therefore treatment is mandatory [5]. Another forms of presentations and differential diagnoses include granulomatous rosácea; acne; benign appendageal tumours; psoriasis, lichen planus, nummular eczema, discoid lupus erythematosus, granuloma annulare cutaneous T-cell lymphoma, secondary syphilis, Kaposi's sarcoma, lupus pernio discoid lupus erythematosus, scar furunculosis, cellulitis and inflammatory panniculitis [6].

Case Report

A 28-year-old female patient presented with a discrete and isolated 5mm infiltrated papule on the eyebrow (Fig. 1) that had started within a period of 6 months.
Cutaneous examination revealed presence of also another asymptomatic infiltrated apple jelly coloured papule (Fig. 2) on the left forearm. Punch biopsy was proceeded and showed confluent non-caseating granulomas with epithelioid cells and few lymphocytes, with negative staining for tuberculosis and fungi (Fig. 3).
Clinical investigation was initiated. When first asked, she replied negatively with regard to respiratory symptoms, but following further questioning, she remembered a persistent dry cough and exertional dyspnoea that had been happening over a period of some months. Her past medical history, personal, occupational and family histories were insignificant.
Peripheral lymph nodes were not enlarged. Clinical examination of cardiovascular, respiratory and neurological systems were normal. The hematological and bio-chemical liver and kidney function tests were normal but urinary calcium was slightly increased.

Erythrocyte sedimentation rate was normal. Contrast enhanced computed tomography of chest revealed enlarged lymph nodes in the mediastinum and involvement of the pulmonary parenchyma consistent with stage II of pulmonary sarcoidosis [7,8] (Figs 4A and B). Spirometry and abdominal ultrasound scan were normal.

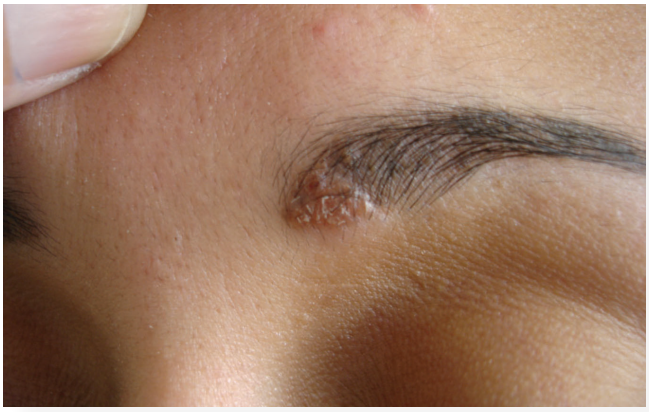


Figure 1. Discrete millimetric seborreic-like eyebrow lesion.

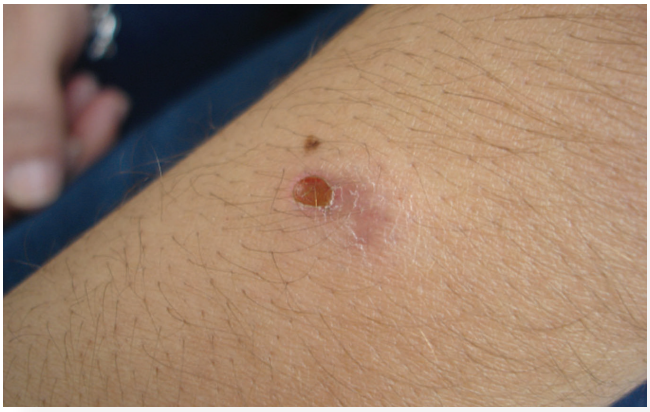


Figure 2. After biopsy of the left forearm lesion.

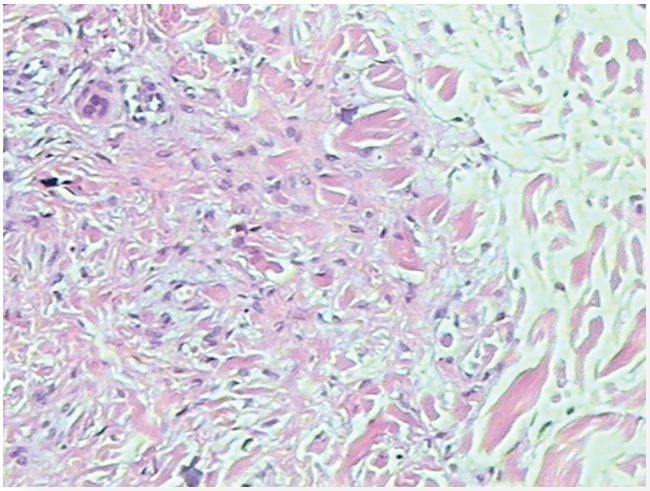


Figure 3. Histopathology: confluent non-caseating granulomas with epithelioid cells and few lymphocytes. Stainings for tuberculosis and fungi were negative.

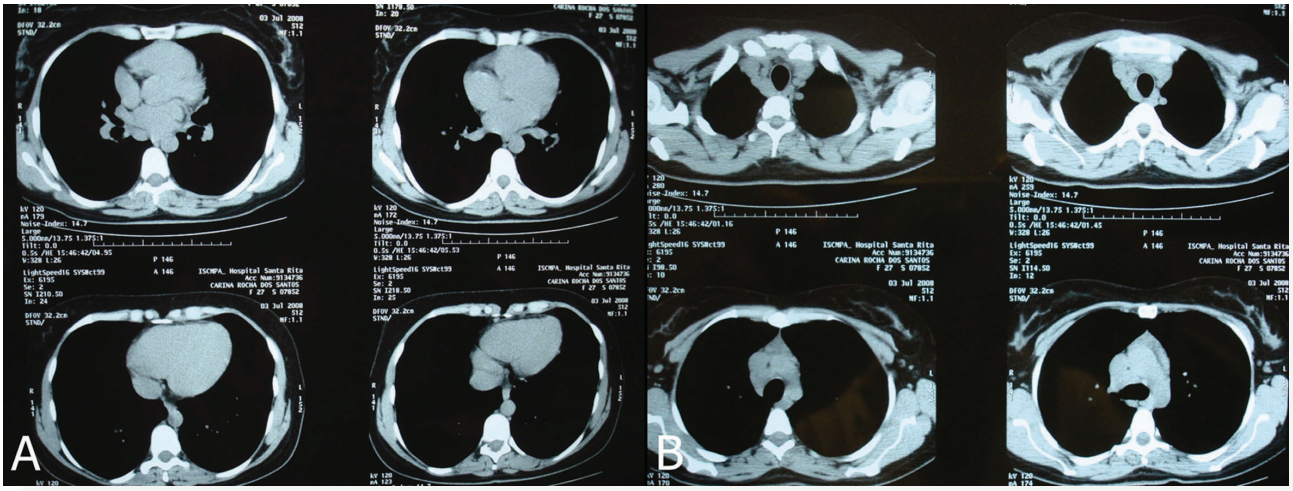


Figure 4 A and B. The patient had stage II pulmonary sarcoidosis as well as reticulo-endothelial system involvement manifested by enlarged mediastinal lymph nodes.

Discussion

Sarcoidosis is a multisystemic granulomatous disorder that affects primarily the lungs and lymphatic tissues. Cutaneous involvement may be the first indication of its presence in other organs. Pulmonary sarcoidosis leads to restrictive lung function impairment with a variable prognosis ranging from a self-limiting course (60%) to progressive fibrosis (10–30 %) with currently no good predictor of outcome [9]. A wide variety of morphologic forms of cutaneous sarcoidosis are possible, although many of these are extremely rare.

Although no breathing issues were raised by this patient until she was asked more specifically, 90% of patients have pulmonary involvement although half of them are usually asymptomatic.

Early investigation of cardiac sarcoidosis is also critical because sudden death can be the initial presentation [10].

The skin is said to mirror internal disease. Various systemic illnesses manifest in the skin and skin offers the advantage of easy access for biopsy and the possibility of early diagnosis and better prognosis.

Recent over emphasis of dermatology on cosmiatric subjects may lead to lack of interest on the investigative aspects. In every dermatologist, there should be something of the detective to put the pieces together by posing the right questions at the right time, and more than that, to have an open mind for seemingly unimportant details [11,12].

Keen observation, intense inspection of the subject, attention to details and apparent trifles, so much emphasised by Sherlock Holmes, are particularly pertinent to the dermatologist. In Sherlock Holmes, the early master detective, there was something of the dermatologist [11].

The early diagnosis was of substantial benefit to the patient in that with just 40mg of prednisone [13] for a short period of time, respiratory symptoms, skin lesion and reticulo-endothelial pathological findings disappeared.

This case hightlights the importance of close inspection of even tiny, otherwise unimportant lesions, that often represents just the tip of the iceberg. Also, adds seborrheic dermatitis to the extensive list of differential diagnosis of cutaneous sarcoidosis.

REFERENCES

1. Johns CJ, Michele TM. The clinical management of sarcoidosis: a 50-year experience at the Johns Hopkins Hospital. Med (Baltimore). 1999;78:65-111.
2.Thomas KW, Hunninghake GW. Sarcoidosis. JAMA. 2003;289:3300-3.
3. Katta R. Baylor College of Medicine, Houston, Texas. Am Fam Physician. 2002;65:1581-5.
4. Tchernev G. Cutaneous sarcoidosis: the „great imitator": etiopathogenesis, morphology, differential diagnosis, and clinical management. Am J Clin Dermatol. 2006;7:375-82.
5. Gawkrodger DJ. Sarcoidosis. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. Vol 3. 7th ed. Oxford: Blackwell Science; 2004. p. 58.1-24.
6. Pandhi D, Sonthalia S, Singal A. Mortimer's Malady revisited: a case of polymorphic cutaneous and systemic sarcoidosis. Indian J Dermatol Venereol Leprol. 2010;76:448.
7. Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med. 2001;164:1885-9.
8. Baughman RP, Lynch JP. Difficult treatment issues in sarcoidosis. J Internal Med. 2003;253:41-5.
9. Remy JM, Beuscart R, Sault MC, Marquette CH, Remy J. Subpleural micronodules in diffuse infiltrative lung diseases: evaluation with thin-section CT scans. Radiology. 1990;177:133–39.
10. Schuller JL, Olson MD, Zipse MM, Schneider PM, Aleong RG, Wienberger HD, et al. Electrocardiographic characteristics in patients with pulmonary sarcoidosis indicating cardiac involvement. J Cardiovasc Electrophysiol. 2011;22:1243-8.
11. Sherlock Holmes, Esq., and John H. Watson, M.D.: An Encyclopaedia of Their Affairs William Blake Gibson. Arch Dermatol. 1963;88:240-1.
12. Oderwald A, Sebus J. The physician and Sherlock Holmes. J Royal Society Med. 1991;84:151-2.
13. Paramothayan S, Jones PW. Corticosteroid therapy in pulmonary sarcoidosis: a systematic review. JAMA. 2002;287:1301–07.

DOI: 10.7241/ourd.20144.107

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

DEEP VARIANT OF ERYTHEMA ANNULARE CENTRIFUGUM

Ahu Yorulmaz[1], Ferda Artuz[1], Devrim Tuba Unal[2]

[1]*Department of Dermatology, Ankara Numune Research and Training Hospital, Samanpazari, Altindag, Ankara, Turkey*
[2]*Department of Pathology, Ankara Numune Research and Training Hospital, Samanpazari, Altindag, Ankara, Turkey*

Corresponding author: Dr Ahu Yorulmaz *ahuyor@gmail.com*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 426-427 Date of submission: 15.07.2014 / acceptance: 29.08.2014

Cite this article:
Yorulmaz A, Artuz F, Unal DT. Deep variant of Erythema Annulare Centrifugum. Our Dermatol Online. 2014; 5(4): 426-427.

A 29-year-old woman came to our outpatient clinic with a several-month history of itchy red lesions over her trunk. There was no family history and past history of any other diseases or medication. Dermatological examination revealed annular and oval-shaped plaques up to several cm's in size, one of which was polycyclic in configuration, on back of the patient (Fig. 1). It was also noticed that lesions had erythematous indurated bordes with paler central areas (Fig. 1). In addition there was an erythematous, firm, solitary papule with prominent pallor on the centrum of one of the large plaques which was situated on the right posterior thoracic area (Fig. 2). A lesional skin biopsy demonstrated superficial and deep perivascular 'sleeve-like' lymphohistiocytic infiltrate (Figs 3, 4). Laboratory investigations including complete blood count and differential, erythrocyte sedimentation rate, serum chemistry profile, urinalysis, thyroid panel, chest X-ray, antinuclear antibodies, antibodies against borrelia, cultures for fungi, purified protein derivative test, screening for anti-HIV were within normal limits and malignancy workup was negative.

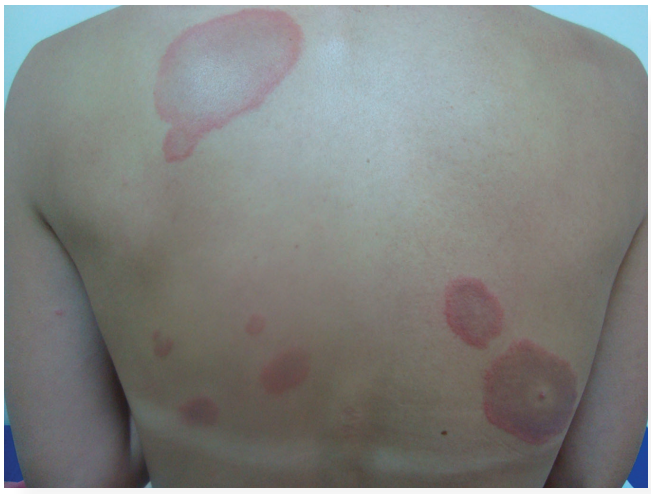


Figure 1. Erythematous oval, annular and polycyclic plaques with central paling on back of the patient.

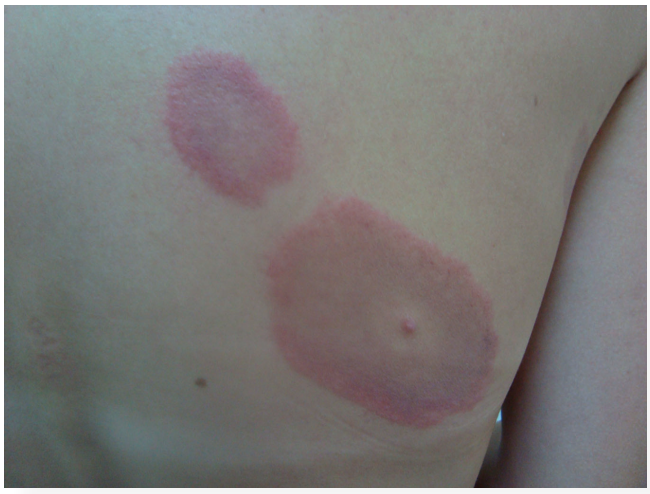


Figure 2. Two oval-shaped plaques with their long axes parallel to Langer's cleavage lines on right posterior thoracic area and apparent central fading especially on the inferior lesion with centric solitary papule.

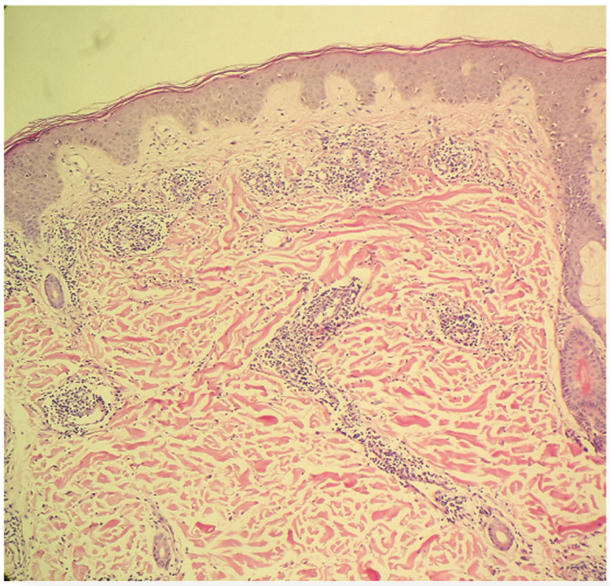


Figure 2. Superficial and deep perivascular mononuclear cell infiltrate. (H&Ex100)

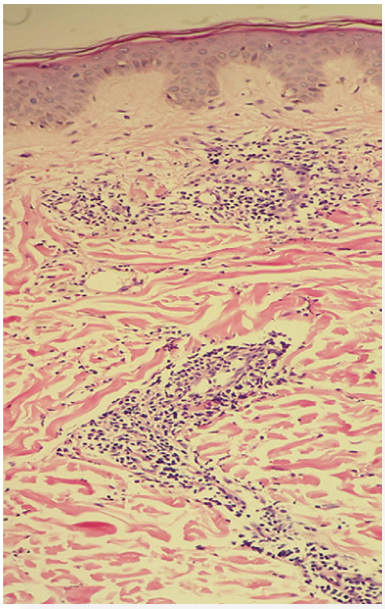


Figure 2. 'Coat sleeve-like' lymphocytic infiltrate around superficial and deep blood vessels. (H&Ex200)

Discussion

Erythema annulare centrifugum (EAC) is a type of gyrate erythema which is considered as a reaction pattern of several underlying etiological factors [1-4]. Originally described by Darier [5], EAC essentially represents annular, indurated, erythematous lesions [3]. However after Darier's original description, EAC has been divided into two clinical subtypes, superficial and deep variants. While supeficial type is typically characterized by scaly, slightly elevated erythematous lesions, deep variant is recognized as nonscaly, apparently elevated plaques with indurated borders. Analogous to deep variant's firm, indurated border, the scale of superficial type is typical and known as peripheral trailing scale, since initial lesions gradually enlarge leaving a peripheral ridge of scale that typically trails behind the advancing edge of erythema. Indeed, EAC consistently begins as a small, firm papule slowly expanding into annular, polycyclic lesions with central clearing. As the lesions extend centrifugally, the innermost area flattens and fades [1-4,6]. The underlying etiologies can rarely be established and EAC generally runs a chronic and recurrent course without evidence of significant response to treatment [1,2].

REFERENCES

1. Weyers W, Diaz-Cascajo C, Weyers I. Erythema annulare centrifugum: results of a clinicopathologic study of 73 patients. Am J Dermatopathol. 2003;25:451-62.
2. Cox NH, Coulson IH. Systemic Disease and the Skin. In: Burns T, Breathnach S, Cox N, Grittiths C, eds. Rook's Textbook of Dermatology. 8 th ed. Oxford: Wiley—Blackwell; 2010. p.62.110-112.
3. Bressler GS, Jones RE Jr. Erythema annulare centrifugum. J Am Acad Dermatol. 1981;4:597-602.
4. Ziemer M, Eisendle K, Zelger B. New concepts on erythema annulare centrifugum: a clinical reaction pattern that does not represent a specific clinicopathological entity. Br J Dermatol. 2009;160:119-26.
5. Darier J. De l'erytheme annulaire centrifuge. Ann Dermatol Syphilol. 1916;6:57–76.
6. Nayak SU, Shenoi SD, Prabhu SM. Erythema annulare centrifugum: deep variant with vasculitis like histopathology. Indian J Dermatol. 2013;58:329.

DOI: 10.7241/ourd.20144.108

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

A METH MOUTH CASE

Jerry E. Bouquot[1,2,3]

[1]Department of Diagnostic & Biomedical Sciences, University of Texas School of Dentistry at Houston, Houston, Texas 77054
[2]Department of Rural Health & Community Dentistry, Past Chair of the Department of Oral & Maxillofacial Pathology, West Virginia University School of Dentistry, Morgantown, WV 26506, USA
[3]Director of Research, The Maxillofacial Center for Education & Research, 212 Tibbs Road, Morgantown, WV 26508

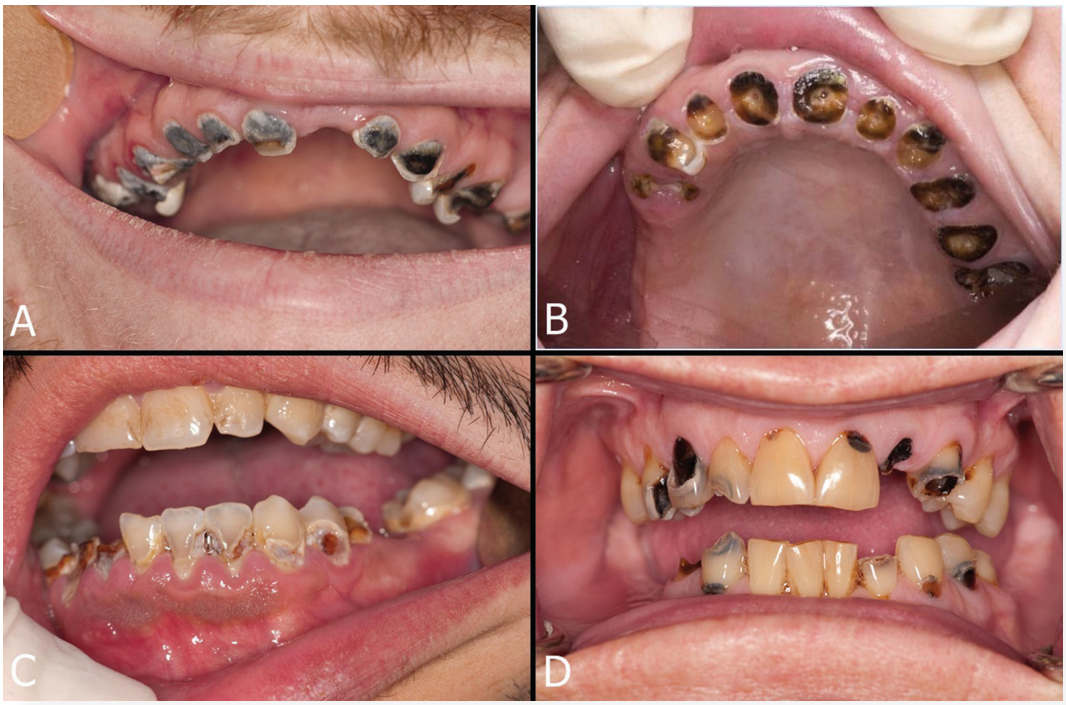
Corresponding author: Prof. Jerry E. Bouquot Jerry.Bouquot@uth.tmc.edu

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 428 Date of submission: 27.05.2014 / acceptance: 18.07.2014

Cite this article:
Bouquot JE. Meth mouth case. Our Dermatol Online. 2014; 5(4): 428.

Darkly discolored, cariously destroyed teeth were „normal" 18 months previously. Methamphetamine, plus the lack of oral hygiene and craving for sweet foods and drinks, can destroy teeth in adults more rapidly than any other process.



Figures 1A - D. patients with darkly discolored, cariously destroyed teeth caused by long-term use of methamphetamine.

DOI: 10.7241/ourd.20144.109

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

MARJOLIN'S ULCER

Niloofar Mehrolhasani

Department of Dermatology, Kerman Medical University, Iran

Corresponding author: Dr Niloofar Mehrolhasani *mehrolhasaniniloofar@gmail.com*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 429 Date of submission: 24.07.2014 / acceptance: 29.08.2014

Cite this article:
Mehrolhasani N. Marjolin's Ulcer. Our Dermatol Online. 2014; 5(4): 429.

A 45 years old man who had sustained a burn injury to his right hand 20 years ago come to our dermatology clinic with complaint of a rapidly growing fungating mass in burn scar from 4 months ago (Fig. 1). A biopsy of the mass revealed invasive squamous cell carcinoma consistent with Marjolin Ulcer (Fig. 2). The patinet underwent wide local excision and placement of a split thickness skin graft. No evidence of tumor was identified in the sentinel lymph nodes.

MU is a rare and aggressive cutaneous malignant transformation with an incidence of 0.1% to 2.5% after a long-term inflammatory or traumatic insult to the skin [1,2]. The main etiology tends to be post-burn scars and traumatic wounds [3]. Since biopsy remains the gold standard for the diagnosis of MU, it should be applied for suspicious lesions that have not healed in 3 months [4]. MU is more aggressive than primary skin tumors, therefore nodal assessment and wide surgical excision are recommended [5]. This potentially fatal complication may be preventable and treatable by surgical management of initial injuries and early diagnosis and treatment of unhealed ulcers [4].

REFERENCES

1. Dupree MT, Boyer JD, Cobb MW. SC arising in a burn scar. Cutis. 1998;11:49–51.
2. Gül U, Kiliç A. Squamous cell carcinoma developing on burn scar. Ann Plast Surg. 2006;11:406–8.
3. Kerr-Valentic MA, Samimi K, Rohlen BH, Agarwal JP, Rockwell WB. Marjolin's ulcer: modern analysis of an ancient problem. Plast Reconstr Surg. 2009;11:184–91.
4. Yu N, Long X, Lujan-Hernandez JR, Hassan KZ, Bai M, Wang Y, et al. Marjolin's ulcer: a preventable malignancy arising from scars. World J Surg Oncol. 2013;11:313.
5. Copcu E. Marjolin's ulcer a preventable complication of bums. Plast Reconstr Surg. 2009;11:156e–64e.

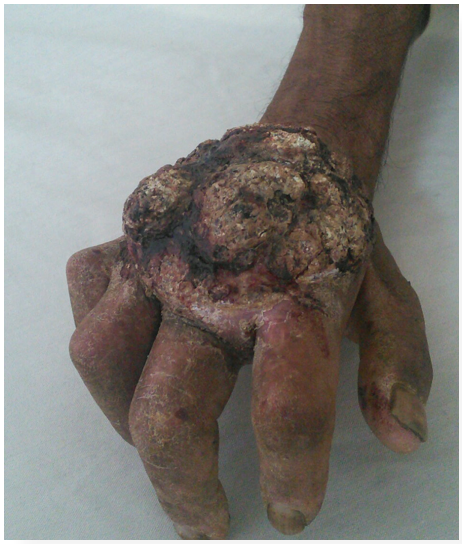


Figure 1. Rapidly growing fungating and necrotic mass in burn scar.

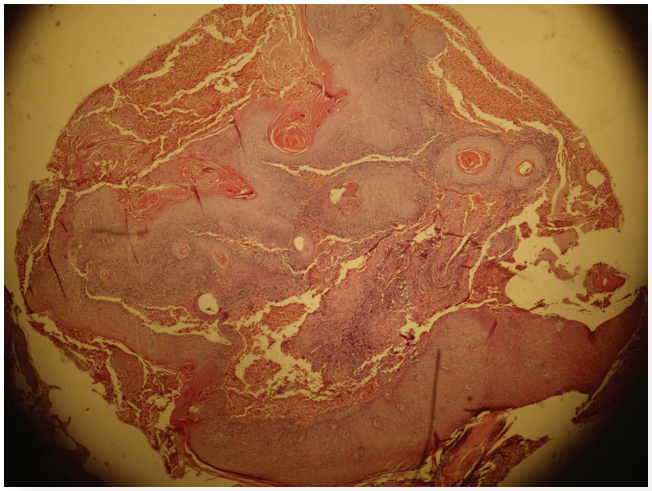


Figure 2. Haphazardly oriented lobules of atypical keratinocytes with an infiltrative growth pattern within the dermis. Some lobules show formation of squamous pearl.

DOI: 10.7241/ourd.20144.110

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

LAPTOP-INDUCED ERYTHEMA AB IGNE - A CASE REPORT

Cesar Bimbi[1], Piotr Brzezinski[2]

[1]*Member of Dermatological Comittee of State Medical Council of Rio Grande do Sul Brazil, Brazilian Society of Dermatology*
[2]*Department of Dermatology, 6th Military Support Unit, Ustka, Poland*

Corresponding author: Dr. Cesar Bimbi *cbimbi@terra.com.br*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 430-431 Date of submission: 21.07.2014 / acceptance: 03.09.2014

Cite this article:
Bimbi C, Brzezinski P. Laptop-induced Erythema ab Igne - a case report. Our Dermatol Online. 2014; 5(4): 430-431.

Introduction

Erythema ab igne is now more commonly related to heating pads, water bottles, infrared lamps and laptop computer use with skin contact. Heat damages superficial skin vessels leading to vasodilatation and leakage of blood and deposition of hemosiderin that presents in a net form. Any surface of the body is susceptible but mostly lower limbs, lower back and abdomen areas are affected.

Case Report

A 8-year-old boy presented with a four month history of dark brown pigmentation only to the anterior aspects of right and left thighs, symetrically (Fig 1). The distribution was reticular, the lesions were not blanchable and there were no symptoms.
There was no need of biopsy since clinical diagnosis of erythema ab igne was obvious.
His mother mentioned the fact of him using laptop positioned atop thighs (Fig. 2). Using his anterior thighs to prop up his laptop - and she added the fact that he used to work on his computer in that position several hours and every day.

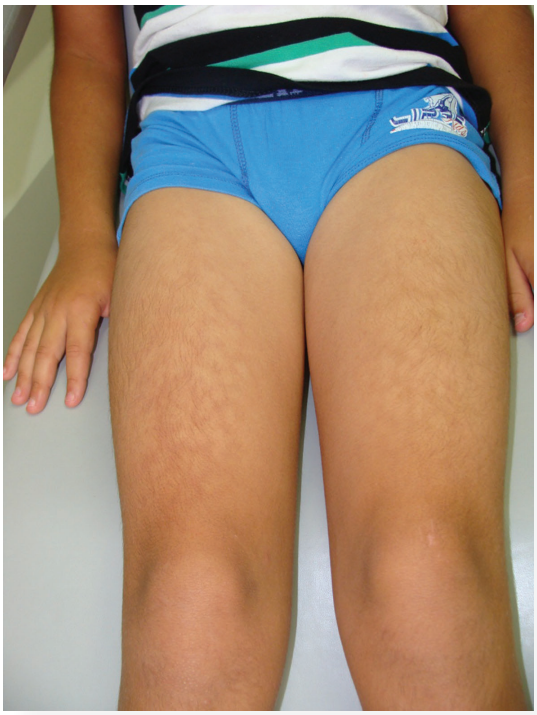


Figure 1. Dirty appearing eruption of reticulate violaceous brown patch on anterior thighs.

Figure 1. Laptop positioned atop thighs in a 8-year-old boy.

Discussion

Erythema ab igne is rare and not commonly seen on daily practice. It was once related to standing long periods of time in front of open fires or stoves to warm the body or using water bottles or heating pads for chronic backache. With introduction of heating systems it turned out to be a rare condition at least in developed countries. Bakers and foundrymen are at occupational risk. Heat damages superficial skin vessels leading to vasodilatation and leakage of blood with deposition of hemosiderin that presents in a net form [1]. It is very characteristic and one of those clinical features that deserves dermatologycal saying that "once seeing, never forgotten". Nevertheless, Livedo Reticularis [2] can be a point of confusion but then the changes are to be strictly symetrical and telangiectatic.

Laptop use is a modern inducer of this reaction [3,4]. Concentrated infrared radiation at the bottom of the laptop heats the skin only

not enough to burn it but sufficient to affect skin superficial vessels. With the passage of time, the repeated heating leads to Erythema ab igne [5,6].

Always good to keep in mind that heat damage has been also associated with skin cancer and Merkel carcinoma. There may be epithelial cellular atypia resembling actinic damage, and some cases eventually go to thermal keratosis and squamous cell carcinomas [7,8].

Educate patients on avoiding prolonged laptop to thigh contact is essential. With removal of the heat source from the skin, no further treatment is required.

The skin changes usually clear spontaneously in several weeks to months, if the repeated exposure to heat is discontinued.

REFERENCES

1. Poustinchian BR, Pohlman DJ. Erythema ab igne. J Am Osteopath Assoc. 2012;112:808.
2. Riahi R, Cohen P, Robinson F, Gray J. Erythema ab igne mimicking livedo reticularis. Int J Dermatol. 2010;49:1314-7.
3. Billic M, Adams BB. Erythema ab igne induced by a laptop computer. J Am Acad Dermatol. 2004;50:973–4.
4. Erythema ab igne caused by laptop computer gaming--a case report. (English) By: Fu LW; Vender R, International Journal Of Dermatology [Int J Dermatol], ISSN: 1365-4632, 2012 Jun; Vol. 51 (6), pp. 716-7; Publisher: Blackwell Science; PMID: 22607292
5. Botten D, Langley R, Webb A. Academic branding: erythema ab igne and use of laptop computers. Canadian Med Assoc J. 2010;182:E857.
6. Bachmeyer C, Bensaid P, Bégon E. Laptop computer as a modern cause of erythema ab igne. J Eur Acad Dermatol Venereol. 2009;23:736-73.
7. Brzezinski P, Ismail S, Chiriac A. Radiator-induced erythema ab igne in 8-years-old girl. Rev Chil Pediatr. 2014;85:239-41.
8. Hewitt JB, Sherif A, Kerr KM, Stankler L. Merkel cell and squamous cell carcinomas arising in erythema ab igne. Br J Dermatol. 1993;128:591-2.

DOI: 10.7241/ourd.20144.111

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

PYODERMA GANGRENOSUM TRIGGERED BY SURGICAL PROCEDURES IN PATIENTS WITH UNDERLYING SYSTEMIC DISEASES

Tomoko Hiraiwa, Hirotoshi Furukawa, Toshiyuki Yamamoto

Department of Dermatology, 1Fukushima Medical University, and 2Hoshi General Hospital, Fukushima, Japan

Corresponding author: Dr. Tomoko Hiraiwa tmk429313@yahoo.co.jp

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 432-433 Date of submission: 13.08.2014 / acceptance: 20.09.2014

Cite this article:
Hiraiwa T, Furukawa H, Yamamoto T. Pyoderma gangrenosum triggered by surgical procedures in patients with underlying systemic diseases. Our Dermatol Online. 2014; 5(4): 432-433.

Introduction

Pyoderma gangrenosum (PG) is a disease characterized by refractory, sterile, deep ulcers, predominantly in the extremities, occasionally in association with several systemic diseases. We herein describe three cases of PG, which were triggered by iatrogenic or surgical procedures in patients with acute myeloid leukemia, Takayasu's arteritis (TA), and ulcerative colitis, respectively.

Case Report

Case 1

A 68-year-old female was diagnosed with acute myeloid leukemia, and hospitalized for chemotherapy. A central venous catheter was inserted into her chest. A few days later, erythema appeared at the site of insertion, which spread rapidly with redness and swelling. Initial treatment with antibiotics was ineffective, and she was referred to our department. Physical examination revealed a well-circumscribed, large deep ulceration with ring-shaped, elevated edematous borders (Fig. 1), and a reddish granulated surface. Skin biopsy from the edge of the ulcer showed dense neutrophilic infiltration in the dermis as well as the epidermis. Vasculitis was not noted. Laboratory tests showed increased levels of C-reactive protein (CRP; 6.5 mg/dl), anemia, leucopenia and thrombocytopenia due to chemotherapy. Bacterial culture of the ulcer was negative. We therefore diagnosed the patient with pyoderma gangrenosum triggered by catheter insertion. She was successfully treated with oral prednisolone (30 mg/day).

Case 2

A 28-year-old Japanese man was seen in a hospital complaining of fever and diarrhea lasting 5 to 6 days. Laboratory findings showed leukocytosis in the peripheral blood (25.47×103/µl) and an increase of CRP (30.47 mg/dl). He was admitted to our hospital and treated with antibacterial agents for suspected infection, which was ineffective. A few days later, contrast enhanced CT results showed that there was a circumferential thickening of the vessel wall from the ascending aorta to the aortic arch, a part of the descending aorta, brachiocephalic artery, and left common carotid artery. He was then diagnosed with TA, and treatment with steroid pulse therapy and anticoagulant therapy with heparin was begun. During admission, he had complained of an abscess formation and painful subcutaneous induration on his left arm at the site where a drip was inserted (Fig. 2). A puncture and drainage resulted in deep ulceration. Bacterial culture was proved aseptic.

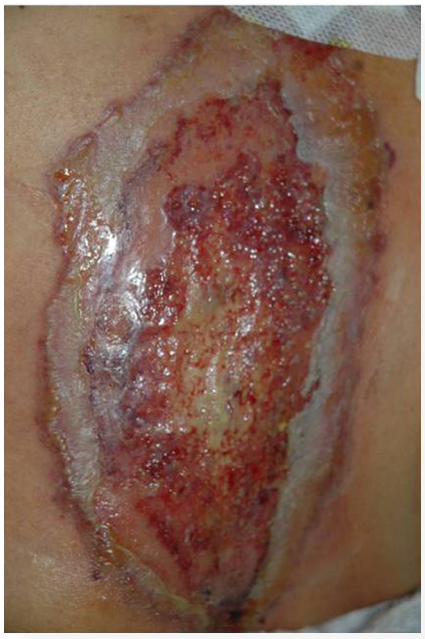


Figure 1. Pyoderma gangrenosum lesion showing large ulceration surrounded with edematous borders and erythema.

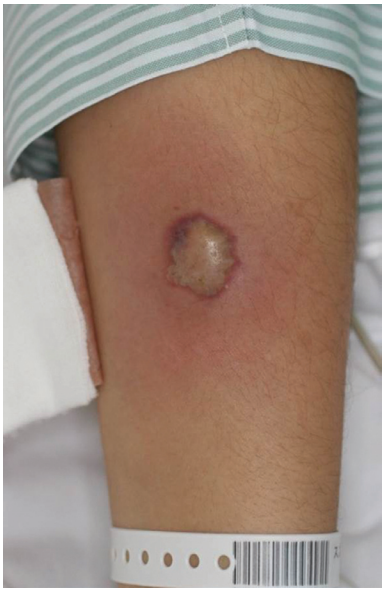


Figure 2. Large abscess formation at the site of intravenous infusion on the forearm.

Case 3

A 75-year-old male was suffering from ulcerative colitis for 2 years. He got operation for left inguinal hernia, at this time he was treated with prednisolone (15 mg per day). Three weeks later, the operation scar was ulcerated and got enlarged. Laboratory examination showed increased levels of white blood cells (34,000/μl) and CRP (14.3 mg/dl). Bacterial cultures were negative. Physical examination showed a deep ulceration covered with necrotic tissues, with erythematous borders on the left lower abdomen (Fig. 3). Histological examination revealed a number of neutrophilic infiltration in the dermis. He was successfully treated with hydrocortisone sodium succinate pulse therapy (500 mg/day for 3 days).

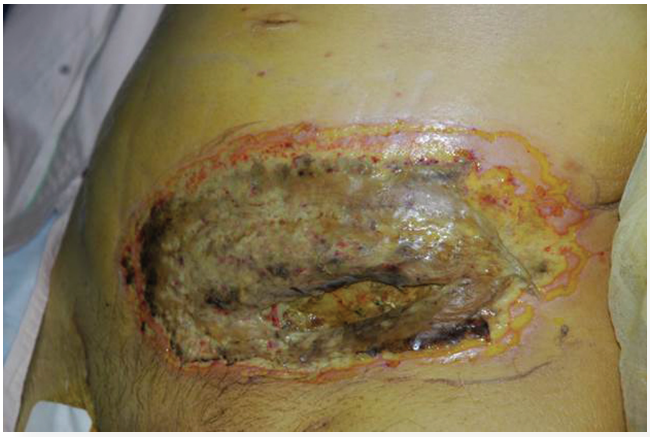


Figure 3. Deep ulceration covered with necrotic tissues bordered by edematous ring.

Discussion

There are several reports of PG occurring at percutaneous surgical sites, after procedures such as breast surgery, pacemaker implantation, splenectomy, hysterectomy, endoscopic tube insertion, cholecystectomy, appendectomy, and cesarean delivery [1]. In the present study, Case 1 was suffering from leukemia. He underwent central vein catheter insertion, which rapidly developed into PG. Similar cases have been reported which were triggered by injection of interferon [2] or tattoo placement [3] in patients with leukemia. Occasionally, PG is the initial presentation prior to the onset of leukemia, however the pathogenic link between PG and leukemia remains poorly understood. Case 2 had TA, who developed a large abscess at the infusion site of an intravenous drip in the forearm that resulted in deep ulceration after puncture. TA is characterized by stenosis or occlusion affecting mainly the aorta and its branches in young women. Several kinds of cutaneous manifestations are occasionally seen in association with TA, with representative lesions such as erythema nodosum and PG. To date, the association of PG and TA has not been frequently reported. PG occurring in patients with TA usually involves the upper limbs, followed by the scalp, face, neck, trunk, buttocks, and pubic region, in addition to the lower limbs [4]. Inflammatory cytokines, such as TNF-α, are considered to play an important role in the pathogenesis of TA. Recent studies have shown that TNF-α targeting therapies are effective for both TA [5] and PG [6], suggesting possible pathogenic similarities between these disorders. Case 3 developed PG following surgical operation of hernia. Cases of postoperative PG following hernia operation have been reported [7, 8]. Such phenomena are called pathergy, which means hyper-reactivity of the skin in response to even minor trauma. Pathergy can be seen in about 20% of cases [9]. The mechanism is still unknown, however, an aberrant immune response to minor trauma, defective cell-mediated immunity, aberrant integrin oscillations on neutrophils and abnormal neutrophil tracking, have been speculated. Because the majority of patients with PG have systemic disorders, development of PG triggered by surgical operation or iatrogenic procedures should be widely recognized.

REFERENCES

1. Kikuchi N, Hanami Y, Miura T, Kawakami Y, Satoh M, Ohtsuka M, Yamamoto T. Pyoderma gangrenosum following surgical procedures. Int J Dermatol. 2010;49:346-8.
2. Montoto S, Bosch F, Estrach T, Blade J, Nomdedeu B, Nontserrat E. Pyoderma gangrenosum triggered by alpha2b-interferon in a patient with chronic granulocytic leukemia. Leuk Lymphoma. 1998;30:199-202.
3. Jacobson S, Martin DB, Deng A, Cooper JZ. Pyoderma gangrenosum following tattoo placement in a patient with acute myelogenous leukemia. J Dermatol Treat. 2008;19:58-60.
4. Ujiie H, Sawamura D, Yokota K, Nishie W, Shichinohe R, Shimizu H. Pyoderma gangrenosum associated with Takayasu's arteritis. Clin Exp Dermatol. 2004;29:357-9.
5. Comarmond C, Plaisier E, Dahan K, Mirault T, Emmerich J, Amoura Z, et al. Anti TNF-α in refractory Takayasu's arteritis: cases series and review of the literature. Autoimmun Rev. 2012;11:678-84.
6. Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum: a comprehensive review. Am J Clin Dermatol. 2012;13:191-211.
7. Strauss A, Storim J, Germer CT, Dietz UA, Wildenauer R. Pyoderma gangrenosum as rare complication of incisional hernia repair in a patient with Werlhof's disease. Hernia. 2011;15:709-12.
8. Kotzampassakis N, Ksontini R. Pyoderma gangrenosum after inguinal hernia repair. Hernia. 2012;16:345-7.
9. Ruocco E, Sangiuliano S, Gravina AG, Miranda A, Nicoletti G. Pyoderma gangrenosum: an updated review. J Eur Acad Dermatol Venereol. 2009;23:1008-17.

DOI: 10.7241/ourd.20144.112

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

PRIMARY CUTANEOUS CD30 +ANAPLASTIC LARGE CELL LYMPHOMA; REPORT OF A SINGLE LARGE SCALP NODULE

Isha Parulkar[1], Jason Micheals[2], Gladys H.Telang[1]

[1]*Department of Dermatology, The Warren Alpert Medical School at Brown University, Providence, RI, USA*
[2]*Private Practice, Aspire Dermatology. Riverside, RI, USA*

Corresponding author: Dr. Gladys H. Telang *gtelangmd@verizon.net*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 434-436 Date of submission: 18.04.2014 / acceptance: 25.08.2014

Cite this article:
Parulkar I, Micheals J, Telang GH. Primary Cutaneous CD30 +Anaplastic Large Cell Lymphoma; Report of a single large scalp nodule. Our Dermatol Online. 2014; 5(4): 434-436.

Case Report

A 93-year -old Caucasian female presented with a 2-month history of a single frontal scalp nodule. The lesion was non-tender however had grown rapidly and was eroded with intermittent bleeding. There were no other skin lesions, lymphadenopathy, or hepatosplenomegaly. Past medical history was significant for breast cancer and review of systems was unremarkable. Physical exam revealed a 10cm x12cm exophytic, fungating, and malodorous tumor of the right frontal scalp (Fig. 1).

A biopsy was performed and revealed a dense diffuse CD30+ atypical lymphoid infiltrate, ulceration, and inflammation. Within the dermis there were sheets of large epithelioid and anaplastic lymphocytes with large vesicular nuclei, prominent one to few magenta nucleoli and ample cytoplasm (Figs. 2 and 3). A few dermal mitoses and numerous neutrophils were present. The large anaplastic lymphocytes were diffusely CD30+ (Fig. 4) and Vimentin positive. CD3 and lymphocyte common antigen were negative. CD4 and CD8 stained approximately 60% and 30% of the T-cells, respectively. Less than 1% B-cells were present and stained positively with CD20 and PAX-5. CD15 highlighted approximately 20-30% positivity on neutrophils and CD68 stained approximately 10% histiocytes within the dermis. These findings supported the diagnosis of CD30+ anaplastic large cell lymphoma. The ALK-1 negativity favored primary cutaneous CD30+ anaplastic large cell lymphoma (PCALCL). Evaluation for underlying systemic disease was advised and the patient declined. Polymerase chain reaction (PCR) study to detect T-cell antigen Beta gene rearrangement showed one band consistent with the expansion of a single clonal T-cell proliferation. PCR was negative for immunoglobulin heavy chain gene rearrangement.

The clinical, histologic, immunohistologic, and PCR findings support the diagnosis of PCALCL. The patient was notified of her diagnosis and treatment options including excision, chemotherapy, and local radiation were discussed. She opted for no treatment and passed away two weeks later. Although an evaluation for systemic disease was not achieved, we present and discuss this case based on our clinical and pathologic diagnosis of PCALCL.

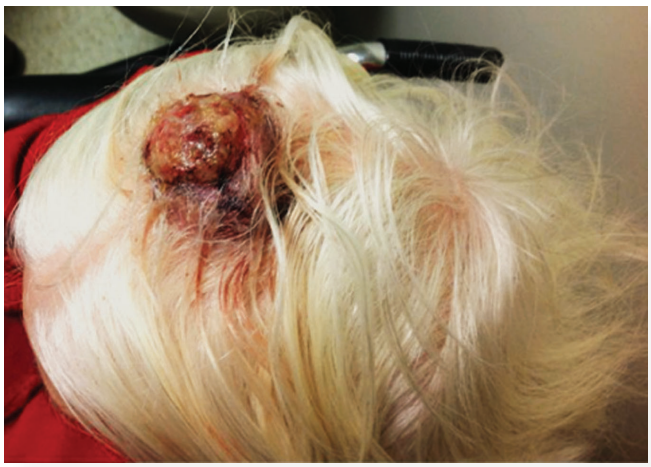


Figure 1. A large, exophytic, fungating tumor on the right frontal scalp.

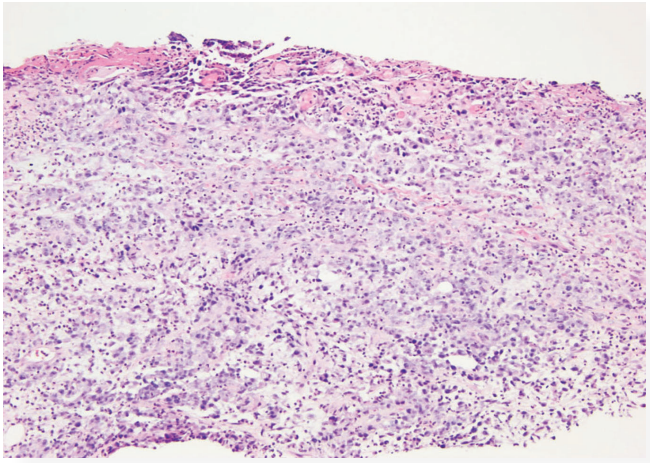


Figure 2. Sheets of large epithelioid and anaplastic lymphocytes with ample cytoplasms within the dermis. (hematoxylin eosin 10x)

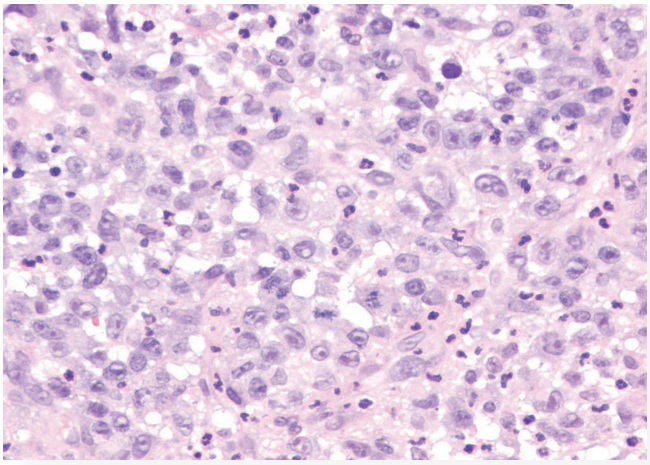


Figure 3. High power of the anaplastic and immunoblastic appearing lymphocytes, "hallmark cells", with prominent mitoses. (hematoxylin eosin, 40x)

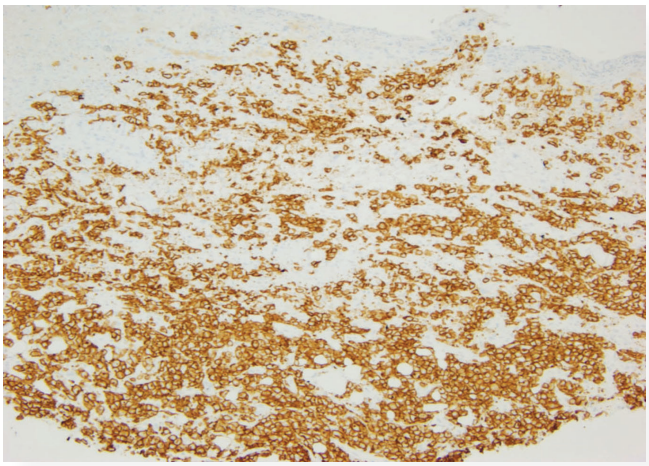


Figure 4. Numerous CD30 positive lymphocytes in dermis and subcutaneous fat. (immunoperoxidase stain, 10x)

Discussion

Primary cutaneous T-cell lymphomas (CTCL) are a clinically and histologically diverse group of non-Hodgkin lymphomas characterized by the aberrant proliferation of skin-homing T-lymphocytes. Together, they represent up to 75-80% of all cutaneous lymphomas [1]. Nearly a third of CTCL are accounted for by primary cutaneous CD30+ lymphoproliferative disorders, the most common subtypes of which are LyP (lymphomatoid papulosis) and PCALCL (primary cutaneous anaplastic large cell lymphoma) [2].

PCALCL are defined according to specific criteria: a) Predominance (>75%) of CD30+ large anaplastic cells on skin biopsy, b) absence of extracutaneous localization at presentation, c) no history or evidence of LyP, mycosis fungoides or cutaneous lymphoma [3,4].

The pathogenesis of PCALCL remains largely unknown [3]. A number of chromosomal imbalances (specifically gains on chromosomes 7q and 17q and losses on 6q and 13q) as well as amplification of several oncogenes have been found in patients with PCALCL [5,6]. The initial activation and clonal expansion of CD30+ T cells is thought to remain in check by an effective host immune response and can only progress when chromosomal alterations or a deficient host immune response confers a growth advantage to cells [7]. Cases in which the immune response remains intact may result in spontaneous regression of the lesion [7].

PCALCL are twice as common in males as in females and tend to present in middle age with median age of 55 at diagnosis [3,7-8]. Clinically, they present as asymptomatic solitary or localized nodules, plaques, or tumors with central ulceration that favor the trunk and extremities. Extracutaneous involvement is rare (occurring in 10% of patients with localized disease), and regional lymphadenopathy, though infrequently seen, is not a predictor of prognosis [6,8]. Though biopsy is conclusive, imaging studies such as CT scan of the head, chest, and abdomen, are necessary to stage the disease and rule out systemic involvement [4].

The histopathology of PCALCL consists of cohesive aggregates or sheets of large CD30 antigen-expressing, atypical lymphocytes in the dermis and subcutaneous fat. Occasionally, epidermotropism may be present [6,10-11]. Rare morphological variants include angioinvasive, neutrophil-rich, histiocyte-rich, and sarcomatoid forms [12-14]. More than 75% of the cellular infiltrates are comprised of "hallmark cells," so called because they are found in all types of anaplastic large cell lymphoma (ALCL) variants [11].

These lymphocytes are anaplastic, pleomorphic, or immunoblastic appearing, with abundant cytoplasm, frequent mitosis, irregular hyperchromatic and horseshoe-shaped nuclei and eosinophilic nucleoli [3,5,6,10]. Immunohistochemical screening reveals three immunophenotypes, the CD3+, CD4+ T-cell phenotype being the most frequent. Other subtypes include B-cell (CD20+) or null (CD3-, CD20-) [11]. A CD4+, CD3-, and CD20- phenotype was present in the case reported.

Immunohistochemical markers are essential to characterize subtypes of ALCL and determine prognosis [3]. Expression of the anaplastic lymphoma kinase (ALK) gene, representing the t(2;5)(p23;q35) translocation is typically absent in PCALCL but often encountered in systemic ALCL [6,9]. Rare cases of ALK+ primary cutaneous ALCL have been reported and are associated with a more aggressive course, similar to systemic ALCL [15]. In contrast, CD30 antigen positivity imparts a good prognosis [3,7]. Epithelial membrane antigen (EMA) expression is seen more frequently in systemic lymphoma and cutaneous involvement secondary to systemic ALCL [3,16].

Treatment options include surgical excision, localized radiotherapy, topical nitrogen mustard therapy, single and multiagent chemotherapy (most commonly Cyclophosphamide, Doxorubicin, Vincristine, Prednisone or CHOP) [4,5,7]. Local radiotherapy is the treatment of choice for solitary lesions [7]. Patients with multifocal lesions may require more aggressive treatment modalities such as systemic chemotherapy. Multi-agent chemotherapy should be reserved for patients who develop extracutaneous or methotrexate-resistant disease [5,7,9]. Novel, less toxic, alternatives include Brentuximab, an anti-CD30 monoclonal antibody drug conjugate that is shown to be effective in patients unsuitable for multi-agent chemotherapy [17]. The rare cases of ALK+ PCALCL could be suitable for treatment with the ALK inhibitor Crizotinib [15]. Prognosis for PCALCL is typically excellent with 10-year disease related survival exceeding 90% [18]. Longitudinal care is recommended in patients given the 10% risk of developing systemic lymphoma [7].

REFERENCES

1. Rosen ST, Querfeld C. Primary cutaneous T-cell lymphomas. Hematology Am Soc Hematol Educ Program. 2006;2006:323–30.
2. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105:3768–85.
3. Chao-Lo MP, King-Ismael D, Lopez RA. Primary cutaneous CD30+ anaplastic large cell lymphoma: report of a rare case. J Dermatol Case Rep. 2008;2:31-4.
4. Rao SD, Ravi R, Govindranajan M. Primary cutaneous CD30+ anaplastic large cell lymphoma. Indian J Srug. 2009;72:283-5.
5. Perry E, Karajgikar J, Tabbara I. Primary Cutaneous Anaplastic Large-cell Lymphoma. Am J Clin Oncol. 2013;36:526-9.
6. Kempf W, Kazakov DV, Kerl K. Cutaneous Lymphomas: An Update. Part 1: T-Cell and Natural Killer/T-Cell Lymphomas and Related Conditions. Am J Dermatopathol. 2014;36:105-23.
7. Willemze R, Meijer CJ. Primary cutaneous CD30-positive lymphoproliferative disorders.Hematol Oncol Clin North Am. 2003;17:1319–32.
8. Liu HL, Hoppe RT, Kohler S, Harvell JD, Reddy S, Kim YH. CD30+ cutaneous lymphoproliferative disorders: the Stanford experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. J Am Acad Dermatol. 2003;49:1049–58.
9. Shehan JM, Kalaaji AN, Markovic SN, Ahmed I. Management of multifocal primary cutaneous CD30 anaplastic large cell lymphoma. J Am Acad Dermatol. 2004;51:103–10.
10. Marrero-Calvo MD, Rodriguez-Serna M, Castejon-Calvete P, Pelaez-Malagon S. Primary Cutaneous Anaplastic CD30+ Large Cell Lymphoma. Actas Dermosifiliogr. 2007;98:194-7.
11. Stein H, Foss HD, Dürkop H, Marafioti T, Delsol G, Pulford K, et al. CD30(+) anaplastic large cell lymphoma: a review of its histopathologic, genetic, and clinical features.Blood. 2000;96:3681–95.
12. Burg G, Kempf W, Kazakov DV, Dummer R, Frosch PJ, Lange-Ionescu S, et al. Pyogenic lymphoma of the skin: a peculiar variant of primary cutaneous neutrophil-rich CD30+ anaplastic large-cell lymphoma. Clinicopathological study of four cases and review of the literature. Br J Dermatol. 2003;148:580-6.
13. Boudova L, Kazakov DV, Jindra P, Sima R, Vanecek T, Kuntscher V, et al. Primary cutaneous histiocyte and neutrophil-rich CD30+ and CD56+ anaplastic large-cell lymphoma with prominent angioinvasion and nerve involvement in the forehead and scalp of an immunocompetent woman. J Cutan Pathol. 2006;33:584-9.
14. Massone C, El-Shabrawi-Caelen L, Kerl H, Cerroni L. The morphologic spectrum of primary cutaneous anaplastic large T-cell lymphoma: a histopathologic study on 66 biopsy specimens from 47 patients with report of rare variants. J Cutan Pathol. 2008;35:46-53.
15. Lamant L, Pileri S, Sabattini E, Brugières L, Jaffe ES, Delsol G. Cutaneous presentation of ALK-positive anaplastic large cell lymphoma following insect bites: evidence for an association in five cases. Haematologica. 2010;95:449-55.
16. Mahalingam M, Bhawan J. Cutaneous anaplastic large cell lymphoma - a case report. Indian J Dermatol Venereol Leprol. 2004;70:168–171.
17. Desai A, Telang GH, Olszewski J. Remission of primary cutaneous anaplastic large cell lymphoma after a brief course of brentuximab vedotin. Ann Hematol. 2013;92:567-8.
18. Kocabas E, Ermertcan AT, Akinci S, Teniz P, Gunduz K. Primary cutaneous CD30-positive anaplastic large cell lymphoma in a 16-year-old girl. Int J Dermatol. 2012;51:1353-8.

DOI: 10.7241/ourd.20144.113

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

MYCOSIS FUNGOIDES – CASE PRESENTATION

Laura Statescu, Dan Vata, Laura Gheuca Solovastru

Dermatology Department, University of Medicine and Pharmacy "Grigore T. Popa" Iassy, Romania

Corresponding author: Dr Laura Statescu laura.statescu@yahoo.com

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 437-438 Date of submission: 18.04.2014 / acceptance: 20.09.2014

Cite this article:
Statescu L, Vata D, Solovastru LG. Mycosis fungoides – case presentation. Our Dermatol Online. 2014; 5(4): 437-438.

Sir,

Mycosis fungoides (MF) is a neoplastic disease of the lymphoreticular system with substrate of T lymphocyte hyperplasia and multifactorial etiology. Usual onset is around age 50, with skin lesions, and in advanced stages affects the internal organs.

Mycosis fungoides has specific histological feature: polymorphous infiltrate located in the papillary dermis which ends abruptly in the middle dermis.

Case Report

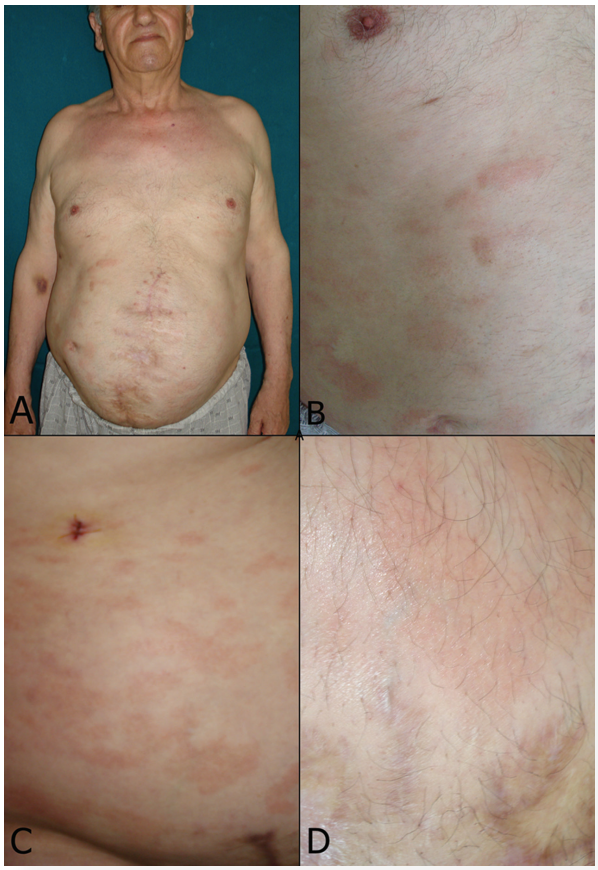
A 72 years old male, pensioner, from urban area, with insignificant heredo-collateral hystory, presented with multiples erythemato-squamous patches, with no pruritus, for six months. The lesiones were located initially on the abdomen, with a digitiform aspect and then were extended on the trunk and limbs (Figs 1A - D). There was no improvement under long-term use of corticosteroides, antifungal and antibacterian ointments. Pacient had no personal hystory of atopic dermatitis, causative drug intake or psoriazis. Eleven years ago he was diagnosticated with internal and external hemorrhoids and whitin the last two years he sufered 11 surgeries for appendicectomy complicated with peritonitis and eventrations. He was using girdle to sustain the abdomen.

The general examination revealed an enlarged abdomen, with generalized tenderness probe and multiple postoperative keloid scars, with difficult defecation and sometimes hematochezia.

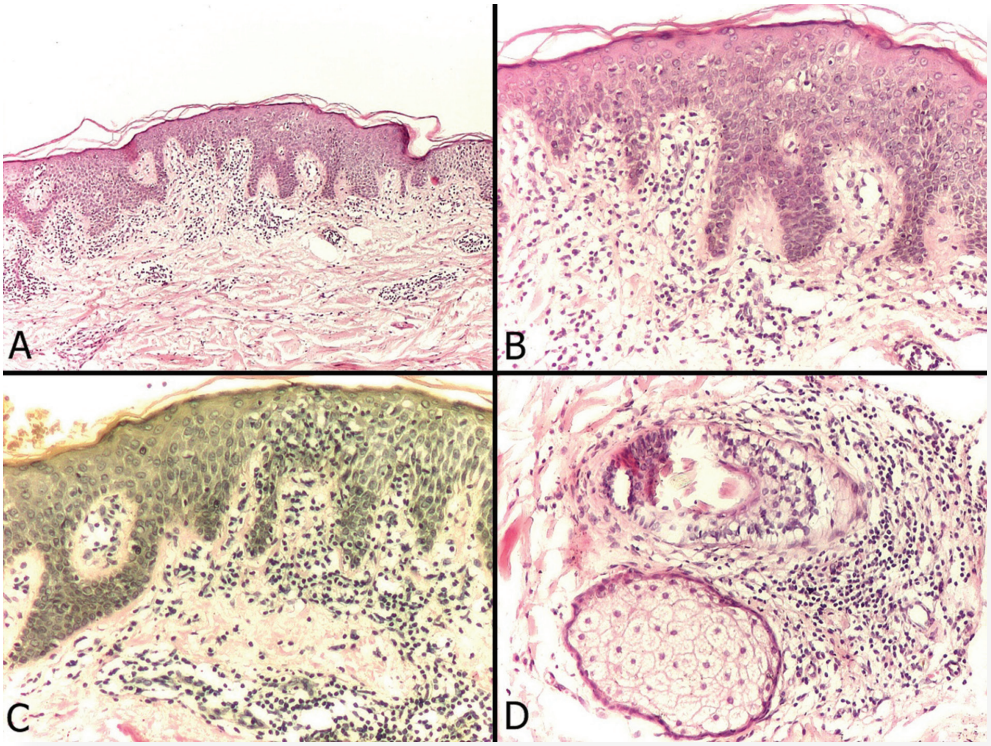
Routine investigations: normal blood and urine tests. Chest X-ray was normal. Abdominal ultrasound: massive aerocolie.

Skin biopsy showed: moderate lymphocytic infiltrate in the superficial dermis. Epidermo-tropism with some intraepithelial halo-Ly and tendency to aggregate (Figs 2A - D).

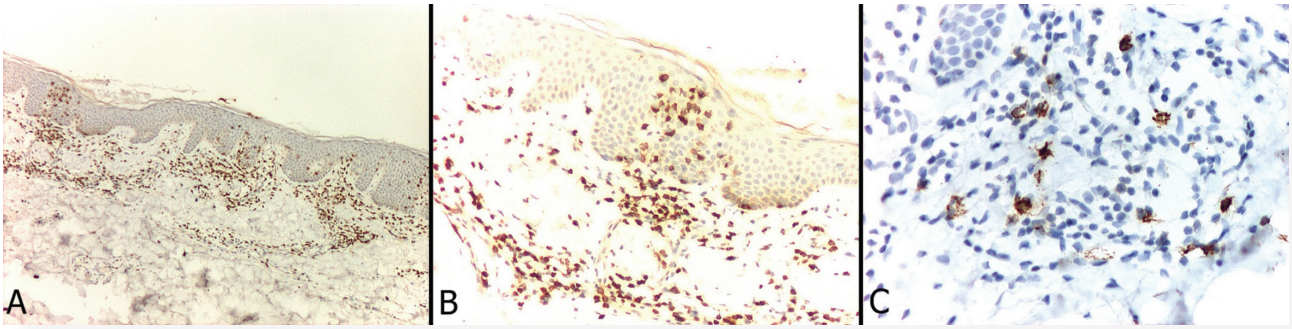
Immunohystochimie: CD20, CD3, CD4, CD8 Ly present in the dermis and rarely in the epidermis (Figs 3A - C).



Figures 1. Clinical images. (A). Enlarged abdomen, with multiple postoperative keloid scars; (B). Enlarged abdomen, with multiple postoperative keloid scars (detail); (C). Foto 3 Multiples erythemato-squamous patches diseminated on the abdomen; (D). Foto 4 Erythematous and scaly plaque, with digitiform aspect, located on the abdomen (detail).



Figures 2. Histopathology. (A). Acanthosis, with epithelial crisis hiperplasis and reduced ortokeratosis. H & E 4; (B). Histological examination reveal moderate dermal edema and lymphocitar inflammatory infiltrate, H & E x 10; (C). Moderate exocitosis with lymphocites, Van Gieson stain, x 10; (D). Chronic perifollicular inflammatory infiltrate, H & E x 10.



Figures 3. Immunohistochemistry. (A). Foto 9 Imunohistochemy reveal inflammatory infiltrate predominent CD3 positiv, x 4; (B). Imunohistochemy reveal inflammatory infiltrate predominent CD3 positiv, x 10; (C). Foto 11 Immunhistochemy show isolated, reactive B lymphocite, x 20.

Conclusion

Based on the clinical examination and histopathological tests the diagnostic was Micosys Fungoides stage IB.

The neoplastic disease apears to a patient with 11 post-operative eventrations shortly after the last abdominal wall plasty, which first is mistaken for a contact dermatitis to the girdle.

As a feature of this case is the relatively sudden onset, pure asymptomatic, in a patient

exposed to a continue surgical stress durring the past two years, malign illnes which does not keeps in with the completly normal laboratory tests, presenting just a bulky abdomen with an important aerocolie which makes imposible the ultrasound investigation of the abdomen.

Following a topical therapy properly conducted according to the lesions stage skin resolve almost completely, but the prognosis remains reserved.

REFERENCES

1. Dubertret L, Aractingi S, Bachelez H, Bodemer C, Chosidow O, Cribier B, et al. Thérapeutique dermatologique, Flammarion Médecine-Science, 2001.
2. Bolognia JL. Dermatology. Third Edition, Elsevier Limited, 2013.
3. Wolff K, Goldsmith LA, Katz SI. Fitzpatrick's Dermatology in General Medicine. Seventh Edition, McGraw-Hill Companies, 2008.

DOI: 10.7241/ourd.20144.114

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

EPONYMS RELATED TO GENETIC DISORDERS ASSOCIATED WITH GINGIVAL ENLARGEMENT; PART I

Ahmad Al Aboud[1], Nora Mohammed Al-Aboud[2], Hanan Barnawi[3], Ahlam Al Hakami[3]

[1]*Dermatology Department, King Abdullah Medical City, Makkah, Saudi Arabia*
[2]*College of Applied Sciences, Umm Al-Qura University, Makkah, Saudi-Arabia*
[3]*Public Health Department, King Faisal hospital, Makkah, Saudi Arabia*

Corresponding author: Dr. Ahmad Al Aboud *ahmadalaboud@hotmail.com*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 4(5): 439-441 Date of submission: 27.05.2013 / acceptance: 14.07.2014

Cite this article:
Al Aboud A, Al-Aboud NM, Barnawi H, Al Hakami A: Eponyms related to genetic disorders associated with gingival enlargement; part I. Our Dermatol Online. 2014; 4(5): 439-441.

Gingival enlargement is common among patients and can be caused by a variety of etiological factors. The most common reason is poor oral hygiene and high bacterial load that leads to gingival inflammation and enlargement. Other implicated factors include systemic drugs, such as Phenytoin, Nifedipine, Verapamil and Cyclosporine. Some enlargements could be associated with other conditions such as puberty, pregnancy or diabetes or be a symptom of a systemic disease (leukemia, Wegener's granulomatosis or sarcoidosis) [1].

There are also genetic disorders associated with gingival enlargement, which can be sorted into four groups, namely, Hereditary Gingival Fibromatosis (HGF), lysosomal storage disorders, vascular disorders and syndromes characterized by the presence of characteristic dental abnormalities .

Hereditary Gingival Fibromatosis (HGF), represents a heterogeneous group of disorders characterized by progressive enlargement of the gingiva. It manifests itself by an enlarged gingival tissue covering teeth to various extents. HGF may appear as an isolated entity i.e. as autosomal dominant Gingival Fibromatosis, which has little consequence apart from a cosmetic problem and occasional associations with hypertrichosis and/or epilepsy, or as part of a syndrome [2-4].

In Table I [5-16], we shed some lights on eponymous syndroms related to gingival fibromatosis.

Eponyms related to disorders associated with gingival fibromatosis	Remarks
Costello syndrome (CS) [5,6]	It is a distinctive rare multisystem disorder comprising a characteristic coarse facial appearance, intellectual disabilities, and tumor and papillomata predisposition. Heart abnormalities are also common. Although the diagnosis can be suspected clinically, confirmation requires identification of a heterozygous mutation in the proto-oncogene HRAS. Oral examination is important as CS patients develop gingival hyperplasia usually within the first years of life and is considered as a quite distinct feature that can also aid in its differential diagnosis from Noonan syndrome and Cardiofaciocutaneous syndrome that phenotypically overlap with CS. CS was discovered by Dr Jack Costello, (Fig. 1), a New Zealand Paediatrician in 1977. Dr Costello died in 2010.

Figure 1. Dr Jack Costello.

Table I. Eponyms related to disorders associated with gingival fibromatosis.

Figure 2. Dr Harold E. Cross.

Figure 3. Dr. Andreas Giedion.

Figure 4. Friedrich Daniel von Recklinghausen (1833-1910

Eponyms related to disorders associated with gingival fibromatosis	Remarks
Cowden syndrome [7,8]	Also known as, „Multiple hamartoma syndrome". It is a rare autosomal dominant inherited disorder characterized by multiple tumor-like growths called hamartomas and an increased risk of certain forms of cancer. Cowden syndrome is associated with loss-of-function mutations in PTEN, a tumor suppressor gene, leading to hyperactivity of the mTOR pathway. Cowden syndrome may cause oral papilloma rather than gingival swelling. Multiple traumatic fibromas, oral fibromas in tuberous sclerosis, Darier-White disease More Details, Heck's disease, lymphangioma, pyogenic granuloma, fibroepithelial polyps, lipoid proteinosis, oral florid papillomatosis, oral papillomas in Goltz syndrome, mucosal neuromas of multiple endocrine adenomatosis, acanthosis nigricans, pseudoepitheliomatous hyperplasia and squamous cell carcinoma should be considered in the differential diagnosis of oral papillomatous lesions Cowden syndrome was first described in 1963 by Lloyd & Dennis. They named the condition after the surname of their patient, Rachel Cowden.
Cross syndrome [3]	Also known s, Cross- McKusick- Breen syndrome or Kramer's syndrome. It is characterized by GE, nanophthalmos, microcornea, hypopigmentation, mental retardation and writhing movement of hands and legs . Named after, a USA ophthalmologist, working in University of Arizona, Harold E. Cross, (Fig. 2), who was born in 1937.
Jones syndrome [9,10]	It is an autosomal dominant disorder characterized by gingival fibromatosis with progressive sensorineural deafness. First reported by Jones et al, in 1977.
Murray-Puretic-Drescher syndrome [11]	This is another name for, Juvenile hyaline fibromatosis (JHF), which is a rare autosomal recessive disease characterized by papulonodular skin lesions, gingival hyperplasia, joint contractures, and bone lesions. JHF was for the first time described by Murray in 1873 and named by Drescher et al, in 1969.
Ramon syndrome [12]	This syndrome comprises the association of cherubism with gingival fibromatosis, epilepsy, mental retardation, stunted growth, and hypertrichosis.Named after an oral surgeon, Yochanan Ramon who and his colleagues reported the condition in 1967.
Rutherfurd syndrome [13]	It is a rare genetic disorder that is primarily characterised by the classical triad of gingival fibromatosis, delayed tooth eruption and corneal dystrophy. First reported, by Rutherfurd in 1931.
Schinzel-Giedion syndrome (SGS) [14]	It is a rare multiple congenital malformation syndrome defined by characteristic facial features, profound developmental delay, severe growth failure, and multiple congenital anomalies. Most individuals affected by SGS die in early childhood mainly because of progressive neurodegeneration and respiratory failure. However, a long-lived patient showed gingival hyperplasia that was progressive even after gingivectomy. The causative gene of SGS, SETBP1, was identified. SGS was first described in 1978 by an austrian geneticist, Dr. Albert Schinzel, born in 1944 and a Swiss radiologist, Dr. Andreas Giedion, (Fig. 3), born in 1925.

Table I. Eponyms related to disorders associated with gingival fibromatosis (continued).

Eponyms related to disorders associated with gingival fibromatosis	Remarks
von Recklinghausen syndrome [15]	This is another name for, Neurofibromatosis type 1 (NF1), which is a neurocutaneous disorder characterized by neural and cutaneous manifestations, as well as skeletal, oral and jaw abnormalities. This syndrome is named after, Friedrich Daniel von Recklinghausen (1833–1910), (Fig. 4), who was a German pathologist.
Zimmermann-Laband syndrome [16]	It is a very rare disorder characterized by gingival fibromatosis, abnormalities of soft cartilages of the nose and/or ears, hypoplastic or absent nails and terminal phalanges, joint hypermobility, hepatoslenomegaly, mild hirsutism and learning difficulties. Named after, Karl Wilhelm Zimmermann (1861-1935), (Fig. 5), who was a German anatomist and histologist, and Peter F. Laband, who was USA dentist born in 1900.  **Figure 5. Karl Wilhelm Zimmermann (1861-1935).**

Table I. Eponyms related to disorders associated with gingival fibromatosis (continued).

Acknowledgment

The authors wish to to express their thanks to the administrators of King Faisal Hospital, Dr Raeef Qutob and Dr Mutlaq Al Malky for their support to their work.

REFERENCES

1. Livada R, Shiloah J. Gummy smile: could it be genetic? Hereditary gingival fibromatosis. J Mich Dent Assoc. 2012;94:40-3.
2. Doufexi A, Mina M, Ioannidou E. Gingival overgrowth in children: epidemiology, pathogenesis, and complications. A literature review. J Periodontol. 2005;76:3-10.
3. Aghili H, Goldani Moghadam M. Hereditary gingival fibromatosis: a review and a report of a rare case. Case Rep Dent. 2013;2013:930972.
4. Haytac MC, Ozcelik O. The phenotypic overlap of syndromes associated with hereditary gingival fibromatosis: follow-up of a family for five years. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103:521-7.
5. Gripp KW, Lin AE. Costello syndrome: a Ras/mitogen activated protein kinase pathway syndrome (rasopathy) resulting from HRAS germline mutations. Genet Med. 2012;14:285-92.
6. Digilio MC, Sarkozy A, Capolino R, Chiarini Testa MB, Esposito G, de Zorzi A, et al. Costello syndrome: clinical diagnosis in the first year of life. Eur J Pediatr. 2008;167:621-8.
7. Melbārde-Gorkuša I, Irmejs A, Bērziņa D, Strumfa I, Aboliņš A, Gardovskis A, et al. Challenges in the management of a patient with Cowden syndrome: case report and literature review. Hered Cancer Clin Pract. 2012;10:5.
8. Balci DD, Çelik MM, Çelik E, Demir M, Yaldiz M. A rare cause of oral papillomatous lesions: Cowden syndrome. Indian J Dermatol Venereol Leprol. 2012;78:230.
9. Kasaboğlu O, Tümer C, Balci S. Hereditary gingival fibromatosis and sensorineural hearing loss in a 42-year-old man with Jones syndrome. Genet Couns. 2004;15:213-8.
10. JonesG, WilroyR S Jr, McHaney V. Familial gingival fibromatosis associated with progressive deafness in five generations of a family. Birth Defects Orig Art Ser. 1977;XIII:195-201.
11. Karaçal N, Gülçelik N, Yildiz K, Mungan S, Kutlu N. Juvenile hyaline fibromatosis: a case report. J Cutan Pathol. 2005;32:438-40.
12. Suhanya J, Aggarwal C, Mohideen K, Jayachandran S, Ponniah I. Cherubism combined with epilepsy, mental retardation and gingival fibromatosis (Ramon syndrome): a case report. Head Neck Pathol. 2010;4:126-31.
13. Raja TA, Albadri S, Hood C. Case report: Rutherfurd syndrome associated with Marfan syndrome. Eur Arch Paediatr Dent. 2008;9:138-41.
14. Ko JM, Lim BC, Kim KJ, Hwang YS, Ryu HW, Lee JH, et al. Distinct neurological features in a patient with Schinzel-Giedion syndrome caused by a recurrent SETBP1 mutation. Childs Nerv Syst. 2013;29:525-9.
15. Asgary S, Aminzadeh N. Unilateral gingival enlargement in patient with neurofibromatosis type I. N Y State Dent J. 2012;78:50-3.
16. Sawaki K, Mishima K, Sato A, Goda Y, Osugi A, Nakano M. Zimmermann-Laband syndrome: a case report. J Clin Pediatr Dent. 2012;36:297-300.

DOI: 10.7241/ourd.20144.115

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

DERMATOLOGY EPONYMS – SIGN – LEXICON – (N)

Piotr Brzeziński[1], Anca Chiriac[2,3], Saroj K. Rath[4]

[1]*Department of Dermatology, 6th Military Support Unit, Ustka, Poland*
[2]*Department of Dermatology, Nicolina Medical Center, Iasi, Romania*
[3]*Department of Dermato-Physiology, Apollonia University Iasi, Strada Muzicii nr 2, Iasi-700399, Romania*
[4]*Department of Periodontics, Armed Forces Medical College, Pune, India*

Corresponding author: Piotr Brzezinski, MD PhD *brzezoo77@yahoo.com*

Source of Support:
Nil
Competing Interests:
None

Our Dermatol Online. 2014; 5(4): 442-447 Date of submission: 17.07.2014 / acceptance: 23.09.2014

Abstract
Eponyms are used almost daily in the clinical practice of dermatology. And yet, information about the person behind the eponyms is difficult to find. Indeed, who is? What is this person's nationality? Is this person alive or dead? How can one find the paper in which this person first described the disease? Eponyms are used to describe not only disease, but also clinical signs, surgical procedures, staining techniques, pharmacological formulations, and even pieces of equipment. In this article we present the symptoms starting with (N) and other. The symptoms and their synonyms, and those who have described this symptom or phenomenon.

Key words: eponyms; skin diseases; sign; phenomenon

Cite this article:
Brzezinski P, Chiriac A, Rath SK. Dermatology Eponyms – Sign – Lexicon – (M). Our Dermatol Online. 2014; 5(4): 442-447.

NAIL SIGN

Sign in oriental sore (leishmaniasis). Nail sign is the the shape of the lesion once the eschar is removed the lesion takes the shape of a deep nail excoriation, which also resembles the nail [1].

HULUSI BEHÇET

Is a famous Turkish dermatologist (1889-1948) (Fig. 1). He was born in Istanbul. Dr. Hulusi Behçet pursued his education at Gülhane Military Medical Academy. After he had become a medical doctor, he specialized in dermatology and venereal disease at Gülhane Military Medical Academy and he completed his specialization in 1914. During World War I (1914–1918), he served at the military hospital in Edirne as a specialist in dermatology and venereal diseases and was assigned to the head of the hospital as an assistant. After the war, between 1918–1919, he first went to Budapest, Hungary and then to Berlin, Germany to improve his medical knowledge. He had the opportunity to meet some well known colleagues there. After his return to Turkey, he went into private practice. In 1923, Behçet was appointed as the head physician at the Hasköy Venereal Diseases Hospital at Golden Horn in Istanbul. Shortly after, he moved to Guraba Hospital, which is now part of the School of Medicine İstanbul University. While he lectured at the university, he continued his private practice as well.

In 1933, Istanbul University was re-established out of the old-fashioned Dar-ul Fünun.

During this period of reform, Behçet founded the department of dermatology and venereal diseases. His curiosity for research, writing and discussion were his intellectual characteristics. Starting from the early years in his profession, his participation in national and international congresses with original articles was very apparent, publishing many articles at home and abroad. The famous German pathologist Schwartz called him once „a scientist who was well known everywhere, but in his country", adding that „you could never find him in Turkey because he was always abroad presenting his findings".

He translated many articles into Turkish to help educate new generations and published original case reports in international reviews in order to make contact with such far countries as Korea. He was interested in syphilis since 1922 and had published many international articles on its diagnosis, treatment, hereditary properties, serology and social aspects. Leishmaniasis (Oriental sore) was another disease, which Behçet worked on, beginning in 1923.

Figure 1. Hulusi Behçet.

He wrote about it in many articles and succeeded in its treatment with diathermic. He first described „the nail sign" appearing by the removal of the crust of an oriental sore. A part of his published work was concerned with parasitosis. In 1923, he described the etiologic agents of „gale cereal" in Turkey. Behçet dealt with superficial and deep mycosis and their treatments. Due to his observations, he described the dermatitis of fig in 1933. In 1935, at the Dermatology Congress in Budapest, he was honoured for his studies on mycosis.

He was also in the publishing vanguard to improve Turkish medicine and he was responsible for the first dermato-venerology journal of Turkey called ''Turkish Archives of Dermatology and Syphilology'' in 1924. In 1939, he was elected as a correspondent member to the German scientific journals ''Dermatologische Wochenschrift'' and ''Medizinische Wochenschrift''. The same year, he has been promoted to ordinary professor.

The most important work that Behçet brought to Turkish medicine was the monograph published in 1940 called ''Clinical and Practical Syphilis, Diagnosis and Related Dermatoses''. Every page of this book contains an aspect of syphilis and the footnotes, provides a wealth of detailed information about the differential diagnosis of other skin diseases. As a result, scientists had the chance to learn about syphilis and dermatology at the same time. This book, despite its outdated style, still retains its value and spirit in medicine as being the only example in its field. Behçet continued as the Head of the Department of Dermatology and Venereal Diseases until 1947. His first observations on Behçet's Disease started with a patient he met between 1924-1925.

Dr. Behçet followed the symptoms of three patients whom he had had for years, then he decided that they were the symptoms of a new disease (1936). He published these cases in the Archives of Dermatology and Veneral Disease.

He died from a sudden heart attack on March 8, 1948.

In 1975, many years after his death, he was honoured with the TÜBİTAK Scientific Award. Several classes, laboratories and libraries had been named in his honour. In national and international congresses, events like „Korean-Turkish Behçet Days" are taking place.

In 1982, he was awarded with the Medical Award of the Turkish Republic by Eczacıbaşı Foundation of Scientific Research. In 1996, the Turkish mint released a silver commemorative coin for Behçet during the National Dermatology Congress [1-3].

NAIROBI SHEEP FEVER SIGN, [Africa]

Headache, fever, and hemorrhagic rash. Caused by zoonotic nairovirus infected tick bites or contact with infected animals. Also called Crimean-Congo hemorrhagic fever [4].

NAZZARO'S SIGN

Follicular hairy hyperkeratosis (horny follicular spicules) commonly located on the face which shows compact follicle bound hyperkeratosis is a rare but typical clinical finding in multiple myeloma [5,6].

PAOLO NAZZARO

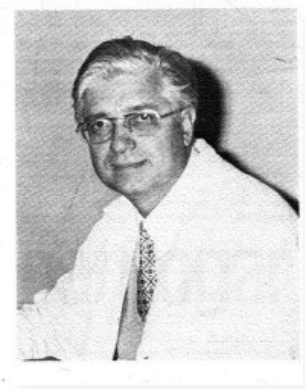


Figure 2. Paolo Nazzaro.

Italian dermatologist, 1921-1975 (Fig. 2). In der dermatologischen Welt war Paolo Nazzaro nicht nur durch sein wissenschaftliches Werk und durch seine aktive Teilnahme an internationalen Kongressen bekannt, sondern auch durch die von ihm in Rom in seinem Krankenhaus organisierten wissenschaftlichen Treffen.

Paolo Nazzaro wurde im Jahre 1945 an der Universitat Rom zum Doktor der Medizin promoviert.

Anschlissend trat er als Assistent in die damals von Prof. Cesare Frugoni geleitete Klinik fur innere Medizin ein. Seine Vorliebe fur die Dermatologie liess ihn dann aber im Jahre 1947 zur Universitatshautklinik in Rom uberwechseln. Hier hat er die Stufen der akademischen Laufbahn durchschritten. Privat-dozent im Jahre 1954, im gleichen Jahre Dozent an der Spezalisie-rungsschule fur Dermatologie, Oberarzt im Jahre 1960.

Im Jahre 1966 erhielt Paolo Nazzaro die Stellung ais Direktor des dermatologischen Krankenhauses San Gallieano in Rom.

This lies on the right bank of the Tiber in Trastevere House is a venerable and illustrious wanted Hospital, which was built in 1729 by Pope Benedict XIII. For a long time this clinic was the only institution in Rome for treatment of skin and venereal diseases. As 1859 in Rome at the Academy training course for dermatology was intro- duced.

It is to mention that he was the period of his activity at the Universitatshautklinik Rome was largely involved in the organization of a Symposium on Behcet's disease nor during, attended by clinicians, pathologists, researchers from around the world. In this period falls the jointly undertaken with the writers creation of the manual „Dermatologia e Yenereologia".

In a hospital has organized Paolo Nazzaro meetings on pediatric dermatology, via porphyria, via comparative mycology, via acne and via Mastocytosen. He was a member of various clinical and experimental Dermatology companies. He was also in the last few years secretary of the Italian Society for Dermatology and Syphiligraphie.
In 1972 Paolo Nazzaro was attacked by a relentless disease whose treatment the fatal results was delayed output only. He was conscious of his fate and spoke about it with an almost stoic attitude without undern to his usual activity somewhat [7-9].

NEGRO TOES SIGN, [Amazon Basin and Rio Negro, South America]
Hair loss, sloughing of the nails, garlic breath odor, pulmonary edema, neurological changes, cirrhosis of the liver, and death. Caused by selenium toxicity [10]. A known source is the consumption of Brazil nuts which have more than 1000 percent of the daily recommended dose of the chemical element.

NEISSER-WECHSBERG PHENOMENON
Complement fixation phenomenon [11,12]. The Neisser—Wechsberg phenomenon resembles the inhibition of agglutination systems by excess antibody. The complement-fixation test is one of the most convenient serological tests available, because it can be applied to the diagnosis of various kinds of infectious diseases just by changing the antigen.

MAX NEISSER


Figure 3. Max Neisser.

German physician and bacteriologist, 1869-1938 (Fig. 3). Max Neisser was the son of Salomon Neisser and Julie Sabersky. The dermatologist Albert Neisser was his uncle.
Neisser first studied some semesters of science and then medicine in Freiburg, Breisgau and Berlin. Upon graduation, he was graduated in 1893 with a study on the differentiation between cholera vibrios and he discovered water-Vibrio (Vibrio berolinensis). This work, which also contains the description of a method for Vibrio cholera detection was developed in the laboratory of the Berlin hygienist Max Rubner.
1894-1899 Neisser worked as assistant to the hygienist Carl Flügge at the Breslauer Hygiene Institute. After his habilitation in 1899 he was until 1909 a member of the Institute for Experimental Therapy in Frankfurt am Main, which was led by Paul Ehrlich. Appointed professor in 1909, he took over the leadership of the new Frankfurt Hygiene Institute. From 1914 Neisser represented at Frankfurt University as Professor trays hygiene and bacteriology. During the First World War he served as a consulting Army Hygienists. Neisser was retired in 1933 by the Nazi regime forcibly and then lived retired in his country house in Falkenstein in the Taunus.
Neisser employed preferably with sanitary-bacteriological issues such as the transmission of infectious pathogens in drinking water or air dust and the differential diagnosis of diphtheria bacillus (1897). Among other things, Neisser described a steam process for disinfection of drinking water wells. He also dealt with „applied" bacteriology and hygiene in public health (water, food, hygienic living conditions, heating, ventilation, milk disinfection) and the further development of bacteriological methods techniques (culture media, sterilization, animal husbandry), issues of laboratory infection and bacteriological warfare .
He explored the properties of many microorganisms (diphtheria bacillus, staphylococcus, streptococcus, pneumococcus, meningococcus, gonococcus, anthrax, plague, Friedlander, Burkholderia mallei). 1901 Neisser showed that staphylococci two different soluble toxins in the blood serum form (hemolysin and leukocidin).
Neisser developed a biological assay for protein differentiation to distinguish different blood types can (Neisser-Sachs-Complement) and showed that immune serum surpluses may block the antigen-antiserum reaction (Neisser-Wechsberg phenomenon) [13].
The Neisser stain is a microbiological staining showing the polar bodies (metachromatic granules, polyphosphate granules) in the cytoplasm of some gram-positive bacteria. The Neisser staining being particularly important for the diagnosis of Corynebacterium diphtheriae a role. The centrosomes arise after this staining is blue black [14].

FRIEDRICH WECHSBERG
Austrian Internist, (1873–1929).

NEOPOLITAN SIGN
= syphilis. Also called morbus neopolitanus [15,16]. Synonyms: Italian sign [17], French sign [18].

NEUMANN'S SIGN
Pemphigus vegetans. Pemphigus vegetans is a rare variant of pemphigus vulgaris and is characterized by vegetating lesions in the inguinal folds and mouth and by the presence of autoantibodies against desmoglein 3 [19]. Two clinical subtypes of pemphigus vegetans exist, which are initially characterized by flaccid bullae and erosions (the Neumann subtype) or pustules (the Hallopeau subtype). Both subtypes subsequently develop into hyperpigmented vegetative plaques with pustules and hypertrophic granulation tissue at the periphery of the lesions.

ISIDOR NEUMANN, EDLER VON HEILWART

Austrian dermatologist, 1832-1906 (Fig. 4). Neumann received his medical education in Vienna, mainly under Ferdinand Ritter von Hebra (1816-1880), and obtained his doctorate in 1858. In 1863 he received his habilitation, and in 1873 became an associate professor. In 1881 he was appointed professor of dermatology and successor to Carl Ludwig Sigmund (1810–1883) as director of the clinic for syphilis.

In an 1886 publication of Vierteljahrsschrift für Dermatologie und Syphilis, he described a type of pemphigus vulgaris, which later became known as Pemphigus vegetans of Neumann. He was also the first to publish a detailed study (Über die senilen Veränderungen der Haut des Menschen) of prematurely aged skin caused by over-exposure to weather conditions. However it wasn't until several years later that Paul Gerson Unna (1850-1929) gave it a name, calling it seemannshaut or „sailors' skin". During the Austrian government's occupation of Bosnia-Herzegovina, Neumann was sent to the country to manage the public health problem of syphilis and leprosy [20].

Figure 4. Isidor Neumann.

NEW WORLD FEVER SIGN

Muscle pain, fever and pin point bleeding lesions, may have brain involvement. Caused by the zoonotic New World hemorrhagic fever Arenaviridae virus [21].

NIGHTCLIFF SIGN

Hepatitis, pulmonary lesions, abscesses. A zoonotic melioidosis disease, carried by rats, horses, primates, other ruminants, zoo animals, and kangaroos. Also called pseudoglanders, Whitmore disease, and Nightcliff gardener's disease [22].

NIGHTSHADE SIGN

Severe dry mouth, loss of voice, dilatation of the pupils, suppression of urine, sight and hearing hallucinations (Fig. 5). A sign of atropine poisoning. Also known as Atropine and Belladonna sign [23].

Figure 5. atropa belladonna.

NIKOLSKY'S SIGN

Easy separation of the outer portion of the epidermis from the basal layer on exertion of firm sliding pressure by the finger or thumb, as in pemphigus vulgaris and some other bullous diseases (Figs 6a - b) [24-26]. Nikolsky first described the sign that bears his name in 1896. He related how, after rubbing the skin of patients who had pemphigus foliaceus, there was a blistering or denudation of the epidermis with a glistening, moist surface underneath.4 According to his explanation, the skin showed a weakening relationship and contact between the corneal (horny) and granular layers on all surfaces, even in places between lesions (eg, blisters, excoriations) on seemingly unaffected skin. Nikolsky's observations were later confirmed by Lyell in 1956, who described a Nikolsky sign in patients with toxic epidermal necrolysis [27].

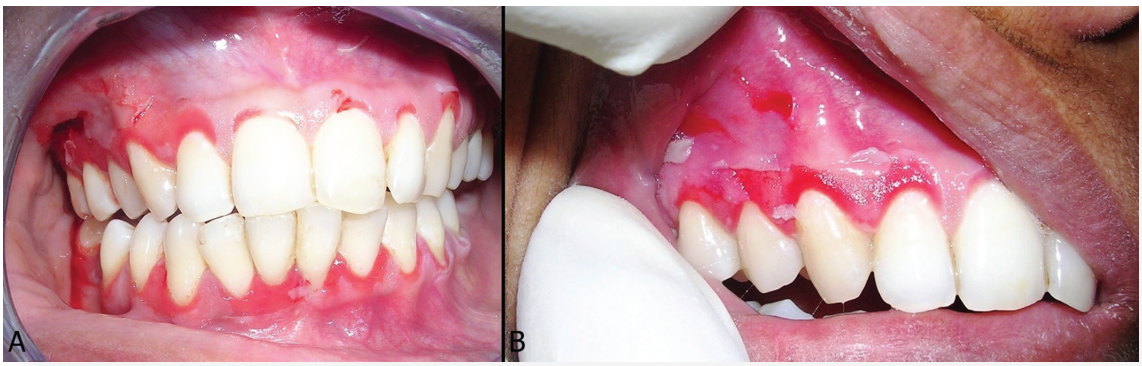


Figure 6. Nikolsky's sign.

PYOTR VASILYEVICH NIKOLSKY

Russian dermatologist, 1858-1940 (Fig. 7). Nikolsky was a dermatologist from Usman who studied medicine and worked in Kiev, now the capital of Ukraine, but at that time, part of the Russian Empire. He studied medicine at the medical faculty of the University of Kiev (now National Medical University), and from 1884 was an assistant to Mikhail Stukovenkov at the dermatology clinic in Kiev. In 1900, he became a professor at Warsaw, and later worked as a professor in Rostov. He published articles in French as well as Russian on skin diseases and on the treatment of syphilis. He was the author of „L'etat de la dermatologie et de la syphiligraphie en Russie jusqu'à 1884" (The state of dermatology and syphiligraphy in Russia up until 1884). In 1896, he published an article on pemphigus, in which he described a dermatological condition involving a weakening relationship among the epidermal layers. The sloughing of skin associated with certain varieties of this condition is now referred to as „Nikolsky's sign" [28,29].

Figure 7. Pyotr Vasilyevich Nikolsky.

NIPAH SIGN, [Malaysia]

Fever, vomiting and encephalitis with high mortality. Caused by contact with pigs, dogs, and fruit bats infected with the zoonotic Nipah vrus [30].

NITRIC SIGN

Burning pains in mouth and throat with vomit containing white lumps of mucous and altered brown or black blood. Stains on skin and mucous membranes appear bright yellow and stains clothing yellow or brown. A sign of nitric acid poisoning [31].

NITROBENZOL SIGN

Extreme blueness of face, lips, and finger-tips, breath and urine have odor of bitter almonds. Indicates poisoning from nitrobenzol [32,33].

NOSE SIGN

It is seen in exfoliative dermatitis in which there is complete absence of erythema and scaling of the nose and perinasal areas. It is hypothesized that sparing of nose in exfoliative dermatitis could be due to greater sun-exposure of nose or it could be explained by the mechanism of island of normal skin [34-36]. The sign described by K Pavithran. Also known as Pavithran's nose sign.

NUP SIGN

Linear gingival erythema, an erythematous band al the free gingiva that follows the contour with a reddish chevron appearance (Fig. 8). An indication of HIV disease [37,38]. Also called ANUG, HiVR and LGE signs.

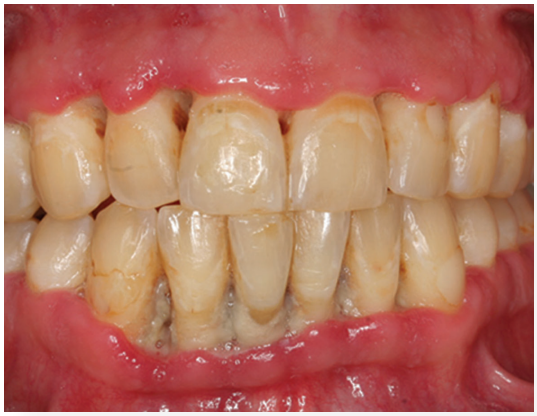


Figure 8. NUP sign.

NUX VOMICA SIGN

Feeling of suffocation, tetanic convulsions with arched back and blueness of the face, accompanied by raised eyebrows and an evil open grin, called risus sardonicas [39]. A sign indicating poisoning with strychnine. This presentation is similar to signs of a tetanus infection caused by the anaerobic bacterium Clostridium tetani, an important differential is the time between infection and showing the first signs in tetanus is at least five days, whereas strychnine poisoning shows signs ten to twenty minutes after exposure. Also known as Strychnine sign after the evergreen tree it is derived from named Strychnos nux vomica.

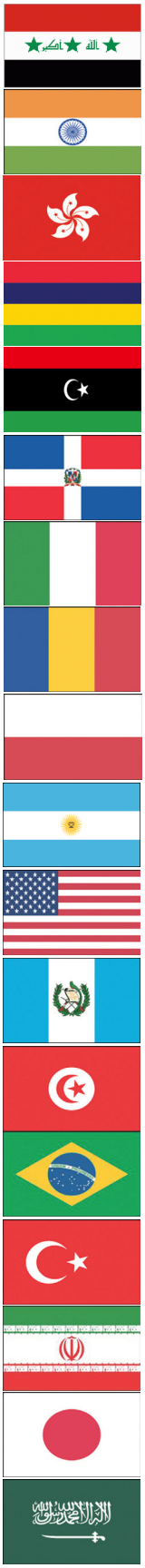
Acknowledgement

Dr Khalid Al Aboud - Department of Public Health, King Faisal Hospital, Makkah, Saudi Arabia

REFERENCES

1. Ustün C. A famous Turkish dermatologist, Dr. Hulusi Behçet. Eur J Dermatol. 2002;12:469-70.
2. Al Aboud K, Al Aboud A. Eponyms in the dermatology literature linked to the oral disorders. Our Dermatol Online. 2013;4:247-50.

3. Demirhan Erdemir A, Öncel O. Prof. Dr. Hulusi Behcet (A Famous Turkish Physician) (1889-1948) and Behcet's Disease from the Point of View of the History of Medicine And Some Results. J Int Soc Hist Islamic Med. 2006;5:51-63.
4. Leblebicioglu H, Eroglu C, Erciyas-Yavuz K, Hokelek M, Acici M, Yilmaz H. Role of migratory birds in spreading crimean-congo hemorrhagic Fever, Turkey. Emerg Infect Dis. 2014;20:1331-4.
5. Izakovic J, Büchner SA, Düggelin M, Guggenheim R, Itin PH. [Hair-like hyperkeratoses in patients with kidney transplants. A new cyclosporin side-effect]. Hautarzt. 1995;46:841-6.
6. Requena L, Sarasa JL, Ortiz Masllorens F, Martín L, Piqué E, Olivares M, et al. Follicular spicules of the nose: a peculiar cutaneous manifestation of multiple myeloma with cryoglobulinemia. J Am Acad Dermatol. 1995;32:834-9.
7. Kocsard E. Professor Paolo Nazzaro. Australas J Dermatol. 1976;17:37.
8. Monacelli M. [In memoriam Paolo Nazzaro 1923-75]. Hautarzt. 1977;28:164-5.
9. Salvati A. [Dermatological aspects of cutaneous pseudocancerosis. (Opinion of Professor P. Nazzaro)]. Minerva Med. 1971;62:1588-91.
10. Boehler CJ, Raines AM, Sunde RA. Toxic-Selenium and Low-Selenium Transcriptomes in Caenorhabditis elegans: Toxic Selenium Up-Regulates Oxidoreductase and Down-Regulates Cuticle-Associated Genes. PLoS One. 2014;9:e101408.
11. Muschel LH, Gustafson L, Larsen LJ. Re-examination of the Neisser-Wechsberg (antibody prozone) phenomenon. Immunology. 1969;17:525-33.
12. Bannai H, Nemoto M, Tsujimura K, Yamanaka T, Kondo T, Matsumura T. Improving a Complement-fixation Test for Equine Herpesvirus Type-1 by Pretreating Sera with Potassium Periodate to Reduce Non-specific Hemolysis. J Equine Sci. 2013;24(4):71-4.
13. Klieneberger-Nobel E. [100th anniversary of Professor Max Neisser]. Zentralbl Bakteriol Orig. 1970;215:279-85.
14. Nittami T, McIlroy S, Seviour EM, Schroeder S, Seviour RJ. Candidatus Monilibacter spp., common bulking filaments in activated sludge, are members of Cluster III Defluviicoccus. Syst Appl Microbiol. 2009;32:480-9.
15. Puri N, Kumari P. A study on sexually transmitted diseases in patients in a STD clinic in a district hospital in North India. Our Dermatol Online. 2014;5:240-4.
16. Brzeziński P, Fiorentino DF, Arunachalam P, Katafigiotis I, Matuszewski Ł, Narita M, et al. Dermatology Eponyms – sign –Lexicon (K). Our Dermatol Online. 2014;5:95-102.
17. Brzezinski P, Hassan I, Chiriac A, Sinjab AT. Dermatology Eponyms – sign –Lexicon (I). Our Dermatol Online. 2013;4:256-9.
18. Brzezinski P, Gijón EG, López-López J, Toyokawa T, Scrimshaw NS, Malard O, et al. Dermatology eponyms – phenomen / sign – Lexicon (F). Our Dermatol Online. 2012;3: 66-78.
19. Son YM, Kang HK, Yun JH, Roh JY, Lee JR. The neumann type of pemphigus vegetans treated with combination of dapsone and steroid. Ann Dermatol. 2011;23(Suppl 3):S310-3.
20. No authors. Isidor Neumann Archiv Dermatol Syphil. 1906;82:158.
21. Milazzo ML, Amman BR, Cajimat MN, Méndez-Harclerode FM, Suchecki JR, Hanson JD, et al. Ecology of Catarina virus (family Arenaviridae) in southern Texas, 2001-2004. Vector Borne Zoonotic Dis. 2013;13:50-9.
22. Wijekoon S, Prasath T, Corea EM, Elwitigala JP. Melioidosis presenting as lymphadenitis: a case report. BMC Res Notes. 2014;7:364.
23. Berdai MA, Labib S, Chetouani K, Harandou M. Atropa belladonna intoxication: a case report. Pan Afr Med J. 2012;11:72.
24. Oishi T, Hanami Y, Kato Y, Otsuka M, Yamamoto T. Staphylococcal scalded skin syndrome mimicking toxic epidermal necrolysis in a healthy adult. Our Dermatol Online. 2013;4:347-8.
25. Abreu Velez AM, Calle J, Howard MS. Autoimmune epidermal blistering diseases. Our Dermatol Online. 2013;4(Suppl.3):631-46.
26. Lezcano L, Di Martino Ortiz B, Rodríguez Masi M, Knopfelmacher O, de Lezcano LB. [Toxical epidermal necrolysis. Report of two cases. Severe skin rash caused by common drugs]. Our Dermatol Online. 2013;4:517-21.
27. Urbano FL. Nikolsky's Sign in Autoimmune Skin Disorders. Hosp Physician. 2001;:23-24.
28. Al Aboud K, Al Aboud A. Eponyms linked to ,'signs'' in the dermatology literature. Our Dermatol Online. 2013;4:579-81.
29. Al Aboud A, Al Aboud K. Eponyms in the dermatology literature linked to Russia. Our Dermatol Online. 2013;4(Suppl.1):414-5.
30. Dups J, Middleton D, Long F, Arkinstall R, Marsh GA, Wang LF. Subclinical infection without encephalitis in mice following intranasal exposure to Nipah virus-Malaysia and Nipah virus-Bangladesh. Virol J. 2014;11:102.
31. Yanagawa Y, Matsukawa T, Yokoyama K, Hirano Y, Ri T, Aihara K, et al. [Case of dyspnea due to toilet cleaner containing nitric acid for household use]. Chudoku Kenkyu. 2013;26:240-3.
32. Delfino U, Del Prete S, Pattono R. [Resuscitative treatment in acute nitrobenzol poisoning]. Minerva Anestesiol. 1968;34:1419-27.
33. Martínez MA, Ballesteros S, Almarza E, Sánchez de la Torre C, Búa S. Acute nitrobenzene poisoning with severe associated methemoglobinemia: identification in whole blood by GC-FID and GC-MS. J Anal Toxicol. 2003;27:221-5.
34. Kanwar AJ, Dhar S, Ghosh S. ,Nose sign' in dermatology. Dermatology. 1993;187:278.
35. Agarwal S, Khullar R, Kalla G, Malhotra YK. Nose sign of exfoliative dermatitis: a possible mechanism. Arch Dermatol. 1992;128:704.
36. Pavithran K. Nose Sign of Exfoliative Dermatitis. Indian J Dermatol Venerol Leprol. 1988;54:42.
37. Brzezinski P, Pessoa L, Galvão V, Barja Lopez JM, Adaskevich UP, Niamba PA, et al.
Dermatology Eponyms – sign –Lexicon (H). Our Dermatol Online. 2013;4:130-43.
38. Brzeziński P, Chiriac A, Arenas R, Urge Dori G, Monteiro R, Cairncross S, et al. Dermatology Eponyms – sign –Lexicon (L). Our Dermatol Online. 2014;5:217-30.
39. Parker AJ, Lee JB, Redman J, Jolliffe L. Strychnine poisoning: gone but not forgotten. Emerg Med J. 2011;28:84.



Our Dermatology Online

www.odermatol.com

4.2014 (03.October.2014)