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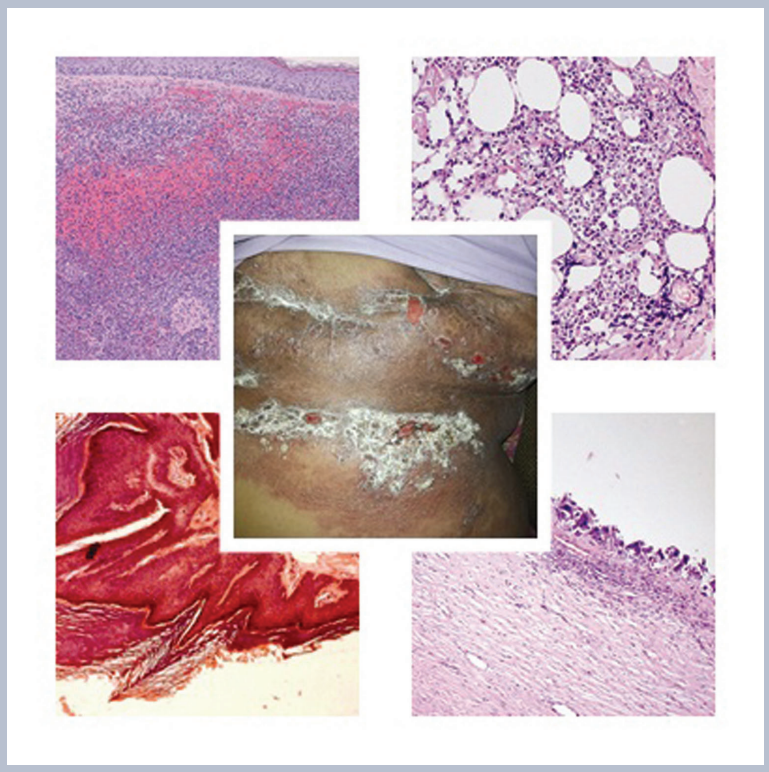

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NASZA DERMATOLOGIA Online
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A CLINICAL STUDY OF GERIATRIC DERMATOSES

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Abstract
Introduction: The geriatric population is composed of persons over 65 years of age and very few studies are available on the dermatologic diseases in this group. This study was done to study the spectrum of cutaneous manifestations and prevalence of physiological and pathological changes in the skin of elderly people.
Material and Methods: Two hundred consecutive patients aged more than 65 years of age attending the outpatient clinic or admitted as inpatients in the Department of Dermatology at Vydehi Institute of Medical Sciences and Research Centre were subjects for the study. A detailed history of cutaneous complaints, present and past medical ailments was taken. A complete general physical, systemic examination and dermatological examination was done and all findings were noted in a pre designed proforma. Skin changes observed due to ageing were classified as physiological and pathological. Findings were collated in a master chart and results analyzed.
Results: Out of 200 patients studied, 71% were males and 29% were females. Pruritus was the single most common complaint elicited (44%). Among the physiological changes, xerosis was the commonest (93%). Among the pathological changes skin tumours, eczemas, infections were the common findings.
Conclusions: The geriatric dermatoses are different in different populations as some of the skin changes seen in western skin and Indian skin are not identical.

Key words: geriatric; dermatoses; cutaneous manifestations

Cite this article:
Raveendra L. A clinical study of geriatric dermatoses. Our Dermatol Online. 2014; 5(3):235-239.

Introduction

Ageing is a natural process. In the words of Seneca; "Old age is an incurable disease". But more recently, Sir Sterling Ross says "You do not heal old age. You protect it; you promote it; you extend it". The geriatric population is composed of persons over 65 years of age and very few studies are available on the dermatologic diseases in this group [1]. In India, there were 72 million elderly persons above 60 years of age as of 2001 and this number is likely to increase to 179 million in 2031 and hence dermatologic care in geriatric population needs emphasis [2].
The dermatology practice of the future will see an increase in the number of geriatric patients [3] and geriatric health care has become a major international issue [4]. In India, very few studies have been done to look into the cutaneous manifestations in the elderly people [5] though several studies have been carried out in the west [6]. Geriatrics as a branch of medicine is beginning to take a foothold in our country too.
In this scenario, with life expectancy in India going up to 63.9 years in males and 66.9 years in females in 2004 [7], this study was undertaken to study the spectrum of cutaneous manifestations and prevalence of physiological and pathological changes in the skin of elderly people.

Material and Methods

Two hundred consecutive patients aged more than 65 years of age attending the outpatient clinic or admitted as inpatients in the Department of Dermatology, STD and Leprosy at Vydehi Institute of Medical Sciences and Research Centre were subjects for the study.

Method of data collection

A detailed history of cutaneous complaints, present and past medical ailments was taken. A complete general physical and systemic examination was carried out irrespective of the complaints. Detailed dermatological examination was done and all findings were noted in a pre designed proforma. Routine blood haemoglobin, complete blood counts, urine routine examination, blood sugar estimation was carried out whenever it was necessary. Skin scrapings, nail clipping for fungus, Tzanck smears and skin biopsies were done wherever indicated.

Skin changes observed due to ageing were classified as physiological and pathological. Findings were collated in a master chart and results analyzed. They were compared with findings from similar studies.

Results

The following observations were made in the study and the results analysed.

Total of 200 patients above the age of 65 years were studied of which, (142) 71% were males and (58) 29% were females. The male: female ratio was 2.44 : 1. The maximum number of patients 124 (62%) belonged to the age group of 65-70. The mean age of these patients was 68 years. Pruritus was the commonest single complaint in 88 patients (44%).

Fifty four percent of patients had associated systemic illness. These were tabulated in a bar graph (Fig. 1). Pruritus was the commonest single complaint in 88 patients (44%). All the patients had physiological changes and the commonest was xerosis. The physiological changes were tabulated in a bar graph (Fig. 2).

Papulosquamous disorders were seen in 24 patients (12%). Fourteen patients (7%) had psoriasis and 10 (5%) had lichen planus. Eczema was present in 62 patients (31%). Among the various types of eczema, lichen simplex chronicus was the commonest, seen in 20 (10%) patients. Ten patients (5%) each had gravitational eczema and seborrhoeic dermatitis. Irritant contact dermatitis and allergic contact dermatitis was seen in 6 patients (3%) each. Asteatotic eczema was seen in 5 patients (2.5%). Hand eczema was seen in 3 patients (1.5%) and 1 patient (0.5%) had atopic dermatitis.

Infections and infestations were seen in 64 patients (32%). These were tabulated in a table (Tabl. I). Of the various infections, fungal infection was the commonest. Pigmentary disorders were seen in 28 patients (14%). Among the various pigmentary disorders, vitiligo was seen in 16 patients (8%), melasma in 10 patients (5%) and ashy dermatosis in 2 patients (1%).

Skin tumours present in patients were noted and tabulated in Table II. The incidence of benign tumours exceeds the number of cases because most patients had more than 1 type of tumour. No malignant or premalignant tumours were seen in this study.

Skin tumours present in patients were noted and tabulated in Table II. The incidence of benign tumours exceeds the number of cases because most patients had more than 1 type of tumour. No malignant or premalignant tumours were seen in this study.

Senile purpura was the commonest vascular disorder seen in 14 cases (7%). Varicose veins were seen in 8 cases (4%). Bullous pemphigoid was the only bullous disorder encountered in this study, seen in 3 patients (1.5%). Disorders of keratinization were seen in 12 cases (6%). Plantar hyperkeratosis was seen in 8 patients (4%) and corns in 4 patients (2%). Trophic ulcers were seen in 8 cases (4%), keloid in 5 cases (2.5%) and keratolysis exfoliativa in 3 cases (1.5%).

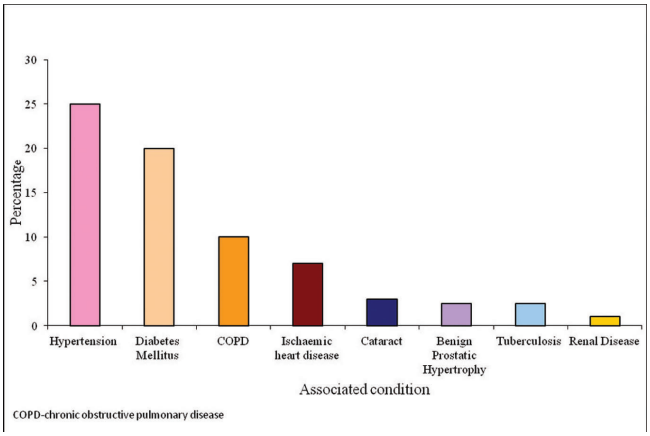

Figure 1. Associated systemic illness- Comorbidities.

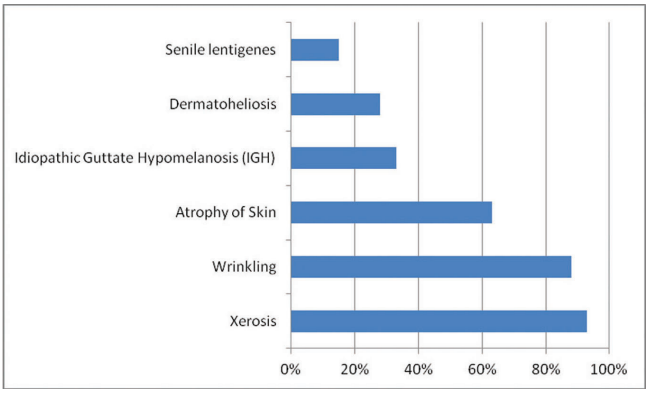

Figure 2. Physiological changes.

Sl. No.	Condition	No. of cases	Incidence (%)
1	Fungal Infections	22	11
	a) Dermatophytosis	15	7.5
	b) Candidiasis	05	2.5
	c) Pityriasis Versicolor	02	01
2	Viral Infections	16	08
	a) Herpes Zoster	08	04
	b) Verruca Vulgaris	08	04
3	Leprosy	12	06
4	Pyoderma	08	04
5	Scabies	06	03
	Total	64	32

Table I. Infections and Infestations.

Sl. No.	Condition	No. of cases	Incidence (%)
1	Seborrhoeic Keratosis	102	56
2	Dermatosis Papulosa Nigra	94	47
3	Cherry Angiomas	74	37
4	Achrochordon	39	19.5
5	Melanocytic Naevi	11	5.5
6	Dermoid Cyst	07	3.5
7	Sebaceous Cyst	01	0.5

Table II. Benign tumors of the skin.

Greying of hair was the commonest hair change seen in 180 patients (90%). Hypertrichosis of pinna was seen in 76 male patients (38%) and androgenic alopecia was seen in 36 male patients (18%). Hirsutism was seen in 12 patients (6%). The nail changes seen in patients were tabulated in Table III. The incidence of nail changes exceeds the number of cases since some cases showed more than one nail change due to ageing. Oral mucosal hyperpigmentation was seen in 49 patients (24.5%).

Sl. No.	Condition	No. of cases	Incidence (%)
1	Vertical Ridging	94	47
2	Loss of Lustre	88	44
3	Onychomycosis	14	07
4	Paronychia	08	04
5	Nail psoriasis	06	03
6	Subungual Hyperkeratosis	02	01
7	Nail Dystrophy	02	01
8	Nail Lichen Planus	02	01
9	Beau's Lines	01	0.5
10	Pterygium	01	0.5

Table III. Nail Changes.

Discussion

In this study, a total of 200 patients varying in age from 65 to 85 years were examined. The oldest patient was 85 years. Of these, 142 (71%) patients were males and 58 (29%) were females. In the present study, the number of males outnumbered the females which coincide with most of the other studies [1,6,8].

Pruritus was the commonest symptom seen in this study and was given by 88(44%) patients. Patange and Fernandez [6] noted pruritus in 78.5% of patients, of which 3.8% had senile pruritus and the rest were associated with cutaneous dermatoses (91.1%). In all the studies, pruritus has been the commonest complaint noted varying from 11.5% to 49.6% [1,8-11]. About 108 (54%) of patients in the present study had co morbid conditions like diabetes mellitus, hypertension, chronic renal failure, ischemic heart disease, chronic obstructive lung disease etc with multiple drug usage which may have contributed to development of pruritus.

In evaluating the older person's skin, the greatest problem is deciding what is abnormal and what is physiological. Many changes and lesions are normal, except occasionally in degree and number. In this study xerosis, wrinkling, atrophy (thinness of skin), idiopathic guttate hypomelanosis, dermatoheliosis and senile lentigens are considered physiological.

Xerosis was the commonest physiological change seen in the present study in 93% of patients. Xerosis was noted in7% [6], 12.5% [12], 77% [13], 85% [9] and 99.8% [11] of patients in various studies. The high incidence of xerosis in this study is comparable to few of the studies [9,13]. The high incidence of xerosis could be attributed to less use of emollients and usage of harsher soaps by the subjects of the study who mostly hail from semi rural areas.

Wrinkling was seen in 88% (156) patients in this study. Tindall and Smith [13], Grover and Narasimhalu [14], Beauregard and Gilchrest [9], and Durai, Thappa et al [11] have reported wrinkling in 94%, 95.5%, 95.6% and 99% patients respectively which coincides with the results of our study. Most of the wrinkling seen in this study was on sun exposed areas like the face, neck, forearms and dorsa of hands in the form of glyphic wrinkles. Slight lower incidence of wrinkling in this study may be because of increased tolerance of racially pigmented skin to sunlight.

Atrophic wrinkled skin was seen in 63% (126) of patients in this study. The aged skin becomes fragile, translucent, lax and wrinkled [15]. Tindall and Smith [13] found an incidence of atrophic wrinkled skin in 94% patients. Most of the patients in our study were in the age group of 65 to 70 years which may explain the decreased incidence of atrophy as compared to the other study as atrophy is just beginning to manifest at this age. More so, pigmented skin is less susceptible to skin damage and atrophy of the skin is more common in females than in males [16] and in this study, females form only 29% of the total cases.

Idiopathic guttate hypomelanosis was present in 66 (33%) cases in this study. Three Indian studies mention an incidence of about 25% [6,9,11] and one other study by Grover and Narasimhalu [14] mentioned an incidence of 76.5%. IGH is statistically more often seen in darkened skin than in fair skinned subjects [9]. This may explain a slightly higher incidence (33%) of IGH in the present study compared to other studies. Also, most patients present themselves to be reassured that IGH is not vitiligo, due to the cultural bias against vitiligo.

The range of changes due to chronic sun damage is called dermatoheliosis. The skin change includes senile comedones, irregular pigmentation, wrinkling, scaling, actinic keratoses, elastoses and malignancy [17]. Senile comedones were found in 56 (28%) cases in this study. Senile comedones was seen in 95.6% [9], 81% [13] and 11.5% [6] in various studies. In the present study, 2% patients had Favre-Racouchot syndrome, which was similar to that seen in the study by Patange and Fernandez [6].

The incidence of senile lentigens was 30 (15%) in this study. The incidence of senile lentigens in various studies ranges from 0.2% to70.6% [6,9,11,13,18]. The incidence of senile lentigens is well in concordance with the findings of Patange and Fernandez [6] which was carried out in the same ethnic population. The incidence of senile lentigens is lesser than most of the western studies as fair skin is more prone for senile lentigens.

Among the various pathological skin changes seen in the elderly the following conditions are discussed: papulosquamous disorder, eczematous conditions, infections and infestations, pigmentary disorders, benign tumors, vascular disorders, bullous disorders, disorders of keratinization and miscellaneous skin condition.

In this study psoriasis was seen in 14 (7%) patients. The incidence of psoriasis ranges from 1% to 11.2% in various studies [9,6,12,13,18-20]. The incidence of psoriasis in the present study is in concordance with that of the study by Patange and Fernandez [6] and Sahoo, Singh et al [12]. An incidence of 5% of lichen planus was noted in this study which is concordant with study by Sahoo, Singh et al [12].

In the present study eczematous conditions were seen in 62 (31%) patients. The total incidence of eczemas in various studies ranges from 11.9% [4] to 58% [8]. The incidence of lichen simplex chronicus (LSC) and contact dermatitis correlates well with the study by Patange and Fernandez [6]. The incidence of stasis dermatitis in the study is in concordance with the study by Beauregard and Gilchrest [9]. Incidence of seborrhoeic dermatitis correlates well with few studies [8,20]. The increased incidence of LSC and stasis dermatitis in our study may be because of the associated xerosis and pruritus which is high in the patients of this study.

Infections and infestations of skin were seen in 64 (32%) patients. Fungal infections were seen in 11% (22), viral infection in 8% (16), leprosy in 6% (12), pyoderma in 4% (8) and scabies in 3% (6) of patients. The incidence of infections and infestations in our study compares well with few studies. Fungal infections are the commonest infections seen in the elderly as noted in our study and in few other studies [4,6]. Leprosy was seen in 6% of patients in the study. The incidence of leprosy was 1.5% in the study by Grover and Narasimhalu [14].

Pigmentary disorders were seen in 28 (14%) cases, of these vitiligo was seen in 16 (8%) cases, melasma in 10 (5%) and ashy dermatosis in 2 (1%) cases. Various studies report an incidence of vitiligo between 1.2% to 19% [6,12,20]. Our study, as well as that of Patange and Fernandez shows that the incidence of vitiligo is higher in Indian patients. Also, since vitiligo is culturally a dreaded disease in Indian subcontinent, self referral is higher in all hypo-pigmentary disorders.

The incidence of seborrhoeic keratosis ranged from 37.5% to 88% [6,9,13] and of cherry angiomas 49.5% to 75% [6,9,13] respectively in various studies. The findings in this study of seborrhoeic keratosis (56%) and dermatosis papulosa nigra (47%) are comparable to that of the study by Beauregard and Gilchrest [9]. The incidence of cherry angiomas (37%) in this study is comparable to that of the study by Patange and Fernandez [6] but the incidence of melanocytic naevi is less compared to the other studies which have an incidence of 46.3% [9] and 32.5% [6]. No malignant skin conditions were noted in this study. This could be because of the lower incidence of skin cancers in racially pigmented skin

Vascular disorders were seen in 22 (11%) patients, of these senile purpura was seen in 14 (7%) of cases and varicose veins in 8 (4%) of cases. The incidence of senile purpura is in concordance with few other studies [6,9,11,13] but the incidence of varicose veins is much less than that noted by Tindall and Smith (48%) [13]. Senile purpura was mostly noted in the exposed atrophic skin in our patients. Most of our patients being agriculturists have increased solar exposure which may be the cause of senile purpura.

Among the bullous disorders, only bullous pemphigoid was noted in 3 (1.5%) patients. In various studies incidence of bullous disorders ranges from 0.5% to 4.4% [1,8,11,14,19]. The findings in the present study matches with that of the other studies.

Trophic ulcer was seen in 8 (4%) cases and keloids in 5 (2.5%) cases in the study. Only one study by Liao YH, Chen KH [8] et al mention incidence of keloid as 1%. Other studies do not mention the incidence of keloids. Weismann, Krakauer [20] et al mention pressure sores in 2.2% of cases.

Longitudinal ridging of nails was the commonest physiological change seen in 94 (47%) cases followed by loss of luster in 88 (44%) cases. Among pathological changes onychomycosis was seen in 14 (7%) cases, paronychia was seen in 8 (4%) cases and psoriasis was seen in 6 (3%) cases.

Conclusion

A sizeable demographic percentage of many dermatologist populations are geriatric patients. India has thus acquired the label of „an ageing nation" with 7.7% of its population being more than 60 years old [21]. The geriatric population is afflicted with a great many dermatology concerns, not only because of normal ageing process but the additional stressors acquired from the environmental causes. The long term effect of the exterior causes such as UV radiation, chemical irritants, temperature, humidity, dryness, pathogens and so forth are compounded for those who have had to endure longer. This cumulative damage profoundly affects the health of the elderly.

More epidemiologic investigations concerning dermatologic diseases in the elderly population are needed to complement the information in this study, which presents an interesting profile of the various skin diseases and notes changes in western and Indian skin.

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A STUDY ON SEXUALLY TRANSMITTED DISEASES IN PATIENTS IN A STD CLINIC IN A DISTRICT HOSPITAL IN NORTH INDIA

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Abstract

Introduction: The Sexually transmitted diseases (STDs) are a global health problem of great magnitude. The pattern of STDs differs from country to country and from region to region. The increased risk of the transmission of HIV is known to be associated with the presence of sexually transmitted diseases (STDs) and despite the presence of the National STD Control Program in India the number of people with STDs remains high.

Aim: The aim of our study was to study the profile of patients in a STD clinic in North India and to study various sexually transmitted infections in both male and female patients.

Material and Methods: A prospective study of the patients attending STD clinic in a district hospital in North India from December 2009 to December 2012 was done. A total of 2700 patients attending the STDclinic in three years from December 2009 to December 2012 were taken up for the study.

Results: The commonest sexually transmitted infection in males was herpes genitalis (30%) followed by 20% cases of genital warts. 10% patients had gonorrhoea, genital molluscum contagiosum, syphilis and genital scabies each and 5% patients had nongonococcal urethritis. Only 5% of the total patients had chancroid, donovanosis and LGV. The commonest sexually transmitted infection in females was vaginal discharge seen in 40% patients, lower abdominal pain in 20% patients, herpes genitalis in 15% patients followed by 20% cases of genital warts and syphilis each. Genital molluscum contagiosum was seen in 5% patients only.

Conclusions: The treatment of STD's is important as both non-ulcerative and ulcerative STDs increase the susceptibility to or transmissibility of HIV infection and as such, an increase in STD prevalence as revealed by clinic attendance in this study was bound to facilitate the spread of HIV/AIDS. Perhaps it is high time health planners adopted a more aggressive and result oriented HIV/AIDS/STD awareness campaign strategy.

Key words: Sexually transmitted diseases; HIV; infections; laboratory; investigations

Cite this article:
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Introduction

Sexually transmitted diseases (STDs) have great impact on health of the individual and community. Control of STDs has been given priority since the advent of the HIV/ AIDS epidemic, in recognition of their role in facilitating the sexual transmission of HIV [1,2]. Although the course of many of these STDs is benign even without treatment, some infections may lead to long-term sequelae, including pelvic inflammatory disease, infertility and cervical cancer. Their epidemiological profile varies with geography and depends upon ethnic, demographic, social and economic factors. In addition to the burden on youth, women are also severely affected. Biological factors place women at greater risk than men for the severe health consequences of STDs. Sexually transmission requires the agent to be present in one partner, the other partner to be susceptible to infection with that agent and that the sex partners engage in sexual practices which can transmit the pathogen. STDs rank among the five leading health problems in the developing countries.

The majority of these diseases affect men and women during their reproductive years. Eighty-six percent of STDs occur among persons 15-29 years of age.

The health and economic costs of STDs are heightened because many STDs, especially those among women, produce no symptoms and can remain undetected until more serious health complications, such as pelvic inflammatory disease (PID) or cervical cancer, have developed [3]. STD clinics have served as the primary avenue for assessing disease patterns in high-risk groups and implementing control programs. Since most data about persons with STDs have been obtained from government STD clinics, little is known about patterns of seeking medical care for STDs outside of government clinics. NACO(National aids control organization) data based on STD clinic data may not provide reliable information about the treatment of STDs, because an estimated 30% - 40% of STD cases are treated outside of STD clinics.

Aim

1. To study the profile of patients in a STD clinic in North India.
2. To study various sexually transmitted infections in both male and female patients.

Material and Methods

A prospective study of the patients attending STD clinic in a district hospital in North India from December 2009 to December 2012 was done. A total of 2700 patients attending the STD clinic in three years from December 2009 to December 2012 were taken up for the study. Prior approval of hospital ethical committee was taken before the start of the study. The consent of patients was taken before the start of the study. All the patients were subjected to laboratory investigations including HIV & VDRL. In patients of vaginal discharge, KOH examination for fungus, whiff test, wet mount and gram stain was done in all the patients. In patients of urethritis, smear was made from urethral discharge and stained with grams stain.

Results

The data of all the patients was compiled and tabulated Tabl. I - IV).

Sr no	Age distribution (years)	Number	Percentage %
1	11 - 20	108	4
2	21 - 30	1512	56
3	31 - 40	918	34
4	41 - 50	135	5
5	51 - 60	27	1
	TOTAL	2700	100

Table I. Aga distribution of patients.

Sr no	Sex Distribution	Number	Percentage %
1	females	1620	60
2	males	1080	40
	TOTAL	2700	100

Table II. Sex distribution of patients

Sr no	Occupation	Number	Percentage %
1	students	540	20
2	farmers	270	10
3	housewives	810	30
4	labourers	270	10
5	female sex workers	540	20
6	unemployed	270	10

Table III. Occupation of patients.

Sr no	Sexually Transmitted Infections	Number	Percentage %
1	herpes genitalis	324	30
2	genital warts	216	20
3	gonorrhoea	108	10
4	non gonococcal urethritis	54	5
5	genital molluscum	108	10
6	syphilis	108	10
7	genital scabies	108	10
8	chancroid, donovanosis & LGV	54	5
	TOTAL	1080	100

Table IV. Sexually transmitted infections in male patients.

Sr no	Sexually Transmitted Infections	Number	Percentage %
1	vaginal discharge	648	40
2	lower abdominal pain	324	20
3	herpes genitalis	243	15
4	syphilis	162	10
5	genital warts	162	10
6	genital molluscum	81	5
	TOTAL	1620	100

Table V. Sexually transmitted infections in female patients.

Discussion

There were total 2700 patients for this study. The commonest age group (56%) in our study was 21-30 years, followed by 34% patients in the age group of 31-40 years. Females outnumbered males and th female: male was 1.5:1. Regarding the occupation of the patients, housewives comprised 30% patients followed by students and female sex workers having percentage of 20% each. Farmers, labourers amd unemployed persons formed 10% each of the total population. The commonest sexually transmitted infection in males was herpes genitalis (30%) followed by 20% cases of genital warts (Figs. 1, 2). 10% patients had gonorrhoea, genital molluscum contagiosum (Fig. 3), syphilis and genital scabies each and 5% patients had non gonococcal urethritis. Only 5% of the total patients had chancroid, donovanosis and LGV (Figs. 4, 5). The commonest sexually transmitted infection in females was vaginal discharge seen in 40% patients, lower abdominal pain in 20% patients, herpes genitalis in 15% patients followed by 20% cases of genital warts (Fig. 6) and syphilis each. Genital molluscum contagiosum (Fig. 7) was seen in 5% patients only. 40% of the patients were educated upto the tenth standard. 60% patients were from urban areas and 40% patients were from rural areas. Out of the total of 1080 males, 35% of the males were involved in premarital sex and 24% had extramarital sex. Out of 1620 females, 10% were involved in premarital sex and 15% indulged in extramarital sex. 90% of the female patients were married whereas only 50% of the males were married. Out of all the patients 11% were HIV positive and 21% were VDRL positive.

In our study, females outnumbered males which is in contrast to the previous studies in which males exceeded females [4]. The reasons for increased female patients in our study may be due to the STD awareness campaign launched in our region. Second possible reason for increased female patients in our study might be due to the fact that the incharge of the STD clinic in the district hospital is a female consultant (STD specialist) and most of the male STD patients have certain inhibitions in getting themselves examined from a female doctor.

In addition to STDs awareness campaign already in progress, the invitation of sexual partners using partner notification cards in syndromic case management might have been responsible for increased number of male and female outpatients observed in this study.

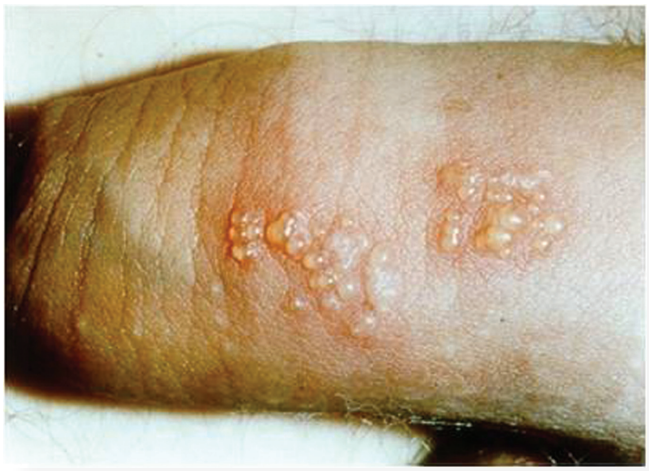

Figure 1. Herpes genitalis in a 28 years old male patient.

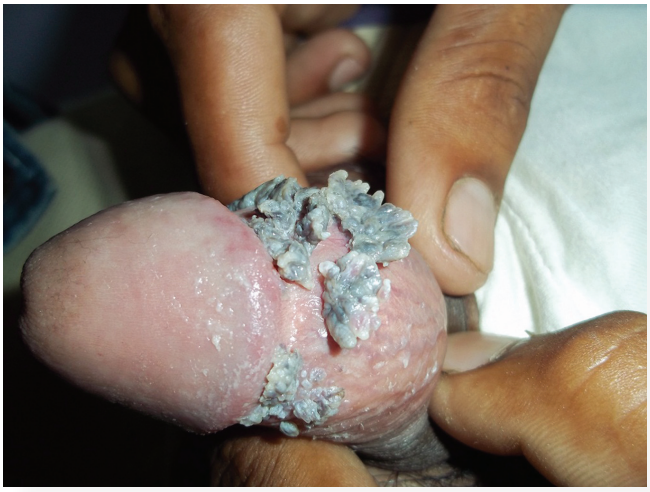

Figure 2. Genital warts in a 20 years old male.

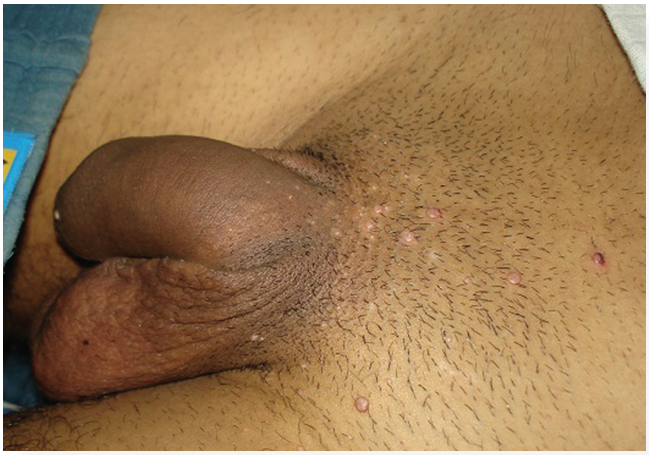

Figure 3. Genital moluscum contagiosum in a 30 years old male.

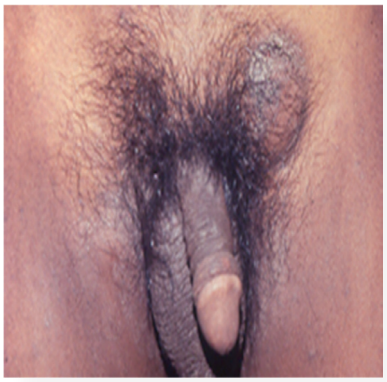

Figure 2. Iguinal bubo (LGV) in 37 years old male.

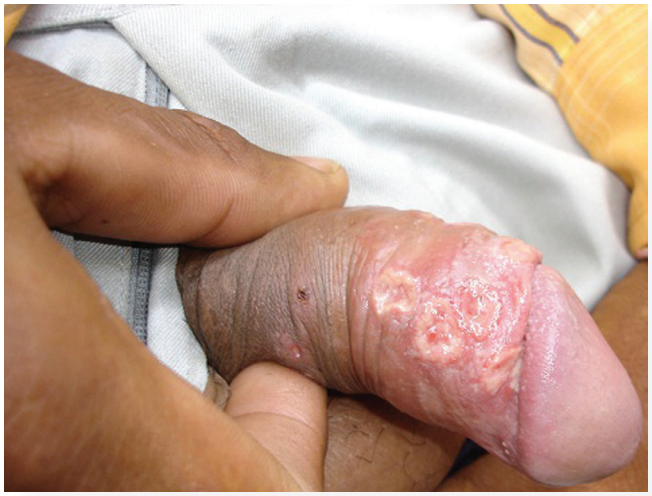

Figure 5. Multiple chancroidal ulcers in a 33 years old male.

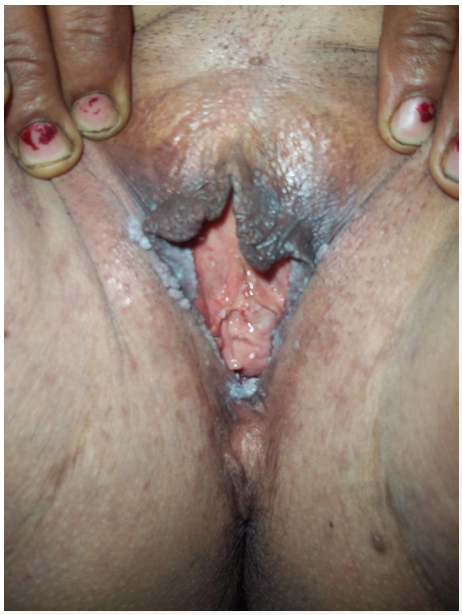

Figure 6. Genital warts in a 17 years old female.

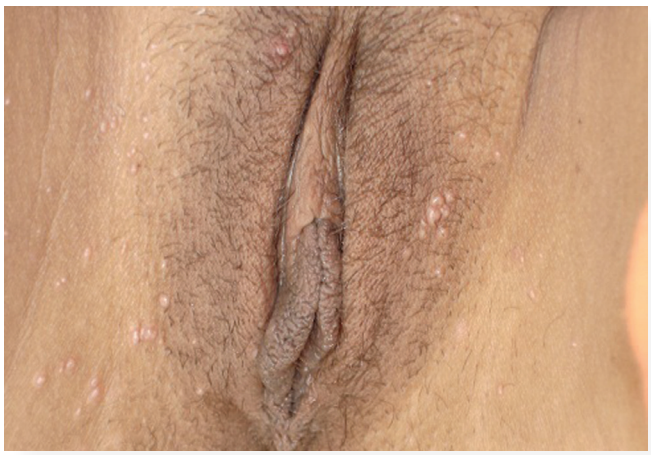

Figure 7. Genital moluscum contagiosum in a 35 year old female.

It was seen from our study that the trends of STD are more toward viral origin (e.g. genital herpes, warts or molluscum Contagiosum) as compared to bacterial origin (e.g. syphilis, chancroid). This is probably due to the fact that most of the bacterial and treponemal STDs are treated at the primary level by virtue of large number of currently available antibiotics and these organisms are responding to antibiotics [5,6]. Genital herpes is the second most prevalent STD worldwide and the commonest cause of GUD in the developed World. There has been a constant increase, both in the incidence and prevalence of genital herpes. The increasing incidence of genital herpes infection may be attributed to a decreased in the incidence of bacterial STD owing to their treatment at primary level and change in the pattern of sexual behavior [7].

The most commonly associated risk factor for the spread of sexually transmitted infections was multiple sexual partners. Men reported that they had multiple partners because this practice supports their sense of masculinity [8-10]. Many other parts of the developing world, including South Asia where the HIV epidemic is now spreading rapidly, are having high rates of STDs as both HIV and STDs are closely interlinked, early diagnosis, treatment and control of STDs offers a rational approach to the control of HIV [11,12].

Conclusion

treatment of STD's is important as both non-ulcerative and ulcerative STDs increase the susceptibility to or transmissibility of HIV infection and as such, an increase in STD prevalence as revealed by clinic attendance in this study was bound to facilitate the spread of HIV/AIDS. Perhaps it is high time health planners adopted a more aggressive and result oriented HIV/AIDS/STD awareness campaign strategy.

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A PRELIMINARY STUDY ON CLINICAL OUTCOME OF CORTICOSTEROID THERAPY IN PEMPHIGUS PATIENTS

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Abstract

Introduction: Pemphigus is life threating blistering of autoimmune disease of the skin and mucous membrane characterised by autoantibodies (auto ABs) against desmoglein-3 (DSG-3). Desmosomal adhesions, protein expressed on the surface of epidermal keratinocytes.

Aim: The present study was to assess the incidence rate of pemphigus, to evaluate the clinical course along with clinical manifestations, Complications and Metabolic factors of patients with pemphigus and to investigate the disease severity and induction of remission during the clinical course and whereas to assess the oxidative stress and antioxidant status in pemphigus patients in our hospital.

Material and Methods: A prospective study was conducted over a period of January 2012 to December 2012 at dermatology department, MGM Hospital, Warangal. The data was collected from 32 cases of Pemphigus on the basis of Age, Sex, Social Habits, BMI, Histopathological forms, Clinical manifestations and Drug therapy. This hospital is 1200 bedded government hospital provided Outpatient and Inpatient care for Indian citizen especially in Telangana region free of cost.

Results: Of the 32 pemphigus patients, 75% were diagnosed with Pemphigus Vulgaris (PV), 12.5% with Pemphigus Foliaceus (PF) and 12.5% with Bullous Pemphigoid (BP). The male to female ratio was approximately 1:1.3. The mean age of onset was 40.8 years in Pemphigus patients. The Onset of disease was 29.85. 34% of patients with Pemphigus had both the mucosal and skin involvement during the clinical course while 25% at the onset of disease. The most common complication was found to be increase blood sugar (40%). Most commonly prescribed adjuvant is dapsone. Majority attained the complete remission and remaining of them attains partial remission. Oxidative stress levels were higher and antioxidant status levels were lower in study subjects when compared to controls.

Conclusions: PV is the most common subtype of Pemphigus in our Hospital and usually affects females more than males. Our study reveals that mucosal and skin involvement is common. Corticosteroids and dapsone as adjuvant is majorly prescribed. Most of patients attain complete remission and remaining of them achieves partial remission. Oxidative stress levels were higher and antioxidant status levels were lower in our study subjects when compared to controls.

Key words: Clinical course; Pemphigus; Remission; Treatment

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Introduction

Pemphigus is an uncommon disease with an incidence rate ranging 0.5-3.2/100,000/year. The peak incidence of pemphigus vulgaris occurs between the fourth and sixth decades of life with a male-to-female ratio of 1:2 [1]. The prevalence of disease in various countries are United states (32%), Jews (16.1%), Greek (9.3%), Bulgarian (4.7%), Malaysian (2%), Saudi Arabian (1.6%). Epidemiology of pemphigus has shown different trend in India compared with Western literature in various counts. The incidence of pemphigus among the dermatology outpatient attendees has varied widely, 0.09 to 1.8% [2]. The incidence assessed by clinic-based questionnaire survey conducted in Thrissur district, Kerala, was 4.4 per million per year. The incidence was found to be higher than available data from Germany, France, and lower than Tunisia [3].

Therefore, the aim of present study to assess the incidence rate of pemphigus and to evaluate the clinical course along with clinical manifestations, Complications and Metabolic factors of patients with pemphigus. In additon to that to investigate the disease severity and induction of remission during the clinical course and to assess the oxidative stress and antioxidant status in pemphigus patients in a tertiary care hospital.

Materials and Methods

The present study was conducted at the department of Dermatology of a tertiary care teaching hospital, i.e., Mahatma Gandhi Memorial Hospital, Warangal, Andhra Pradesh, India, which is 1200 Bedded multidisciplinary Tertiary Care government hospital. The study was carried out for the period of one year. The patients included in the study who was suffering with Pemphigus. Sample/ Data collection was performed according to hospital regulations after approval by the Hospital administration / Ethical committee. The study was conducted in various steps.

Step 1: Identify or selection of Patient inclusion in the study.

All patients diagnosed pemphigus on the basis of history, skin biopsy report of the patient along with the clinical features like fluid filled lesions, multiple hyperpigmented lesions all over the body and "Nikolsky sign" were included in our study. All subjects attendee completed a detailed standardized questionary. The victims were also sorted for different epidemiological factors like age, gender, marital status, socio-economic status and life style pattern. All patients were reviewed and admitted in dermatology department based on severity of disease. The treatment included with corticosteroids, emollients (liquid paraffin), multivitamin tablet and dapsone.

Step 2: Design of the study.

Study period: The study was planned to be carried out for a period of one year consent from the hospital authority. The Protocol of the study which includes the Introduction, Objective and Methodology was submitted to the Superintendent of our hospital and to Kakatiya Medical College to obtain the Ethical Committee approval and was obtained to carry out the present study.

Step 3: Defining criteria, Standards and Design of Data Entry Format Inclusion Criteria.

Patients with Pemphigus undergoing prednisolone treatment of Age ≥ 20, either sex.

Exclusion Criteria:

- Patients without Pemphigus
- Patients with Pityriasis versicolor, Eczema, Candida infections

Step 4: Literature Survey.

The literature supporting the study was collected and analysed. The different sources used to collect the literature were Micromedex drug information databases, various websites like PubMed, Dove Press, Science alert, Bentham Publisher, Pharmaintelligence, Journal on Web, Science direct, DOAJ, Medline, etc.

Step 5: Data collection.

Data were recorded in a case record form that was particularly designed for this study. Data concerning age of onset, sex, presenting symptoms, characteristic of skin and mucosal lesions, laboratory investigations, treatment outcomes and clinical course were obtained.

Step 6: Sample Collection.

Five (5ml) venous blood samples were collected from the patients after obtaining the Informed consent form from the patient or the attendee. The samples were collected in 5ml EDTA vials (for serum) and 5ml heparin tubes (for plasma). The samples were immediately transferred to the cooling centrifuged at 6000 rpm for 20 minutes. The supernatant was separated into a labelled eppendroff's tubes and kept at 40ºC till biochemical analysis. The amount of lipid peroxidation products present in the serum samples were estimated by the Thiobarbituric acid reactive substances (TBARS) method [4]. The Glutathione is endogenous antioxidant; it forms a coloured complex with DTNB, which is measured spectrophotometrically [5,6]. For the estimation of total antioxidant status, we used a stable free radical- diphenyl-picryl hydrazyl (DPPH) at the concentration of 0.2mM in methanol [7,8].

Disease severity and remissions of Pemphigus

Disease severity was classified according to the severity scale created by Herbst and Bystryn. The scale is based on the compilation of the extent of disease and the intensity of therapy. The extent of disease was classified by the number of body areas involved, including scalp, face/neck, upper trunk, lower trunk, arms, legs, oral mucosa and genitals. A score 0 was given for no lesions, ½ for lesions healed within 48 hours, 1 for 1 site involved, 2 for 2 to 3 sites involved, 3 for 4 to 5 sites involved and 4 for ≥ 6 sites involved. The score for the intensity of therapy was given as follows: 0 for no treatment required, ½ for only topical treatment needed, and 1, 2, 3 and 4 for ≤ 15, 16 to 49, 50 to 89 and ≥ 90mg of Prednisolone (or equivalent) per day respectively. If ≤ 100 mg/day of azathioprine or cyclophosphamide or gold or dapsone or cyclosporine was used, an additional score of 1 was added. An extra score of 2 was added if > 100 mg/day of azathioprine/cyclophosphamide or plasmapheresis were used. Then the sums of these scores of ≤ 2+, 3 to 6+ and ≥ 7+ were used to classify the disease as mild, moderate and severe disease respectively. Complete remission was defined as a period of more than 1 month during which the patient was receiving no systemic therapy and was lesion free. Partial remission was defined as a period greater than 1 month during which the patient was lesion free and receiving no more than 15 mg/day if prednisone or its equivalent, receiving only 100 mg/day or less of cyclophosphamide or azathioprine, or receiving only gold or dapsone. Duration of remission was classified as short if it was at least 1 month but less than 6 months in duration and was classified as long if it lasted 6 months or longer.

Statistical analysis

Statistical analysis was carried by student t-test using Graph Pad Prism Version-5. Results were expressed in Mean±SD. Probability values of $P < 0.05$ were considered to be statistically significant. t-test: The t-test was performed to compare the average of biochemical parameters.

Results

In this study, total 32 patients were diagnosed with Pemphigus. Out of them 14 were male and 18 were female. Ratio of men to women is 1:1.3.

Table I shows the mean age limit of cases was found to be 40.81±13.72. Whereas, control was found to be 43.91±11.52. Of 32 cases onset of disease < 1 year includes 22% of patients, 1-4 years includes 47%, 5-8 years includes 31%. The greater mean value of age was 23.29±3.208 and it was found to be 41-50 years.

Gender	Number of Patients (n=32)	Percentage (%)
Male	14	44
Female	18	56
Total	32	100
Onset of diseases	08	04
<1	10	22
1-4	15	47
5-8	07	31
Age and BMI of study subjects	Mean value of BMI	Standard Deviation
Below 30	21.31	4.430
31-40	20.93	3.851
41-50	23.29	3.208
51-60	22.90	3.746
Above 60	24.20	2.828
Age in years	Control (n=32)	Case (n=32)
Below 30	07	07
31-40	05	11
41-50	12	08
51-60	06	04
Above 60	02	02

Table I. Patient characteristic of pemphigus in our study population.

The prevalence of pemphigus among study subjects shows, 75% of patients had Pemphigus Vulgaris, 12.5% of had Pemphigus Foliaceus and 12.5% had Bullous Pemphigoid are shown in Table II.

Type of Pemphigus	Number of Patients (n=32)	Mean value of age
Pemphigus Vulgaris	24	40.29±12.78
Pemphigus Foliaceus	04	31.50±10.91
Bullous Pemphigoid	04	53.25±15.78

Table II. Prevalence of Pemphigus among study subjects.

The clinical manifestation of study subjects show vesicle/bullae 100%, 81% erythematous base, 66% normal skin base, 53% patch/plaque, 88% erosion/ulcer, 13% pustules and remaining 13% show scar as morphology of skin lesions respectively as shown in Table III.

Morphology of skin lesions	Number of Patients (n)	Mean value of age
Vesicle/bullae	32 (100%)	40.29±12.78
Base: Erythematous base	26 (81%)	31.50±10.91
Normal skin base	21 (66%)	53.25±15.78
Patch/plaque	17 (53%)	
Erosion/ulcer	28 (88%)	
Pustule	04 (13%)	
Scar	04 (13%)	

Table III. Clinical manifestations of study subjects.

Among 32 patients, 1 patient had lesions beginning on the oral mucosa at the onset of disease and 1 of them still show only oral mucosal involvement during the follow-up period (pure oral pemphigus). 23 patients had lesions beginning on the skin at the onset of disease and 20 of them still show skin involvement during the follow-up period, remaining 8 of them had both mucosal and skin involvement at the onset of disease and 11 of them still show both during the follow-up period as shown in Table IV.

Site of involvement	At onset	During clinical course
Oral mucosa	01 (3%)	01(3%)
Skin involvement	23 (72%)	20 (63%)
Both oral mucosa and skin	08 (25%)	11 (34%)

Table IV. Site of involvement at onset and during clinical course.

Biochemical factors	Mean value ± SD	'P' value
ESR (mm)	33.75±20.91	<0.0001
RBS (mg/dl)	129.3±39.83	
B. Urea (mg/dl)	28.06±5.73	
S. Creatinine (mg/dl)	0.887±0.21	
Hb (gm %)	11.02±1.18	

Table V. Biochemical profile of study subjects.

The mean values of Biochemical factors such as ESR, RBS, B.Urea, S.Creatinine and Hb were estimated. *P (<0.0001)* was statistically significant (Table V).

Of 32 pemphigus patients, Anemia was the most common side effect found (56%), followed Hyperglycemia (40%), Infection (3%), Weight gain (31%). Serious infection associated with mortality occurred in 1 patient (3%) of PV as shown in Table VI and were treated with high dose corticosteroid and had been admitted to the hospital. During the hospital stay, he later developed septic shock which resulted in death.

Complications	Number of Patients
Hyperglycemia	13 (40%)
Infection	01 (3%)
Weight gain	10 (31%)
Anemia	18 (56%)
Death	01 (3%)

Table VI. Associated complications of study subjects.

Distribution of lesions in subjects	Number of patients (%)
Mouth	34
Trunk	65
Face	68
Upper extremities	78
Lower extremities	78
Genital	28
Scalp	46

Table VII. Associated complications of study subjects.

The extent of disease is more in Upper and Lower extremities (78%), followed by Face (68%), Trunk (65%), Scalp (46%), Mouth (34%) and Genital (28%) as shown in above Table VII.

Among 32 patients, 75% of patients treated with systemic steroids, 9% of patients treated with adjuvant, 13% with both adjuvant and steroids and 3% of them treated with topical medications was represented above Table VIII.

Among the study patients, none of them show mild severity, 23 (72%) patients moderate severity of disease and 9 (28%) patients show severe as shown in Table IX.

Treatment	Number of Patients
Systemic Steroids	24 (75%)
Adjuvant	03 (9%)
Adjuvant and Steroids	04 (13%)
Topical Medications	01 (3%)

Table VIII. Intensity of therapy in study subjects.

Disease severity	Number of Patients (%)
Mild	Nil
Moderate	23 (72)
Severe	09 (28)

Table IX. Disease severity of study subjects.

Table X shown relation between initial disease severity response to treatment and induction of remissions of study subjects.

Two factors were found to be predictive of remission induction: disease severity at the time of diagnosis and an early response to therapy as shown in Table XI. Patients with moderate disease at onset manifested by a severity score of 6 or less were twice as likely to have complete remission as those with severe disease (severity score of ≥7). Patients with a rapid response to therapy were twice as likely to have a complete remission than those who did not, regardless of the patient's initial disease severity (ie, complete remission in 75% compared with 40% of patients with moderate disease and in 33% compared with 17% of those with severe disease).

Levels of MDA, a major oxidation product of peroxidised polyunsaturated fatty acids, have been considered as an important indicator of lipid peroxidation was presented in Table XII.

Disease Severity at Onset	Number of Patients	Number (%) with Complete remission
Mild	Nil	Nil
Moderate	23	12 (52)
Severe	09	02 (22)

Table X. Relation between initial disease severity response to treatment and induction of remissions of study subjects.

Rapid Responders		Slow Responder	
Number of Patients	Number (%) with Complete Remission	Number of Patients	Number (%) with Complete Remission
Nil	Nil	Nil	Nil
08	06 (75)	15	06 (40)
03	01 (33)	06	01 (17)

Table XI. Rapid responders vs slow responder.

Parameter	Case	Control	'P' value
MDA (µ mol/ml)	17.95±10.48	17.71±5.22	<0.0001
GSH (µg/ml)	24.20±22.24	37.98±10.08	<0.0001
TAS (nmol/ml)	31.86±13.37	38.23±10.50	<0.0001

Table XII. Levels of MDA, a major oxidation product of peroxidised polyunsaturated fatty acids, have been considered as an important indicator of lipid peroxidation.

Discussion

Pemphigus has a variety of epidemiological profiles in different regions of the world. This was the preliminary study done by us in Telangana region. Our study reveals that PV is the most common subtype of pemphigus. Our data show that pemphigus affected females more than males. Male to female ratios is 1:1.3 which is similar to Ameneh Yazdanfar [9]. In our study, the mean age of onset was in the fifth decade of life which is similar to the previous studies of Piamphongsant et al. [10] (mean age = 40.8 years). The Onset of disease ranged from <1 to 8 years and the mean duration of pemphigus was found to be 29.85±25.97 which is similar to Yu-Huei Huang et al [11]. The mean BMI was 22.05±3.72.

The nature and distribution of the lesions as well as mucosal involvement seen in different types of Pemphigus in our study was similar to b. Flaccid bullae/vesicle were seen in all cases. Patients with Pemphigus often have mucosal and skin involvement. In our study, 34% of patients with Pemphigus had both the mucosal and skin involvement during the clinical course while 25% had skin and mucosal lesions present at the onset of disease which is similar to the results reported by Chams Davatchi et al [12]. Approximately half of patients with Pemphigus in our study had the eroded lesions as clinical manifestations. Our study also showed the Mean values of ESR, RBS, B.urea, S.creatinine and Hb%.

In our study disease severity was showed to be moderate and similar to Kanokvalai Kulthanan et al [13]. Corticosteroids are the major drugs used in pemphigus patients because are able to reduce autoantibody levels and also dramatically decrease the mortality rate. Nevertheless, high dose administration and prolonged usage of corticosteroids may bring about serious complications in our study. Most common complication was increase blood sugar after using corticosteroids and anaemia, which was seen in 40% and 56% of the patients. The mortality rate in our study was 3% (1 patient) which is similar to Ameneh Yazdanfar [9]. In our study 75% of patients with Pemphigus received prednisolone. Adjuvant drugs were additionally prescribed to 13% of patients to achieve disease control. The advantages of adjuvant drugs are the steroid-sparing effect and the augmentation of steroid efficacy. The most common prescribed adjunctive drug in our centre was dapsone. 9% patients with pemphigus treated with dapsone monotherapy and achieved remission and 13% patients treated with dapsone concurrently with prednisolone which is similar to Gurcan et al. analysed 55 pemphigus patients treated with dapsone from the literature published between 1969 and 2008. They state that 86% of PV patients and 78% of PF patients responded to treatment either with dapsone alone or dapsone concurrently with prednisolone.

The other parameter commonly used to judge response to therapy in pemphigus is the induction of a remission.

Review of all major studies of pemphigus conducted during the past 4 decades describes these as occurring fewer than one-third of patients the average incidence of remissions in the more recent studies is similar to the results reported in earlier studies. The proportion of evaluable patients in complete remission was 33% and 75% respectively. The remaining patients were in partial remissions controlled with only an adjuvant which is similar to Andrew Herbst et al [8].

In pemphigus, the increased production of reactive oxygen species from activated neutrophils decreases concentrations of antioxidant vitamins and enzymes in plasma and red blood cells (RBC), resulting in oxidative stress. We compared lipid peroxidation, a measure of reactive oxygen species production, total antioxidant status, reduced glutathione (GSH). Lipid peroxidation levels (malonyldialdehyde) were significantly higher ($p < 0.0001$) in Pemphigus patients than in control subjects. Significantly lower concentrations of total antioxidant status $p< 0.0001$) and reduced glutathione levels ($p < 0.0001$) were found in Pemphigus patients when compared to controls is similar to the Naziroğlu M et al. showed Plasma and RBC lipid peroxidation levels (malonyl dialdehyde) were significantly higher ($p<0.05$) in pemphigus vulgaris patients than in control subjects.

Conclusion

The present study is the first to reveal the incidence, clinical manifestations, complications, metabolic factors, management and clinical course of Pemphigus patients in tertiary care hospital. In our study we found that Pemphigus is the most common form and affects females more often than males meanwhile our study reveals that mucosal and skin involvement is common in Pemphigus patients, whereas, Corticosteroids are majorly prescribed to study subjects and dapsone is the most common adjuvant drug prescribed. The majority of patients attain complete remission and remaining of them achieves partial remission. In addition to that Oxidative stress seems to be responsible for the onset/aggravation of many disease conditions. It is considered as one of the factor for the etiopathogenesis of Pemphigus. The oxidative stress levels in study subjects were found to be higher when compared to controls and antioxidant status levels were found to be lower in study subjects when compared to controls.

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CLINICAL PROFILE OF HERPES ZOSTER IN A RURAL TERTIARY CARE HOSPITAL IN SOUTH INDIA

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Abstract

Introduction: Herpes zoster (Hz), which presents as localized, painful cutaneous eruption is a common clinical problem, particularly among adults of above 50 years of age and immunocompromised patients. It results from reactivation of varicella zoster virus.

Aim: To analyze the clinical pattern of herpes zoster with special emphasis to the precipitating factors and incidence of post herpetic neuralgia.

Material and Methods: 100 clinically diagnosed cases of herpes zoster, attending the Dermatology department of MVJ Medical College and Research Hospital Bangalore, India from a period of June 2010 to May 2012 were included in the study. The clinical pattern of herpes zoster with special emphasis to the precipitating factors and incidence of post herpetic neuralgia were analyzed.

Results and Conclusion: The study showed a male preponderance. Age group varied from 8-80 years. 42% of the total patients presented during summer season when the incidence of varicella is also high. Past history of chicken pox was present in 68% of the patients. 11% of the patients were on immunosuppressive treatment. 8% of the patients had associated diabetes mellitus and 7% showed HIV seropositivity. Thoracic dermatomal involvement was seen in majority of patients. Most commonly observed complication was post herpetic neuralgia which was encountered in 36% of the patients and most of these patients were (77%) were above the age of 60years.

Key words: Herpes Zoster;Varicella Zoster; Postherpetic Neuralgia

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Introduction

Herpes zoster (HZ), which presents as localized, painful cutaneous eruption is a common clinical problem, particularly among adults of above 50 years of age and immunocompromised patients. It results from reactivation of varicella zoster virus (VZV). After primary infection of varicella, the virus persists asymptomatically in the ganglia of sensory cranial nerves and spinal dorsal root ganglia. As cellular immunity to VZV decreases with age or because of immunosuppression, the virus reactivates and travels along the sensory nerves to the skin, causing the distinctive prodromal pain followed by eruption of the rash [1]. Clinical presentation is dependent on rapidity of immune response and ranges from typical zoster to scattered vesicles, zoster sine herpete or disseminated zoster. It is a cause of considerable morbidity, especially in the elderly and can be fatal in immunocompromised or critically ill patients.

Aim of the Study

To analyze the clinical pattern of herpes zoster with special emphasis to the precipitating factors and incidence of post herpetic neuralgia.

Materials and Methods

100 clinically diagnosed cases of herpes zoster, attending the Dermatology department of MVJ Medical College and Research Hospital, Bangalore, India from a period of June 2010 to May 2012 were included in the study.

Detailed history was recorded with emphasis to the presenting symptoms, chicken pox in the past, risk factors, associated systemic diseases and complications. Clinical examination including the segment of involvement, morphology of lesions and any evidence of complications was carried out. Tzanck smear examination and hematological investigations including complete hemogram, blood sugar and HIV serology was done. Patients were followed up once a week for 2 weeks and once a month for 6 months. The data was tabulated and analyzed statistically.

Results

The study showed a male preponderance with a male to female ratio of 3:2 (*p= 0.00186*). Age group varied from 8-80 years. 38% of the patients were above the age of 60 years and 6% of the patients belonged to less than 20 years of age (*p=0.002*) (Tabl. I). 42% of the total patients presented during summer season when the incidence of varicella is also high.

Past history of chicken pox was present in 68% of the patients (*p=0.0001*). 11% of the patients were on immunosuppressive treatment either on long term steroid therapy or on chemotherapeutic agents. 8% of the patients had associated diabetes mellitus and 7% showed HIV seropositivity.

36% of the patients complained of a prodromal symptom of pain 3-7 days prior to the developmentof lesions and 24% had paraesthesia. Thoracic dermatomal involvement was seen in majority of patients (62%) followed by lumbar (16%) and cranial (14%) and cervical (8%) dermatomes (p=0.0001) (Tabl. II). Among the cranial nerves, trigeminal nerve was involved in 11 patients and one patient had Ramsay-Hunt syndrome. 9 patients had herpes zoster ophthalmicus, of which 4 had corneal involvement. Multidermatomal involvement was observed in 11 patients and disseminated herpes zoster and herpes zoster duplex bilateralis were observed in one case each. All these patinets were immunocompromised.

In majority of the patients lesions resolved within 10-14 days except in immunocompromised individuals which prolonged upto 21 days. Most commonly observed complication was post herpetic neuralgia which was encountered in 36% of the patients and among them 28 (77%) were above the age of 60years.

Age Distribution (Yrs)	Percentage of Cases (%)
<20	6
20-40	24
40-60	32
>60	38

Table I. Age distribution.

Segmental Distribution	Percentage of Cases (%)
Thoracic	62
Lumbar	16
Cranial	14
Cervical	8

Table II. Segmental distribution.

Discussion

In the present study majority of the patients (38%) belonged to the age group of >60 years followed by 32% of patients in 40-60 years group. An increase in the reactivation of varicella zoster virus (VZV) with increasing age is reported in the literature. One study reported a 0.3% rate of VZV reactivation in the overall population, compared with 1.0% in persons older than age 80 [2]. This is thought to result from the decline in virus-specific, cell-mediated immune responses that accompanies advancing age [3]. A male preponderance with a male to female ratio of 3:2 is observed in this study which is in accordance with other studies from south India [4,5]. Trauma and stress as a result of their occupation and outdoor activity may be the predisposing factor for the male preponderance in Indian rural setup [4]. Increased incidence noticed during the summer months in this study could be attributed to reactivation of latent infection on exposure to varicella virus as chicken pox is also more in these months. This is in contrast to the reports of herpes zoster risk reduction through exposure to chicken pox patients. This exogenous boosting hypothesis states that re-exposure to circulating VZV can inhibit viral reactivation and consequently also herpes zoster in VZV-immune individuals which is also the basis for varicella zoster vaccination [6].

Past history of chicken pox was present in 68% of patients and none of our patients had taken the varicella vaccination. Various prodromal symptoms usually preceeds herpes zoster by 2-10 days; the most common being pain, paraesthesia,tingling and itching. Rarely other symptoms like hiccup also can preceed herpes zoster of the cervical and thoracic dermatome [7,8]. In this study similar to the other studies, pain (36%) and paraesthesia (24%) were the common prodromal symptoms.

In our study thoracic dermatomal involvement was seen in majority of patients (62%) followed by lumbar (16%) and cranial (12%) and cervical (8%) dermatomes. This is in contrast to the study by Goh and Khoo where the most commonly involved dermatomes were thoracic in 45% and cervical in 23% [9]. In our study multidermatomal involvement was observed in 11 patients and herpeszoster duplex bilateralis and disseminated herpes zoster was observed in one case each ,all of them were immunocompromised. This is in concordance with other studies [4,10] where as Gahalaut et al has reported a case of herpeszoster duplex bilateralis in an immunocompetent individual [11].

HIV seropositivity was seen in 7% of the patients in our study and two of them had multidermatomal and one had disseminated zoster.This is similar to the study by Kar et al where they observed a seropositivity of 9.5% in 115 cases studied [12]. Smith et al in their study of 912 HIV-1 seropositive patient, found that 53 patients (16%) of the study population had herpes zoster. Approximately 15% of their patients had previous history of herpes zoster [13].

Post herpetic neuralgia (PHN) was encountered in 36% of cases and 77% of these patients belonged to the age group of >60 years. A higher incidence of PHN (82%) was observed in patients with ophthalmic zoster which is in contrast to study by Abdul Latheef et al [4]. Among these patients one of them progressed to to trigeminal neuralgia as reported in one study [14].

Conclusion

Majority of our patients were above age of 60 years and males outnumbered females. An increase in incidence of herpes zoster was noticed during the summer months. Disseminated zoster and multidermatomal involvement was encountered in immuno compromised individuals. Post herpetic neuralgia was seen more in the elderly patients, especially in cases of ophthalmic zoster.

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DERMATOLOGY REFERRALS IN A NEUROLOGICAL SET UP

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Abstract
Introduction: Dermatology is a specialty, which not only deals with dermatological problems with outpatient but also inpatients referrals. The importances of Dermatologist in hospital setting are rising due to changing condition of medical care. Since no peer-reviewed articles are available for dermatological problems in a neurological set up, we conducted this study to know about pattern of skin disorders in neurological patients.
Material and Methods: The present study was a prospective study in a neurological setup, which included data from hospital dermatology consultation request forms over a period of one year. The data included demographic profile of the patient investigation where needed, neurological diagnosis and final dermatological diagnosis. The data was analyzed using SPSS.
Results: A total of 285 patients who were requested for consultation were included in the study. Face was the commonest site of involvement (19.6%). Laboratory examination of referred patients revealed abnormal blood counts in 2% cases, renal function tests in 0.7% and urine in 0.4% cases. CT scan showed abnormal findings in 65.6% patients. The most common drug used in these patients was phenytoin (29.1%). The most common dermatological diagnosis was Infection and Infestation (34.7%) followed by eczema (46.6%). Drug rash was seen in 3.9% cases. Out of which one had phenytoin induced Steven Johnson syndrome. Skin biopsy was done in 5 patients. Topicals was advised in 80%. Upon discharge 10% of inpatients didn't require any follow-up. The patients who were followed up after 4 weeks, about 48% had their symptoms resolved with topicals and oral treatment as required. About 38% required more than two follow ups due to chronic course of the diseases.
Conclusions: This present study discussed about various manifestations of skin disorders in a neurological set up and emphasizes the role of dermatologist in treating skin problems both in outpatient as well as inpatient scenarios.

Key words: Dermatology; Infection; Eczema

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Introduction

Dermatology is a specialty with both medical and surgical aspects. It not only covers outpatient setting but also involve in inpatients referrals from other specialties [1]. Due to changing condition of medical care the value of dermatologist as consultants within the hospital setting is scaling high [2]. The reason for dermatology consultations and its impact on diagnosis and treatment would be of interest to doctors and health care delivery workers [3]. Lack of medical literature on dermatological problems in a neurological set up motivated us to work on this issue to find out the pattern of the dermatological diseases in neurological patients.

Materials and Methods

The present study was a prospectively conducted in a neurological setup, which included data collection from hospital dermatology consultation request forms over a period of one year (January 2011- January 2012). The data included demographic profile of the patient including name, age, sex, onset of lesion, type of lesion, provisional dermatological diagnosis, laboratory investigation including skin biopsy when required, CT scan, neurological diagnosis and final dermatological diagnosis. Patients with acute disorders or if admitted were followed up after 1 week. If they have chronic disorder, they were followed after 4 weeks.
The data was analyzed using SPSS software.

Results

A total of 285 neurological patients were evaluated who were requested for dermatological consultation during one-year study period. 62.1% patients among them were males. Patients' age ranged from a newborn to 84 years. Mean age of presentation was 37.48 years. Lesions was distributed commonly on face (19.6%) followed by generalized distribution (16.5%), trunk and lower limbs involvement (13.7% each), scalp (9.8%), upper limbs (7%), soles (5.6%) and nails, genital, palms(<5%). Common morphological lesions were plaque (43.1%), scaling (10.2%), papular (8.8%), macules (7.7%), pustular (4.9%) and comedones (4.9%), nails (3.2%), maculopapular (2.8%), lump (2.8%), hyperkeratotic (2.5%), vesicular on an erythematous base (1.4%), petechiae, vesicular and thickened nerve (0.7% each) and hair loss (5.6%). Onset of rash occurred for > 1 year in 13% cases, for 8 weeks to 1 year in 28.4% patients, between 4- 8 weeks in 23.9%, between 2-4 weeks in 20.7% and <2 week in 14% patients. Laboratory examination of these patients revealed abnormal complete blood count in 2%, abnormal kidney function tests in 0.7% and abnormal urine tests in 0.4%. CT scan head was found to be abnormal in 65.6% cases. Neurological drugs used in these patients were phenytoin 29.1%, steroids 20.4%, and Valproic acid 12.6%, augmentin 0.4%, combination of epileptic drugs in 10% and other miscellaneous drugs in 24%.

The most common dermatological diagnosis (pattern depicted in Table I) was Infection and Infestation 34.7% followed by eczema 46.6%. Among infections, wart was found to be more common and constituted about 27% followed by Hansen's disease about 14%, Impetigo 13%, folliculitis 13%, T. infection 13%. Scabies was found in 20%. Eczema was seen in 24.2%. Xerosis and pilosebaceous disorder was seen in 5.6%. Skin Biopsy was done in 5 patients and was suggestive of Hansen's (2 patients), urticarial vasculitis, psoriasis, traumatic alopecia, and Melanocytic nevus (1 patient each). Drug rash was seen in 3.9%. Out of which one had phenytoin induced Steven Johnson syndrome, nine patients had phenytoin induced maculopapular rash and one had augmentin induced maculopapular rash. Topicals was advised in 80%, which included steroids, antifungal, antibiotics, scabicidals and immune-modulators. Patients who required dermatosurgical procedures were treated accordingly.

Patients who had dermatological diseases were either admitted or seen in outpatient department with neurosurgical diagnosis; of which commonest was RTA (road traffic accidents) in 20% patients followed by brain tumors (17.5 %) and seizure disorders (14%) (Details provided in Table II).

Of the total inpatients, 55% did not require follow up, as they were symptom free before discharge, however 48% of out patients were symptom free after second visit. Patients were followed up in 1 week, for inpatients and acute disorder, which constituted about 18% and in 4 weeks for chronic disorder and later depending upon type of skin diseases constituted about 68%. 14% cases did not require follow up. Out of 18% inpatients and with acute disorder, upon discharge 10% cases didn't require follow-ups. The remaining 68% who was followed up after 4 weeks, about 48% had their symptoms resolved with topicals and oral treatment as required. About 38% required follow up even after 1 month due to chronic course of the diseases.

Diseases	Frequency	Percentage (%)
Drug rash Phenytoin induced –Steven-Jhonson syndrome-1 Phenytoin induced –maculopapular rash-9 Augmentin induced- urticarial rash- 1	11	3.9
Eczema Seborrheic dermatitis-30 Photodermatitis-14 Hand eczema-8 Neurodermatitis-7 Pedrus dermatitis-6 Heal eczema-4	69	24.2
Hair disorder	10	3.5
Vasculitis	7	2.5
Infection and Infestation	99	34.7
Xerosis	16	5.6
Tumors	9	3.2
Pruritus	7	2.5
Pigmented purpuric dermatoses	5	1.8
Papulosquamous disorder	2	.7
Pilosebaceous disorder	16	5.6
Others	34	11.9

Table I. Dermatological diagnoses of patients.

Diseases	Frequency	Percentage (%)
Road traffic accidents	57	20
Arteriovenous malformations	5	1.8
Meningitis	3	1.1
Spondylosis	7	2.5
Neurocysticercosis	7	2.5
Sub occupying lesions	2	0.7
Brain Tumour	51	17.9
Tuberous sclerosis	1	0.4
Hemorrhagic Stroke	22	7.7
Seizure disorder	40	14
Ischemic Stroke	6	2.1
Hydrocephalus	4	1.4
Others	23	8.1
No organic neurological problem	57	20

Table II. Neurological diagnoses of patients.

Discussion

Dermatology is emerging as a specialty, which not only deals with outpatient but also inpatients referrals. In literature there are studies that give information about importance of dermatology referrals in hospital settings. In view of referrals most of the studies had multispecialty referrals. Internal medicine had the highest referrals followed by pediatrics, neurology and psychiatry but none like our study was done in a neurosurgical setup. Though few studies had referrals from Neurology as Mancusi et al 12%, Fisher 9.9%, and Penate 8.3% [2,4,7]. The most common diagnosis in these studies was infections [2-8]. The present study also has found infection as the most common diagnosis about 34.7% however in a higher proportion. In outpatient setting infection is commonly seen [9] but also can be seen in inpatient as in the present study. We saw 20% of inpatients had RTA and they were susceptible to infection. Immunosuppresion in some patients and presentation of cutaneous infection are a reason for hospital admission [4]. Eczema was found in 24.2% cases, which is slightly higher than reported by Mancusi et al (16.6%) and Antic et al (12.6 % cases) [4,10]. Eczema is also one of the common diagnoses in dermatology outpatients and also seen in inpatients due to exposure to sweat, antiseptics, dressing occlusion, diapers and monitoring with catheters and or pressures tubes as per Mancusi et al [4]. In our study we found Drug rash in 3.9%. In literature there are higher incidence of drug reaction found in studies by Mancusi et al 14%, Hardwick et al 10.5%, Itin et al 9.8%, sherertz 9.2%, Arora 9.1%, Penate 7.4% [2,4,6,7,11,12]. The lower incidence of drug rash in our study may be due to only one referral specialty i.e. Neurosurgery as in other studies it was multispecialty referrals dealing with more medications. In our study we found one patient as Stevens Johnson syndrome, which is a fatal skin reaction if not diagnosed early and treated. This condition was recognized early and treated which shows a dermatologist role in patient care. Early diagnosis is of utmost importance for some life threatening dermatological condition and should motivate non-dermatologist to request for dermatology consultation [2].

In the present study patients were followed up at regular intervals depending upon the nature of the disease and chronicity. 55% of the inpatients were symptom free before discharge and 48% of out patients were symptom free after second visit. 38% patients required follow up of more than two visits due to their chronic problems. In literature there are few studies that had follow up their patients and found 85.7%, 71.8% and 58% of the patients complaints were resolved in single visit by Fisher et al [8], Penate et al [2] and Mancusi et al [4] respectively. Fernendes et al [5] found that in 88.7% patients did not require any follow up. About in 65% cases preliminary diagnosis was changed after dermatology consultation and 3.3% dermatologist diagnosis was important as it modified the initial admission diagnosis and had an impact on final prognosis the the dermatological condition [5].

Conclusion

This present study describes dermatological problems in neurological patients and emphasis the role of a dermatologist in managing them. Dermatology referral improves interdisciplinary treatment and thus have an impact on the quality of treatment and facilitate management of the diseases that lead to admission or treat a potentially life threatening dermatological disease. In any health care system there is a role of dermatologist and training for doctors to treat common dermatological problems and its management is justified [13].

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THE COMPARISON STUDY OF 5 FLUOROURACIL VS. CRYOTHERPY IN THE TREATMENT OF THE BACKHAND RESISTANT COMMON WART

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Abstract

Introduction: Wart is a common disease which is caused by a group of viruses called Human Papilloma Virus. The most prevalent type of wart is common wart and the most prevalent site of involvement is hands. Complete recovery, no recurrency and effectiveness in all patients are not obtained by any of therapeutic methods, so in this study we decided to compare therapeutic effects of 5 Fluorouracil (FU) with cryotherapy in treatment of common warts of backhand.

Material and Methods: In this study, in a one year period from March 2012 to March 2013, 60 patients that referred to dermatology clinic of Sina hospital included the study with the diagnosis of backhand wart .Patients were divided into two groups of treatment, one treated with cryotherapy (30 patients) and one threated with 5 FU (30 patients). Age and gender of patients, number of lesions and duration of involvement were documented. Treatment by topical 5 FU was implemented for 4 weeks, twice a day for 4 hours each course. Second group was treated by cryotherapy (liquid nitrogen spray, two sessions with a two-week interval between sessions). Their response to treatment was evaluated as good, moderate and weak.

Results: There was no difference in age, gender and mean of duration of involvement and number of lesions between two groups. Response to treatment was considerably better in 5 FU group ($p=0.02$). Also rate of relapse and complications were lower in 5 FU group of treatment, with a statistically significant difference compared to the cryotherapy group ($P<0.001$). In separate evaluation of complications only scar formation was equal in two groups and pain and bullae formation were lower in 5 FU group with a statistically significant difference ($P<0.001$ both).

Conclusions: According to limited studies in this field, results of this study could be the base of more comprehensive studies in evaluating the efficacy of 5 FU in treatment of common warts. Appropriate therapeutic response in addition to lower rates of relapse and complications by 5 FU treatments can make a major change and lower the psychosocial burden of this disease dramatically.

Key words: Fluorouracil; Cryotherapy; Resistant warts of backhand

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Introduction

Warts are fleshy tumors/lumps that grow on the hands and feet, but it may grow on all parts of the body. They are indeed benign prolife ration of skin and mucous [1-5]. This disease is relatively common and it caused by a group of viruses called ''human papilloma virus'', that can grow on the skin, the inner surface of the mouth and genital and anal areas [6,7].

According to importance of performance, availability and cost of selected method in tearing patients with ''hand warts'', and also the lack of relevant studies about this case (8,9), we decided to compare''5-fluorouracil therapy'' with ''cryotherapy'' in treatment of common warts on hands, if there is one superior to the other methods, we use it as the preferred treatment method.

Materials and Methods

Is this study during the one- year period (1391-1392), 60 patients with ''hand warts'' referred to the dermatology clinic in Sina Hospital, were selected for the study. Patients were treated in two categories (30 of them with cryotherapy and 30 with 5-fluorouracil).

Age and sex, number of warts, and duration of illness were registered in patient's history. Treatment with local 5-flurorouracil was carried out for 4 hours at 2 times / day for 4 weeks.

The patients were taught how to use the cream and then, they use the cream themselves. The second group treated by cry therapy with liquid nitrogen and using spray cryotherapy with a distance of 1-2 cm from the warts in the term of 20-30 seconds depending on the size of warts, to the extent that white halo is formed around the wart.

Results

In our study there were 28 (46.7%) female individuals and also 32 (53.3%) male participants. Average age of all participants was 17.61±8.35 years. The youngest was 6 and the oldest one was 48 years old. Average number of warts were 4.73±2.73 (3-20) also duration time to warts were 14.95±9.55. response to medication in 26 individuals were good (43.3%) in 22 cases were moderate (36.7%) and in 12 cases were low (20%). Response to medication was analyzed between two groups and results proved that 5-fu had a significant different to cryoteraphy group ($p=0.02$). We had compare also side effects of two methods as a due it shows that side effect in 5-fu group were significantly lower than cryoteraphy group ($p<0.001$). In 19 (63.3%) cases in cryoteraphy group pain was reported as side effects but noun of participants in 5-fu show any pain. which was significantly difference between two groups. Scorch reported in 22 (37.3%) in cryotraphy and 0 in 5-Fu also in this point of view there were a significant difference between two groups.

Discussion

This study is a randomized clinical trial that carried out with the aim of comparing the two methods, ''using local 5-FU'' and "Cryotherapy" in response to the treatment, medical complications and recurrence of common hand warts. In this illness, 60 patients were divided into two therapeutic groups, and were evaluated in a prospective study.

In our survey, overall, 53/3% of patients were male. (63/3% in 5-FU group and 43/3% in cryotherapy group, P=0/72) and the mean age of patients in both groups were respectively 19/2 ± 10/02 and 15/96 ± 5/94 (P=0/13). The mean duration of illness in 5-FU group, was slightly significant (16/47±9/42 in comparison to 13/48± 3/48, P=0/27). Average number of warts was similar in the two groups. (4/53±3/12 m 5-FU group in comparison to 4/93 ± 2/3 in Cryotherapy group P=0/57)

Unlike previous studies [10,11], most of our patients were male and mean age of patients was lower compared to previous results. This issue can be caused from epidemiological differences of disease in various locations. The mean duration of illness in Luk et al Survey was about 17-19 months and similar to our study [7]. This value in Valikhani et al study was approximately 30 months and much higher than in our study [11]. Unlike general impression that skin wart is a simple disease with an outpatient and fast treatment, our survey along with other studies shows that many patients are already infected and are trying to treat it. In addition to this issue, such high figures associated with disease duration, notes the importance of effective treatment with low recurrence. Average number of lesions in our study was lower than Valikhani and Sayad Rezayi's [11]

In our study, the therapeutic response of 5-FU group was much better than Cryotherapy (60% positive response in 5-FU group in comparison to 26/7% positive response in Cryotherapy group, P=0/02). Disease recurrence and also complications was lower in 5-FU group, and the difference of these cases with Cryotherapy group was statistically meaningful.

In the separately assessment of treatment effects, having scars was the only effect in 5-FU group that was equal with Cryotherapy group. Having pain (0 in comparison 63/3%) and blisters (0 in comparison 37/3%) was rarely seen in this group, this case has also a significant difference with Cryotherapy group. And the cure rate was 30 and 42/5% (P=0/02)

Also side effects and pain were seen in 27, 19 patient receiving both Cryotherapy and F-U, and 14, 11 patient receiving Cryotherapy and placebo. These differences were not statistically significant. In Valikhani, survey [11], 93/3% of patients in the group treated with Cryotherapy had complete recovery, whereas the complete recovery was seen 66/7% of patients treated with 5-FU (P=0/02)

However in both these studies, clinical improvement was higher in Cryotherapy group, they recommended using 5-FU for certain categories of patients.

Again in Sayad Rezayi, study, however the outcome was more favorable in Cryotherapy group but the difference is not too much (52% positive response in 5-FU group and 60% in Cryotherapy group) , disease recurrence in 5-FU group was lower like our study (8% in comparison to 18%). Unlike our survey, noun of the patients in this study had been scars, and the amount of pain and blisters in the Cryotherapy group of patients was very high, while in 5-FU group were not reported It seems that according to the results of studies conducted by Hursthouse et al [12] and Lee aet al [13], we can consider 5-FU as an appropriate treatment for hand warts.

Conclusion

This study prove the usage of 5-Fu in warts treatment which were significantly low in side effects and reliable in treatment, it would one of basic studies to investigate more about 5-Fu.

Acknowledgments

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THE COMPARISON STUDY OF 5 FLUOROURACIL VS. CRYOTHERAPY IN THE TREATMENT OF THE BACKHAND RESISTANT COMMON WART

by Rahim Asghariazar, Hamideh Herizchi Ghadim, Shahla Babaeinezhad, Sina Nobahari

comment:

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We refer to the study conducted by Asghariazar R et al comparing the efficacy of 5-fluorouracil against cryotherapy in the management of backhand resistant common warts [1]. We congratulate their success in reporting such a high-quality study. We would humbly like to offer a few pieces of advice, which might further augment the clinical relevance and the scientific content for future studies along similar veins.

Firstly, human papillomavirus infection causing cutaneous extragenital viral warts is lifelong, and cannot be eradicated by any active treatment strategy [2,3]. The aims to treat are to alleviate the physical and psychological discomforts of the patients, and to prevent further spread of the infection by autoinoculation [4]. We thus advocate that the inclusion criteria while recruiting patients for future studies should include evaluations of their physical and psychological discomforts, including impacts of the disease on the quality of life of patients. For patients with low impacts, counselling education about the expected disease course and implications for future active treatment might not be indicated clinically, and thus may be excluded from the study recruitments. An example is depicts as Figure 1.

Secondly, many good systemic reviews revealed, there exists little significance for the results of many treatment strategies including cryotherapy to be compared to those of placebo treatment [5,6]. We thus advocate that future studies might include placebo as one of the study arms so that the genuine clinical and psychological benefits of treatments can be validly and reliable quantified. Outcome measures could also be both clinician-rated and patient-rated.

Thirdly, viral warts exhibit Köebner phenomenon. Action ablation treatment might lead to future relapse of lesions. Moreover, as the human papillomavirus infection is lifelong, transient symptomatic remission might not infer long-term disease relief [7]. We therefore advocate future studies to be designed with sufficiently long follow-up periods so that the effectiveness of various treatment strategies could be reliably compared to each other and to placebo on significantly longer time frames.

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CARCINOMA ERYSIPELOIDES MIMICKING RADIATION DERMATITIS - A CASE REPORT AND REVIEW OF LITERATURE

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Abstract
Carcinoma erysipeloides (CE) is a relatively rare variant of cutaneous metastasis more often observed in breast cancer than in other carcinomas in women. Clinically, it appears as a well-defined, warm and tender inflammatory erythematous plaque, thus mimicking Erysipelas, Cellulitis or post mastectomy complications of lymphedema and acute radiation dermatitis. We report a case of CE in a women previously treated for infiltrating ductal carcinoma by modified radical mastectomy, chemotherapy and radiotherapy. An early and accurate differential diagnosis of this disease gives the opportunity to diagnose and halt the systemic spread of the cancer.

Key words: Inflammatory metastatic cancer; cutaneous metastasis; breast cancer

Cite this article:
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Introduction

Carcinoma erysipeloides (CE) is an uncommon cutaneous metastasis arising from visceral carcinoma [1]. It is the result of spread of tumor cells along deep dermal lymphatic vessels. It is a sign of advanced cancer or cancer recurrence. It is most often associated with breast carcinoma but may be observed in the course of some other malignancies.

Case Report

A sixty-one year old female, a known diabetic, was diagnosed as a case of carcinoma left breast with secondaries in left axilla since one and a half years. The Surgical record revealed that she underwent Modified Radical Mastectomy. The tumor was 5*3cm in size. Histopathologically, it was diagnosed as infiltrating ductal carcinoma with metastatic deposits in 10 out of 12 nodes and margins of skin, nipple & areola free of tumor. As the patient did not report for follow-up, so there was a gap of six months between surgery and chemotherapy. She was given six cycles of chemotherapy in the form of Cyclophosphamide 1g, Adriamycin 100mg and 5-Flourouracil 1g. It was followed by twenty-five fractions of radiotherapy with a total tumor dose – 5000 c Gy in a span of five weeks. On a follow-up visit in the Radiotherapy Unit after six months, she was referred to the Department of Dermatology for erythematous lesions over the irradiated area. On muco-cutaneous examination, the afebrile patient had an operative scar which was seen extending from sternum to the left axilla. Lesion was in the form of erythematous plaque of size 12"* 10" with ill-defined and irregular margins extending from the left clavicle to epigastrium and left hypochondrium. It was interspersed at places with superficial ulcers and brown colored adherent crusts with few erythematous papules present at the periphery (Fig. 1). On palpation, entire plaque was slightly warm and tender without any induration. Hematological investigations were within normal range. Histopathological examination revealed nodular infiltrates of neoplastic cells within the reticular dermis and within the lymphatics in the upper and mid dermis (Fig. 2). Thus, the diagnosis of cutaneous metastasis with lymphatic spread was made. She was put on chemotherapy Inj. Ifosfamide 2 g and Inj. Vinorelbine 40mg.

Discussion

Cutaneous metastatic carcinoma is an unusual clinical diagnosis with an overall incidence varying from 0.7% to 10% [2]. In women, it occurs most commonly in breast cancer in contrast to men, where it occurs most often in melanoma [3].

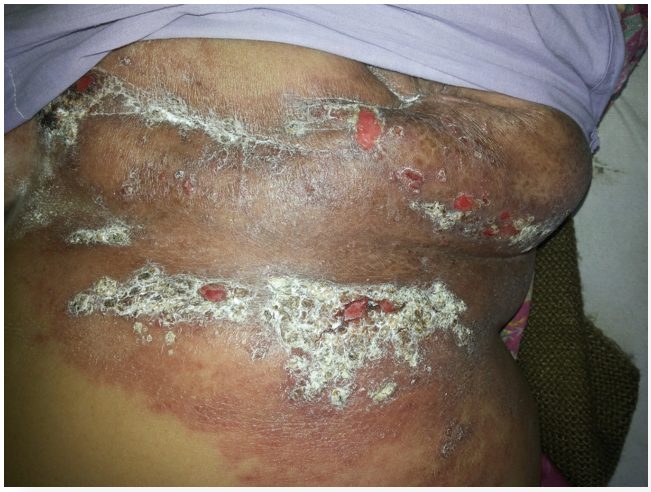

Figure 1. Erythematous plaque with ulcers, crusts and papules in the left mammary region.

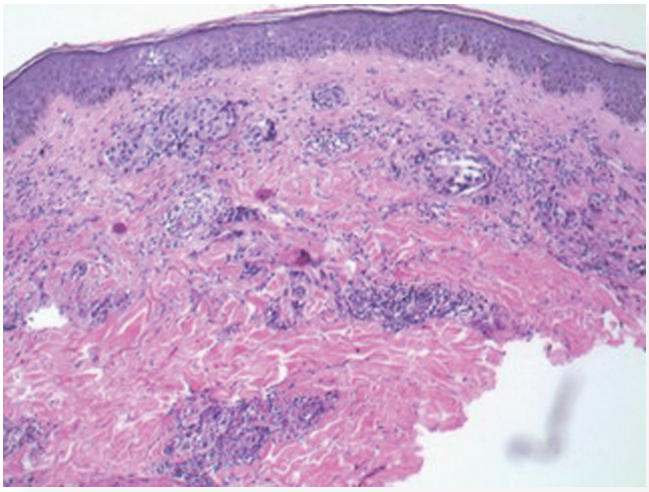

Figure 2. Nodular infiltration of neoplastic cells in reticular dermis and within the lymphatics in the upper and mid dermis.

In a retrospective study, various morphological patterns of cutaneous metastasis from breast carcinoma have been described like nodules/papules (80%), carcinoma telengiectoides (11%), carcinoma erysipeloides (3%), encuirasse carcinomas (3%), alopecia neoplastica (2%) and zosteriform (0.8%) [2].

CE was first described in 1924 by Lee and was named so by Rasch in 1931 because of its similarity to erysipelas [2]. It is a relatively rare variant of cutaneous metastasis (2-3%). Although most commonly associated with breast cancer, it can rarely be observed with other malignant tumors such as adenocarcinomas of pancreas, rectum, ovary, parotid gland and lung [4].

It can be either a primary or secondary (after treatment of primary carcinoma) with secondary being a commoner presentation [1]. It can occur after chemotherapy, radiotherapy, lymphadenectomy or tumor excision surgery of primary breast carcinoma. It has been suggested that these therapies lead to shedding of metastatic cells into subepidermal lymphatics leading to blockage of lymph ducts [5,6].

Clinically, it appears as a well-defined, warm and tender inflammatory erythematous plaque, thus mimicking erysipelas. The most common site involved is anterior chest wall. The other less common involved sites are contralateral breast, incision scar arms and facial skin [4]. In this case; the lesions were situated on the anterior chest wall and covered both above and below the operative scar suggesting the direct spread from the carcinoma breast.

CE is usually associated with intraductal breast carcinoma and is often considered a marker of tumor recurrence with omnious prognosis [3]. The metastasis occurs due to a rapid spread of tumor along subdermal lymphatic vessels leading to blockade and erythema [7].

Clinically CE should be differentiated from other benign dermatological diseases i.e. contact dermatitis, erysipelas, cellulitis or post mastectomy complications of lymphedema, acute radiation dermatitis. The infectious processes were ruled out in this patient because of absence of fever, leukocytosis, neutrophilia and persistence of lesions even after a course of antibiotics [8].

Acute radiation dermatitis usually appear during or with in a period of three months after radiotherapy and tend to resolve soon after the completion of treatment [1] Histopathological examination was also not suggestive of flattening or loss of epidermal rete ridges along with edema or sparse connective tissue beneath the epidermis which are the common findings seen in acute radiation dermatitis.

Although, as reported, the cutaneous metastasis of breast carcinoma are discovered long after the diagnosis of primary tumor with an average time interval of 2.93 years [9]. In this case, it's diagnosis in early stages can be attributed to a delay in chemotherapy cycles which may have led to early spread of disease to the lymphatics.

To conclude, although it is a rare presentation but can have grave prognosis. So early diagnosis with the help of skin biopsy is important to differentiate it from radiation dermatitis as in this case, so that antimitotic therapy may be instituted early for better prognosis.

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CONGENITAL SELF-HEALING RETICULOHISTIOCYTOSIS: A CASE REPORT

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Abstract
Congenital self-healing reticulohistiocytosis (CSHRH) is a benign type of Langerhans cell histiocytosis (LCH) also known as Hashimoto-Pritzker disease. Clinically it presents with skin lesions at birth or in neonatal period, usually without any systemic involvement. Lesions often heal spontaneously in period of weeks to months. We report a case of CSHRH presenting with skin lesions at birth, describing need to make an early diagnosis and to have a multidisciplinary approach with regular follow-up, in managing this rare type of LCH.

Key words: Congenital; reticulohistiocytosis; Langerhans cell histiocytosis

Cite this article:
Shetty S, Monappa V, Pai K, Rao R, Pai S. Congenital self-healing reticulohistiocytosis: a case report. Our Dermatol Online. 2014; 5(3): 264-266.

Introduction

Langerhans cell histiocytosis (LCH) is a clonal proliferative disease of Langerhans cells with broad spectrum of forms. It can be local asymptomatic form with indolent course or symptomatic form involving multiple organs. They commonly show positive S100/CD1a on immunohistochemistry [1]. The annual incidence rate reported to be 0.5–5.4 million children per year [2]. Congenital self-healing reticulohistiocytosis (CSHRH) is a rare benign variant of LCH first described by Hashimoto and Pritzker [3]. It is generally limited to skin and rapidly self-healing. It presents at birth or in the neonatal period as red-brown papulonodules on the skin, which may be superficially ulcerated. Multiple lesions are most common but the presence of a solitary skin lesion has been reported. Due to its non-specific clinical features and rarity, CSHRH is difficult to diagnose and hence its essential to have an understanding of clinical and histological findings. Herein, we report a case of CSHRH.

Case Report

An 8-month-old female infant born full-term via uncomplicated vaginal delivery with normal birth weight, length and APGAR score, presented with reddish brown papules all over the body, progressively developing since birth. Lesions were predominantly present on trunk, distributed on face, upper and lower limbs (Fig.1). Lesions heal leaving behind depigmented macules. The physical examination was otherwise normal. Clinical differential diagnosis of epidermodysplasia verruciformis and disseminated spitz nevi were considered. The skin biopsy revealed thinned out epidermis overlying aggregates of histiocytes with folded nuclei and pale cytoplasm along with scattered eosinophils (Fig. 2). Immunohistochemistry showed CD68 and S100 positivity, suggesting a diagnosis of Langerhans cell histiocytosis (Fig. 3). Laboratory and clinical work up to rule out systemic involvement including complete blood count, coagulation profile, urine analysis, X-Rays of skull, chest and long bones and abdominal ultrasound were normal.

During next few months, the skin lesions resolved considerably with only residual hypopigmentation. No new skin lesions or any systemic involvement were noted. Child is kept under monthly follow-up on out-patient basis.

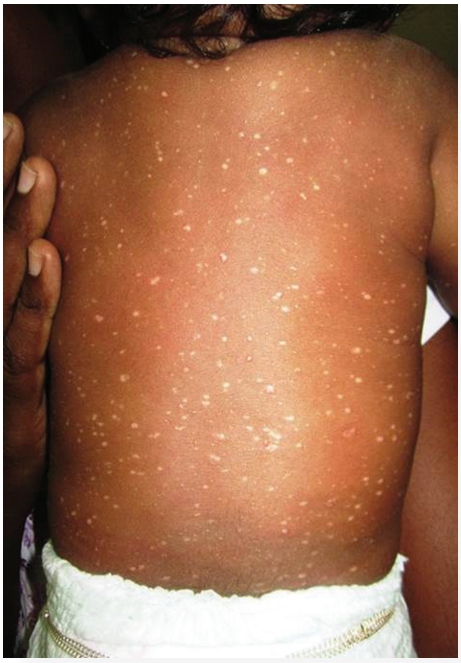

Figure 1. Reddish brown papules over the back leaving behind depigmented macules on healing.

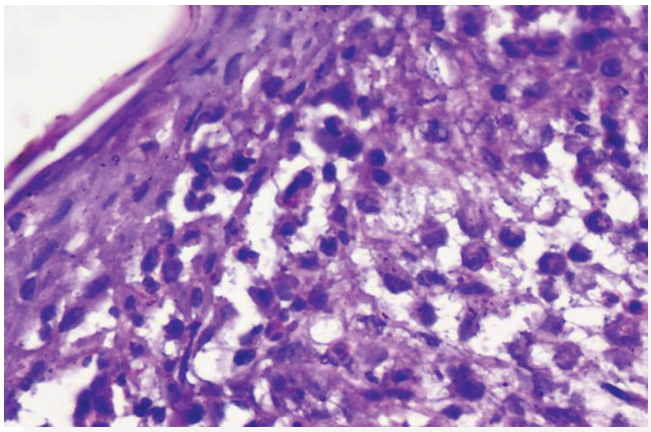

Figure 2. Photomicrograph showing subepidermal histiocytic aggregates and occasional eosinophils. H&E 200 X

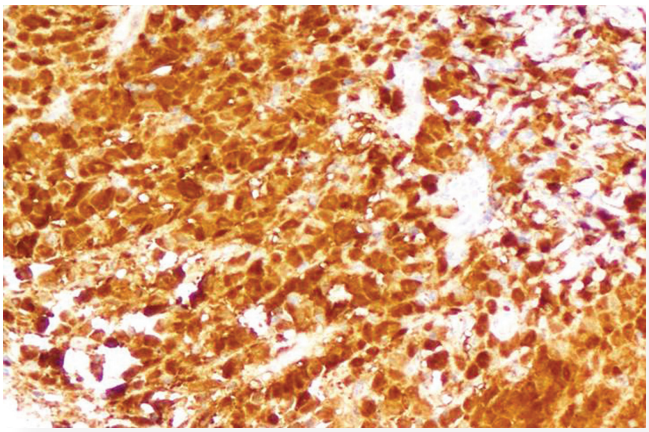

Figure 3. Photomicrograph showing diffuse S100 positivity. IHC, 200 X

Discussion

Langerhans cell histiocytosis is a heterogeneous disease, involving the accumulation of Langerhans cells in various organs. A diagnosis of LCH is typically made with a skin biopsy that shows positive immunohistochemical staining of infiltrative cells in the dermis with CD1a and S-100. These cells also exhibit classic Birbeck granules on electron microscopy, which was once the gold standard for identifying Langerhans cells before immunohistochemistry became more prominent [5].

Congenital self-healing reticulohistiocytosis is a single-system LCH with a benign prognosis. The condition is rare, and the incidence reported in the literature varies substantially, possibly because the disease has the potential to resolve while undiagnosed. The disease is characterized by presence of cutaneous lesions such as papules, nodules and vesicles, usually at birth or in the neonatal period, without systemic involvement. Spontaneous involution and absence of systemic symptoms are marked characteristics for differentiation with the other clinical spectra of Langerhans cell histiocytosis [6]. However, there are rare reports of pulmonary and ocular involvement in CSHRH that resolved along with cutaneous findings [6,7]. There have also been reports of disseminated brown or violaceous non-blanching macules and papules raising concerns of congenital infections or other hematological disorders as seen with the "blueberry muffin" lesions [8].

Patients with CSHRH have excellent survival rate and no report of death have been found in the literature. There are no specific recommended treatments for CSHRH, but if lesions persist, topical corticosteroids, tacrolimus, or nitrogen mustard can be used, or localized lesions may be excised [9]. It is important to follow the patient for long periods to detect possible systemic involvement, since there are reports of recurrence involving skin, mucosa, bones and pituitary gland [10].

As this is a rare disease with variable presentation, it is important for us to diagnose it early and have a multidisciplinary long term follow-up. This will prevent administration of systemic toxic therapy to infant and also help in identifying recurrences, if any.

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SUBCUTANEOUS PANNICULITIS- LIKE T-CELL LYMPHOMA: REPORT OF TWO CASES

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Abstract
Subcutaneous panniculitis-like T-cell lymphoma is a distinct variant of cutaneous T-cell lymphoma, characterized by primary involvement of the subcutaneous fat in a manner mimicking panniculitis. It accounts for less than one percent of all non Hodgkin lymphoma. We describe two such patients who presented with cutaneous nodules. A 28 year old male presented with a one and a half month history of multiple subcutaneous nodules over the thighs, abdominal wall and chest. A clinical diagnosis of panniculitis was made. An excision biopsy of one the nodules was performed and the histopathology revealed subcutaneous panniculitis-like T-cell lymphoma. The other patient was a 44 year old male who underwent excision of a subcutaneous mass in the right thigh and on histopathological examination a diagnosis of subcutaneous panniculitis-like T-cell lymphoma was made. The patients received one cycle of CHOP (cyclophoshamide, vincristine, doxorubicin and prednisolone) regimen, followed by systemic steroids and were advised follow up.

Key words: Subcutaneous Panniculitis-like T-cell Lymphoma; panniculitis; cutaneous T-cell lymphoma; non Hodgkin lymphoma

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Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) originally described by Gonzalez et al is a primary cutaneous lymphoma (PCL) characterized by an aggressive clinical course and hypodermal involvement [1]. The annual incidence of cutaneous lymphoma is estimated to be from 0.5 to 1 per 1, 00,000 persons per year.[2] SPTCL is a rare extranodal non Hodgkin lymphoma (NHL) accounting for less than one percent of all NHL [1-5] and resembles certain benign panniculitis like lupus panniculitis and erythema nodosum clinically and histologically.

We present the clinicopathological features of two such cases and discuss the differential diagnosis, immunohistochemical and molecular features of SPTCL

Case Report

Case 1

A 28 year old male presented with a history of high grade fever followed by eruption of multiple swellings over the thighs, chest and abdominal wall, of one and a half months duration. On examination, a number of firm to hard, indurated, 1-5 cm sized, cutaneous nodules and plaques with scaling and discolouration were seen over the chest, anterior abdominal wall and both the thighs (Fig. 1). A clinical diagnosis of lobular panniculitis was made. His laboratory investigations such as blood counts, peripheral smear, bone marrow, and anti-nuclear antibody were unremarkable. Serum alkaline phosphatase and lactate dehydrogenase were elevated. One of the nodules was biopsied and sent for histopathlogical examination.

Case 2

A 44 year old male underwent excision biopsy of an indurated subcutaneous mass measuring 2 × 2 cm in the right thigh, of one month duration. He had no organomegaly and his laboratory tests including a complete hemogram and bone marrow were within normal limits.

On histopathological examination of the lesion on the thighs of both the patients showed a diffuse cellular infiltrate involving the septae and lobules of subcutaneous fat (Fig. 2) in a lobular panniculitis like pattern, sparing the overlying dermis and epidermis. The atypical lymphoid infiltrate was seen rimming the individual adipocytes in a lace like manner (Figs. 3, 4). These cells had pleomorphic, clefted nuclei with hyperchromasia and coarse chromatin. Interspersed amidst the neoplastic cells were karyorrhectic debris, mitotic figures and histiocytes. There was focal angiocentric distribution of the lymphomatous cells. A diagnosis of SPTCL was made. On immunohistochemistry, the tumor cells were CD45 and CD3 positive (Figs. 5, 6) and negative for CD20 and CD30.

The patients received one cycle of CHOP (cyclophoshamide, vincristine, doxorubicin and prednisolone) regimen, which was well tolerated with healing of the cutaneous lesions. They were discharged on oral steroids and advised follow up after three weeks. The first patient continued to be in remission at the end of one year follow up. The second patient has not come again for review till date.

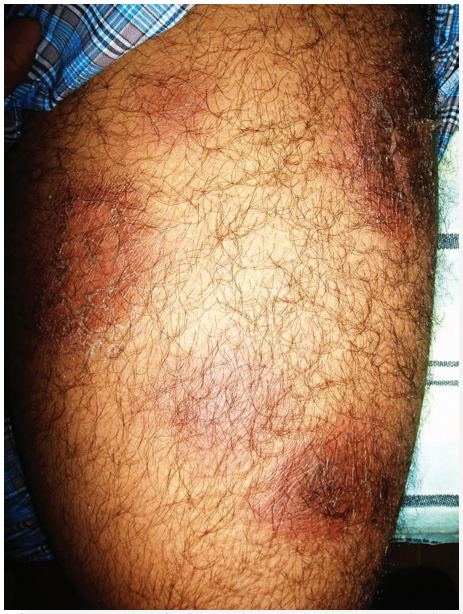

Figure 1. Multiple subcutaneous nodules involving the trunk and thighs with peripheral erythema and induration.

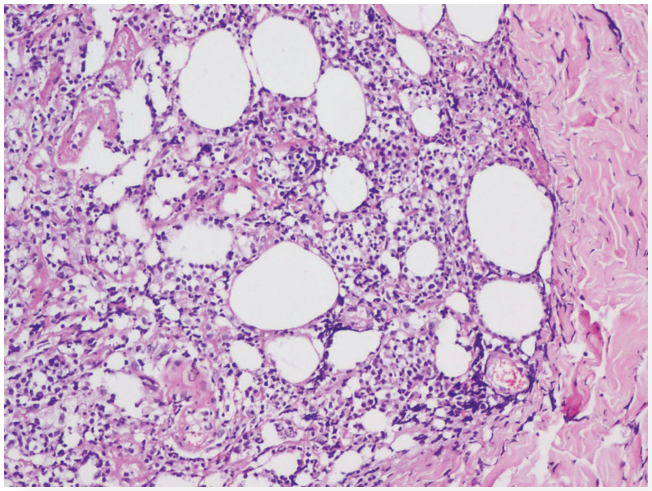

Figure 2. Histological examination revealed a diffuse cellular infiltrate of atypical lymphocytes involving the septae and lobules of subcutaneous fat in a lobular panniculitis like pattern. (Hematoxylin and Eosin stain, × 100)

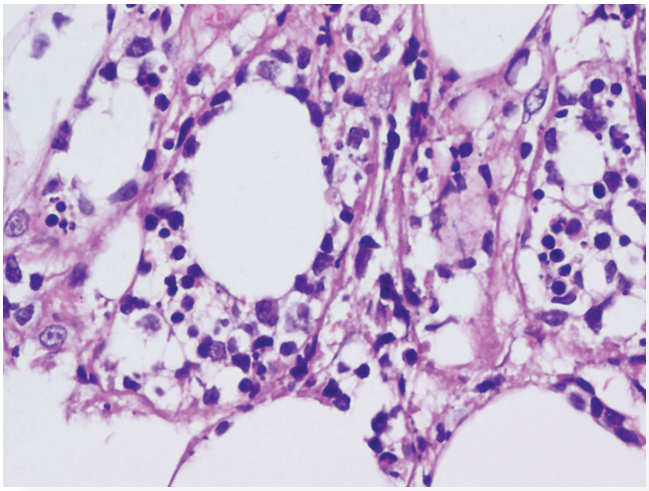

Figure 3. Higher magnification of the tumor in figure 2 demonstrated rimming of individual adipocytes by the neoplastic lymphoid cells. (Hematoxylin and Eosin stain, × 400)

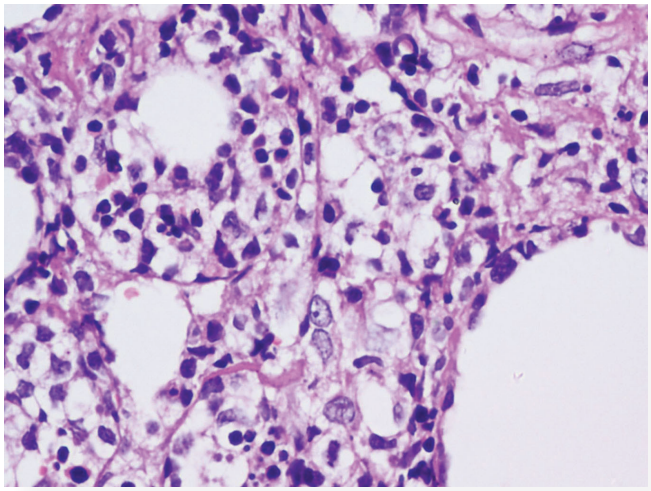

Figure 4. High power view of the neoplasm in figure 2 showed tumor cells with pleomorphic hyperchromatic nuclei, coarse chromatin and scanty cytoplasm. Interspersed amidst the neoplastic cells were karyorrhectic debris and histiocytes. (Hematoxylin and Eosin stain, × 400)

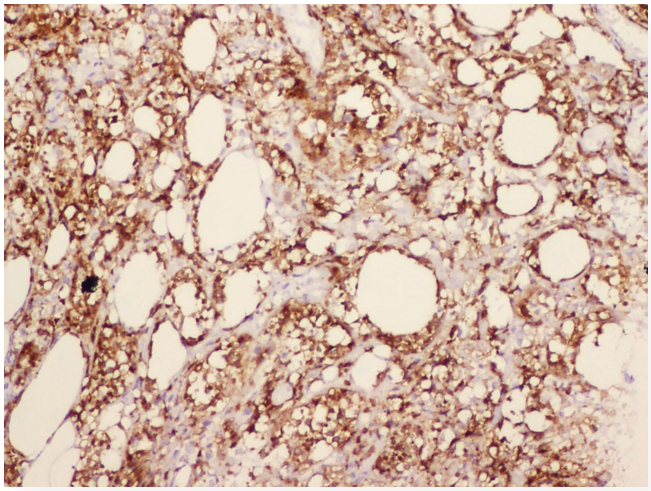

Figure 5. Immunohistochemistry showed the tumor cells were CD45 positive. (× 100)

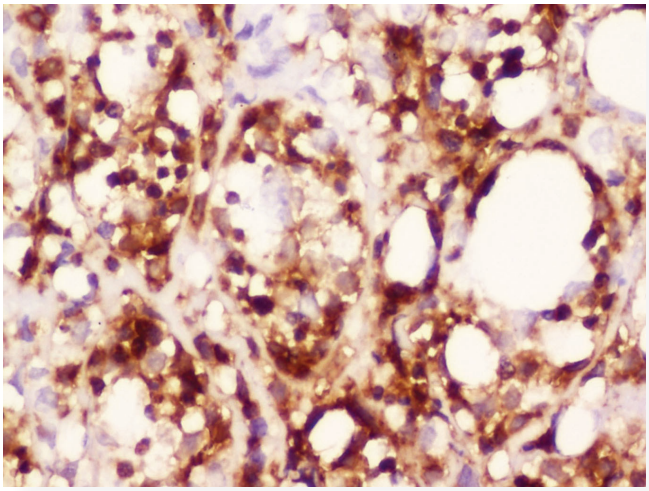

Figure 6. Immunohistochemistry revealed diffuse strong positivity of the tumor cells for CD3. (× 100)

Discussion

Subcutaneous Panniculitis-like T-cell Lymphoma (SPTCL) is the least well defined and rarest subtype of PCL preferentially involving the subcutaneous fat that can clinically imitate panniculitis. It was defined as a distinct entity by the World Health Organization (WHO) classification in 2008 [3]. Lymphoma lesions consist of multiple subcutaneous swellings and/ or erythematous plaques or ulcerated skin nodules mostly located on the trunk, extremities and face.

Histologically the lymphoma infiltrate in SPTCL involves the lobules of the subcutaneous fat, resulting in a characteristic lobular panniculitis like pattern. Immunohistochemical studies have demonstrated that these atypical neoplastic lymphoid cells have a cytotoxic T-cell phenotype. The cells are consistently positive for CD3, CD45 and T-cell intracellular antigen (TIA-1). Previously, two phenotypic subsets had been described based on T-cell receptor and CD56 expression [2-5]. SPTCL has a $CD3^+$, $CD4^-$, $CD8^+$, $\beta F1^+$, TCR $\delta 1$-, $CD56^-$, $CD30^-$ phenotype and a favorable prognosis; while SPTCL γδ or as per recent WHO classification Primary Cutaneous Gamma Delta T cell Lymphoma (PCGD-TC) have a $CD3^+$, $CD4^-$, $CD8^-$, $\beta F1^-$, TCR $\delta 1^+$, $CD56^+$, $CD30^+$ and a poor prognosis [2-7].

SPTCL lesions show only subcutaneous involvement by the mildly pleomorphic neoplastic lymphoid cells as was observed in our patients. There is moderate apoptosis and patchy necrosis. These features were noted in our cases also. In contrast, in PCGD-TCL though subcutaneous involvement is predominant there is infiltration of the overlying dermis or epidermis by the tumor cells. Angiocentric growth may be found. These cells are highly pleomorphic, show extensive apoptosis and areas of massive necrosis [4]. The immunophenotypical features of both have been enumerated above.

Patients with SPTCL type are usually young adults (median age, 36 years) presenting with subcutaneous nodules and erythematous plaques without ulceration [4]. Systemic manifestations such as fever, chills, night sweats and weight loss may be variably present and are usually mild. Cytopenias in the form of anemia, leucopenia, thrombocytopenia or combined can be seen to a mild degree in these patients. Individuals belonging to older age group (median age, 59 years), presenting with ulcerated nodules and disseminated plaques are likely to have the more aggressive PCGD-TC [4,5]. Systemic manifestations and cytopenias are more common and severe in these patients usually with a fatal outcome. Association with autoimmune disease is more common in SPTCL than PCGD-TC.

Distinguishing SPTCL from other types of cutaneous lymphomas is principally based on the subcutaneous localization of these lesions unlike the predominantly dermal involvement seen in mycosis fungoides, anaplastic large cell lymphoma, Natural Killer cell/ T-cell lymphoma [2-5,7,8]. Immunohistochemistry helps in clinching the diagnosis.

SPTCL must be differentiated from non-neoplastic panniculitis including lupus panniculitis. In benign panniculitis, $CD20^+$ B cell aggregates are seen admixed with $CD3^+$ cells containing equal proportion of $CD4^+$ and CD8+ T cells. The absence of malignant lymphocytes rimming individual fat cells classically seen in SPTCL and presence of reactive B- follicles with germinal centers admixed with plasma cells is indicative of lupus panniculitis [4,7,8].

The treatment of SPTCL includes systemic steroids, multidrug chemotherapy, radiotherapy, and/ or bone marrow transplantation [4-7]. Since SPTCL behaves in an indolent manner, these patients can have long term remission with high dose systemic steroids. High dose chemotherapy and stem cell transplantation is usually considered in primary refractory or recurrent cases.[4,6] The response is variable but usually the prognosis is unfavorable in the presence of constitutional symptoms, cytopenia, multiple site involvement and associated haemophagocytic syndrome (HPS) [6,9,10].

In conclusion, SPTCL represents a distinct clinicopathologic entity of clonal, cytotoxic T- cell lymphomas derived from αβ T cells. SPTCL has a prolonged clinical course with recurrent panniculitis, is not commonly associated with HPS and rarely metastasize. The prognosis is favorable in SPTCL except in those cases associated with HPS. Awareness of this rare condition facilitates early diagnosis and appropriate management of these patients.

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SUBCUTANEOUS PANNICULITIS- LIKE T-CELL LYMPHOMA: REPORT OF TWO CASES

by Jyoti Ramnath Kini, Ancy Susan John, Hema Kini, Flora Dorothy Lobo, Pramod Kumar, Krishna Prasad

comment:
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Subcutaneous panniculitis–like T-cell lymphoma (SPTCL), originally described as lymphoma of the cytotoxic T lymphocyte, is characterized by a tendency to infiltrate the subcutaneous tissue. The rapid clinical course and aggressive multidrug chemotherapy was the treatment of choice by many years – but it has been changed since 2008. SPTCL term is used only in relation to disease with TCRαβ phenotype, while TCRγδ+ panniculitis-like T-cell lymphomas have become classified by WHO and EORTC as primary cutaneous γδ T-cell lymphoma - PCGD-TCL. The course and prognosis of those two entities differs significantly. SPTCL occurs in children and adults. The major symptoms include single or multiple nodules or deep-seated infiltrates localized mainly in the skin and subcutaneous tissue of the lower limbs, arms and trunk. The ulcerations are rare (6% of cases – versus 45% in PCDG-TCL) [7]. The general symptoms as fever, fatigue and weight loss and laboratory abnormalities (eg. cytopenia and increased liver enzymes), occur frequently, but full-blown hemophagocytic syndrome (HPS) occurs in only 15% patients [1]. The involvement of other organs beyond the skin is rare – contrary to PCDGL-TCL, where extranodal involvement, as well as mucosal lesions occurs very often [2]. SPTCL has a very good prognosis if it is not accompanied by HPS. Recent reports indicate that the proportion of surviving 5 years is 91% if the disease is not accompanied by HPS and 46% when it is associated with HPS [1]. That is why, the 1st sentence of the article " Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) originally described by Gonzalez et al is a primary cutaneous lymphoma (PCL) characterized by an aggressive clinical course … [3]" is not true anymore. It is very important to remember that the publications written before the last classification had collected the SPTCL and PCGD-TCL into one group– that is why chemotherapy was the first choice before 2008 in many clinical centers. The recommended treatment in SPTCL without HPS nowadays involves the use of systemic corticosteroids and other immunosuppressive agents, while in the case of isolated lesions the radiotherapy can be the first choice. The chemotherapy, especially multidrug one, as well as bone marrow transplantation, should be introduced only in case of patients with progression of the disease, resistance to recommended treatment and/ or SPTCL with accompanying HPS. It is well to remember that in addition to HPS, elevated lactate dehydrogenase enzyme level and low white blood cell count are known poor prognosis factors [2]. But even in those cases, as well as in cases with relapses after chemotherapy – the immunosupressive therapy can be consider - ex. with cyclosporine A – with long lasting follow up [2,4]. Especially that the risk of infection is still lower in case of systemic steroids and / or cyclosporine A than in cases of multidrug chemotherapy.

But anyway – the described cases can be interested because they can remind the difficulties in differentiial diagnose of the disease. Diagnosis of SPTCL is based on pathological examination of skin and subcutaneous tissue, immunohistochemical staining patterns, molecular analysis, and clinical characteristics. The differentiation of Lupus erythematosus profundus (LEP) and SPTCL seems to be the biggest diagnostic challenge. When the vasculitis, mucin deposition, reactive germinal centers, B-cells clusters, considerable number of admixed plasma cells and polyclonal TCR-gene rearrangements are typical for LEP, the atypical cellular infiltrates of the subcutaneosu fat (both lobules and septae), mimicking panniculitis are also typical for SPTCL [5]. Lymphocytes exhibit slight atypical features, including hyperchromatic, angulated nuclei, and indistinct cell borders in SPTCL. Scattered mitoses, apoptotic cells, karyorrhectic debris, focal areas of fat necrosis, and rimming of individual fat cells by neoplastic cells are also common in SPTCL [6]. Immunophenotyping can be very helpful. The neoplastic cells in SPTCL are cytotoxic T cells CD3+ CD4−. TCRαβ cells are CD8+ and usually CD30− CD56− whereas PCGD-TCL is usually CD8−CD30+CD56+. In terms of differential diagnosis, benign panniculitis usually has aggregates of CD20− B-cells mixed with CD3− cells that are both CD4− and CD8−. LEP is commonly CD4+ without CD8+ T cells [6].

Although this is still controversial, some authors suggest that patients with LEP are at risk for the development of abnormal, clonal T-cell proliferations and/or overt SPTCL. In cases of atypical lymphocytic lobular panniculitis that fail to meet diagnostic criteria for subcutaneous panniculitis-like T-cell lymphoma, patients should be clinically followed indefinitely, as future subcutaneous lymphoma cannot be excluded [7].

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SUBCUTANEOUS PHAEOMYCOTIC CYST: A CASE REPORT

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Abstract
Phaeohyphomycosis refers to infection of tissues by dematiaceous fungi which occur most commonly due to traumatic inoculation of fungi. A host reaction to these fungi can ultimately lead to the formation of a cystic cavity or abscess. Here we present a 71 year old woman who presented with a nodular swelling over the left elbow. A surgical excision was performed. On histopathological examination she was found to have a subcutaneous phaeomycotic cyst.

Key words: phaeohyphomycosis; fungi; cyst; elbow

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Introduction

Phaeohyphomycosis refers to a heterogeneous group of mycotic infections that are caused by dematacious fungi [1]. These fungi occur either as soil saprophytes, plant pathogens or contaminants living in the environment, with more than 100 different species [2]. Exophiala and Phialophora species usually cause subcutaneous infection. In tissues they form yeast like cells, pseudohyphae-like elements or hyphae [3]. Phaeohyphomycosis is rare. Subcutaneous infection can manifest as phaeomycotic cyst which commonly occurs in the extremities [3,4]. A male predominance has been noted with majority of patients being more than 30 years of age [4]. Infection usually occurs through traumatic implantation of the fungi into the skin with contaminated vegetable matter, slivers of wood or thorn prick [3,4]. We present a subcutaneous phaeomycotic cyst occurring in a 71 year old woman.

Case Report

A 71 year old woman presented with a slowly progressive swelling over the posterior aspect of the left elbow joint since 6 months. It initially started as a small nodule which then progressed to the present size. It was not associated with pain. There was no obvious history of trauma. On local examination the swelling was about 5x3 cm. A clinical diagnosis of bursitis was rendered, excision biopsy performed and sent for histopathological examination.

Pathological Findings

The biopsy specimen consisted of a skin covered cystic tissue mass which weighed about 44grams and measured 6.5x4.5x3 cm. On cut section a uniloculated cyst was identified, filled with pultaceous material (Fig. 1). On microscopy, the cyst wall was fibrocollagonous and lined by foamy macrophages, necro-inflammatory debris, histiocytes, numerous multinucleate giant cells and chronic inflammatory infiltrate (Fig. 2). Septated pigmented fungal hyphae were identified in the giant cells and extracellularly in H and E stained sections (Fig. 3) and with the help of PAS and GMS stains (Figs. 4 – 6). Constrictions were also noted at few of the septations. The overlying epidermis showed no hyperplasia or ulceration. A diagnosis of subcutaneous phaeomycotic cyst was made based on the above findings. A fungal culture to identify the species could not be performed as the specimen was already preserved in formalin.

Figure 1. Skin covered cystic tissue mass, inset shows uniloculated cyst on cut section,

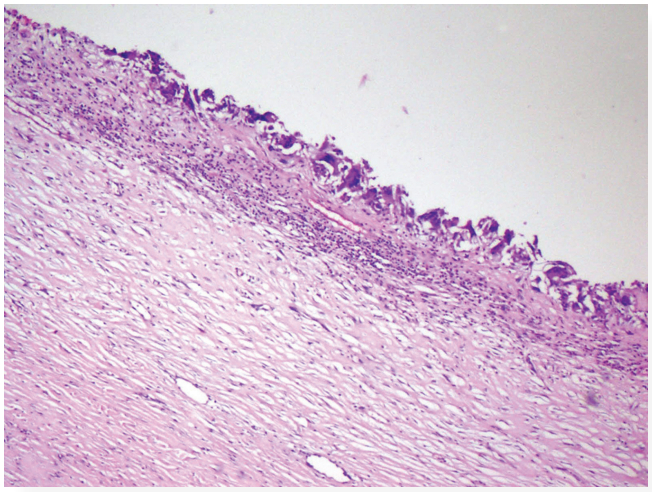

Figure 2. Cyst wall lined by granulation tissue overlying fibrocollagenous wall. [H&E x40]

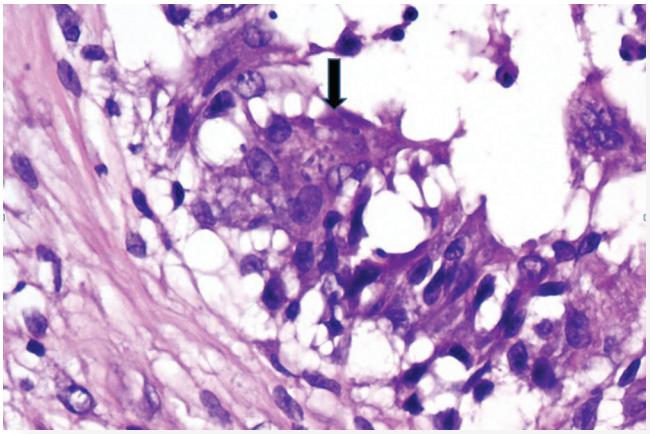

Figure 3. Arrow shows hyphae seen within the multinucleate giant cell. [H&E x400]

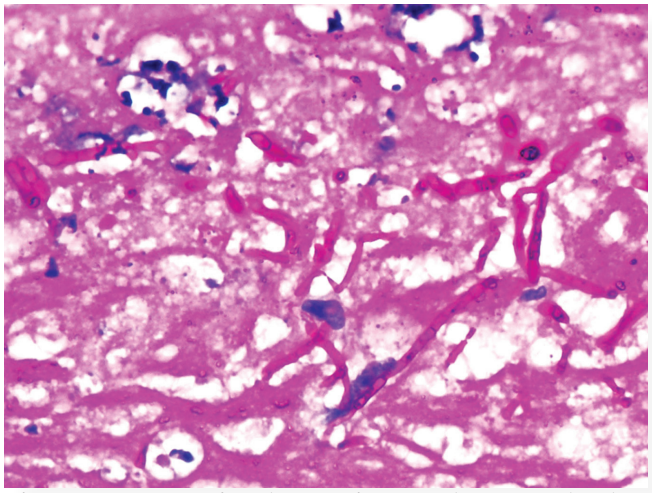

Figure 4. PAS stain shows pigmented septate hyphae extracellularly and intracellualrly respectively. [PAS x200]

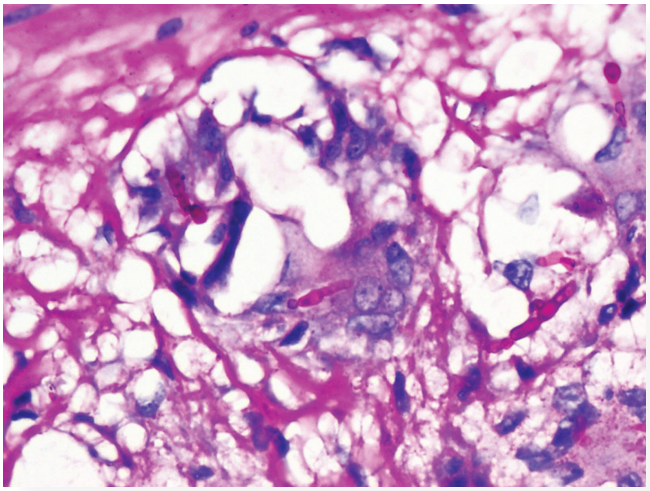

Figure 5. PAS stain shows pigmented septate hyphae extracellularly and intracellualrly respectively. [PAS x400]

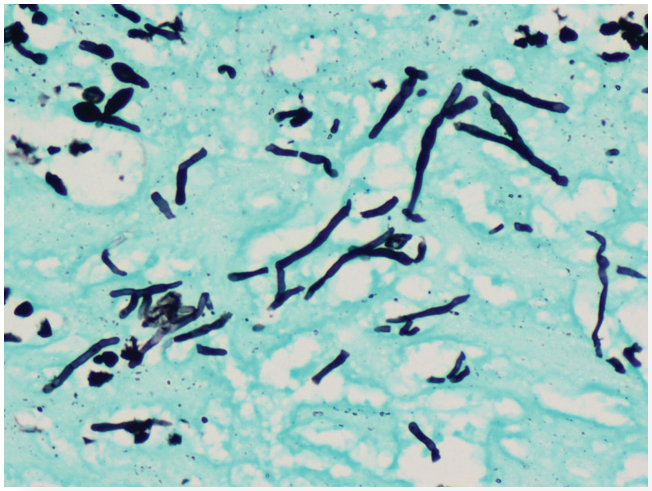

Figure 6. GMS stain shows septate hyphae. [GMS x200]

Discussion

Phaeohyphomycosis is a fungal infection caused by dark-walled, pigmented hyphae in tissue and culture. The term ”phaeo” is derived from the greek word phaios which means black or grey [5,6]. Clinical manifestations vary from local skin lesions to invasive and disseminated infections. McGinnis has classified the disease broadly into superficial, subcutaneous and systemic forms. Subcutaneous infections usually occur as solitary lesions; however multifocal lesions have also been described. Common sites include the hand, arm, face, or neck. These infections are being increasingly being detected in immunocompromised patients [1,2,4].

Histopathologically, the lesions are seen as uniloculated pus filled cavities with a fibrous wall. On microscopy granulomas with epitheloid cells, giant cells, lymphocytes and plasma cells are seen. Fungi are septate and seen both intra and extra cellularly [1,5,6]. Often the brown colour of the hyphae may not be visible on routine H and E stains. Hence PAS and Fontana-Masson stains can aid in diagnosis. Constriction at the septations can sometimes be observed with Gomori methenamine silver stain [3,6,7]. The overlying epidermis does not show ulceration or hyperplasia as observed in cases of chromomycosis and sporotrichosis which should be considered in the differential diagnosis, nor do phaeomycotic cysts form sinus tracts or contain grains, both of which are typical features of mycetoma [1,3].

Excision of the localized lesion is usually curative. However different antifungal agents have been administered of which itraconazole and amphotericin B appear to be the preferable agents [3,4]. No recurrence has been noted in our patient with a 6 month follow up.

Conclusion

Phaeohyphomycosis should always be considered as one of the differential diagnosis while evaluating cystic lesions in the extremities, especially the exposed areas vulnerable to external trauma. Hyphae may appear hyaline on H and E stains with very light brown pigmentation or no pigment at all. However special stains would always be helpful. Some authors suggest that lowering the condenser of the microscope makes these fungi refractile and visible.

Acknowlegement

We wish to thank all the technical staff of pathology department for their support.

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PATOLOGIAS UMBILICALES EN NIÑOS. APORTE DE DOS CASOS Y REVISIÓN DE LA LITERATURA

UMBILICAL PATHOLOGIES IN CHILDREN. REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

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Resumen

Son múltiples las patologías que pueden afectar al cordón umbilical, entre ellas se hallan las de tipo infeccioso, las relacionadas con anomalías del desarrollo, patologías degenerativas, relacionadas con la dinámica del cordón umbilical, de tipo vascular, tumorales y del amnios.

El pólipo umbilical es una anomalía infrecuente por persistencia de parte o todo el conducto onfalomesentérico, histológicamente formado por mucosa intestinal o urinaria. Entre las patologías infecciosas se mencionan las verrugas umbilicales, que son proliferaciones epiteliales benignas, causadas por la infección del virus del papiloma humano.

Se presentan dos casos de patologías umbilicales en niños, el primero en un lactante de sexo femenino de 1.5 meses con un pólipo umbilical, y el segundo caso un escolar de sexo masculino con una verruga umbilical, una localización infrecuente, tratada exitosamente con electrocoagulación. Hacemos además una revisión de las patologías más frecuentes de esta localización en pacientes pediátricos.

Abstract

There are many conditions that can affect the umbilical cord, between them, there are the infectious kind, related developmental abnormalities of the cord, degenerative diseases related to the dynamics of the umbilical cord, vascular type, tumor and amnion.

The umbilical polyp is a rare phatology consistent in a persistence of some or all omphalomesenteric duct, histologically composed of bowel or bladder mucosa. Among the infectious diseases, there is the umbilical warts, that are benign epithelial proliferations caused by infection of the human papilloma virus. Two cases of umbilical disorders in children are presented, the first one in a female infant of 1.5 months, that present a umbilical polyp. The second case, a male child of 12 years old with umbilical wart, an unusual placement, successfully treated by electrocoagulation.

Palabras clave: patología umbilical; verruga; pólipo
Key words: pmbilical pathology; wart; polyp

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Introducción

En la formación del ombligo intervienen una serie de fenómenos desde el propio plegamiento del disco embrionario, la formación y migración del intestino primitivo, hasta la involución de estructuras fetales como el conducto onfalomesentérico, la alantoides y los vasos umbilicales. En los embriones de 75mm ya están constituidas las estructuras definitivas del cordón umbilical: dos arterias, una vena, la gelatina de Wharton y el amnios envolvente [1,2]. Después del nacimiento, las arterias umbilicales y la vena comienzan su obliteración anatómica hasta cerca de los 28 días. En la obliteración de la vena intervienen dos procesos: por un lado la proliferación de la íntima, que llena la periferia y la luz de la vena con nuevo tejido fibroso; y por otro lado la formación de tejido colágeno en la media fibromuscular. Ambos procesos forman al final el ligamento de Teres.

El desprendimiento del cordón suele producirse entre el 5º y 10º días.
Durante la vida fetal el conducto onfalomesentérico o vitelino, une al saco vitelino con el intestino medio y se cierra normalmente para desaparecer por completo. Se encuentra conectado con el intestino primitivo en el saco amniótico. En el desarrollo embriológico normal, el conducto onfalomesentérico involuciona entre las 5a y 7a semanas de vida intrauterina. Un fracaso en la regresión produce varias anormalidades, en dependencia del lugar donde se localice este fallo: en el lado umbilical o en el intestinal [1-4].
Los vestigios del conducto onfalomesentérico pueden presentarse como anomalías relacionadas con la pared abdominal. Sin embargo, puede ocurrir que todo o parte del conducto fetal se mantenga y entonces se produzca sintomatología clínica. También puede persistir como una estructura permeable en toda su longitud o mantenerse como un divertículo o quiste cuando persiste en su periferia, parte central o media; o quizás quede representado simplemente por un resto de epitelio intestinal ectópico a nivel umbilical o como cordón fibroso [5].
El divertículo de Meckel es la lesión más común en su grupo y ocurre en el 2 a 4 % de las personas. La permeabilidad completa del conducto onfalomesentérico (fístula entero-umbilical) es extraordinariamente rara y son muy pocos los casos que aparecen documentados en la literatura. La persistencia de todo el conducto es señalada por la emisión de contenido de fecal por el ombligo, lo cual se observa inmediatamente después del nacimiento y es corregido quirúrgicamente evitándose así la intususcepción o vólvulo [5-7].
A continuación presentamos dos casos clínicos de patologías umbilicales.

Casos clínicos

Caso 1

Lactante de sexo femenino de 1,5 meses de vida procedente de medio urbano, que consulta por lesión sobre elevada en ombligo. Cuadro de 2 semanas de evolución de lesión roja sobre elevada en ombligo, que aumenta progresivamente de tamaño sin otros síntomas acompañantes. Antecedentes neonatales y familiares sin datos de valor.
Examen Físico: tumoración de 5 mm de diámetro, eritematosa brillante de bordes regulares y límites netos en ombligo (Fig. 1).
Diagnósticos clínicos presuntivos: Granuloma umbilical versus Pólipo Umbilical.
Se realizan exéresis y electrocoagulación y se remite el material para estudio histopatológico.
Histopatología: Toma tipo polipoide, constituida por mucosa colónica, glándulas colónicas de morfología preservada, musculo liso, folículos linfoides y gruesos vasos centrales.
Diagnóstico final: Pólipo Umbilical.
Conducta: se deriva a la paciente a cirugía pediátrica para descartar extensión intraperitoneal de este proceso.

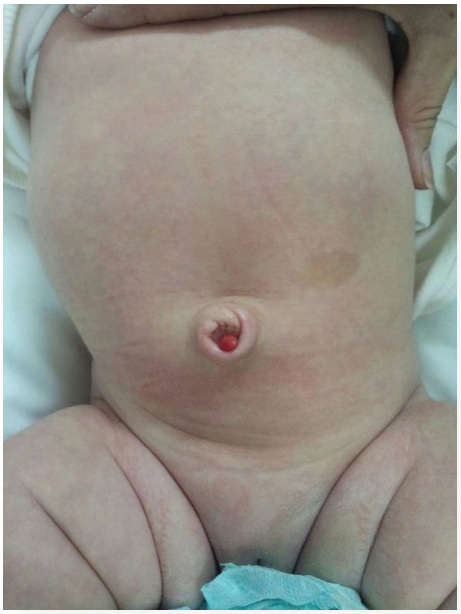

Figura 1. Caso 1. Clínica. Tumoración de 5 mm de diámetro, eritematoviolácea de bordes regulares y límites netos, superficie lisa brillante, que asienta en ombligo.
Figure 1. Case 1. Clinic. Tumor of 5 mm of diameter, erithematoviolaceous, regular margins and net limits, bright smooth surface, which sits at the belly button.

Caso 2

Escolar de sexo masculino de 12 años de edad, procedente de medio urbano, que consulta por presentar desde hace un año lesión sobreelevada en ombligo, asintomática que aumenta de tamaño y se oscurece progresivamente. No realizó tratamiento. Antecedentes patológicos personales y familiares sin datos de valor.
Examen Físico: Tumoraciones hiperpigmentadas de entre 5 y 25 mm de diámetro, bordes regulares y límite netos, superficie hiperqueratósica y verrugosa, localizadas sobre cicatriz umbilical (Fig. 2 y 3). No se aprecian lesiones similares en dedos de manos ni en región genital.
Diagnósticos clínicos presuntivos: Verruga vulgar, Queratosis seborreica, Nevus epidérmico.
Tratamiento: Se realiza shaving de la lesión, electrocoagulación del lecho y se remite la muestra a anatomía patológica, fijada en formol neutro tamponado al 10%.
Histopatología: Macroscópicamente, lesión papulosa de superficie verrugosa, sólida elástica, de 1.5 cm. de eje mayor (Fig. 4). Se procesa de manera rutinaria y se colorea con HE, observándose histológicamente una marcada hiperqueratosis y acantosis (Fig. 5). Hay papilomatosis epidérmica en forma de delgadas agujas. Las columnas de paraqueratosis recubren la proyecciones papilomatosas observándose hemorragia en estas columnas (Fig. 6). Se observa hipergranulosis y las células contienen grupos de densos gránulos de queratohialina. Hay un escaso infiltrado linfocitario en dermis.
Diagnóstico final: Verruga vulgar.
Evolución: El paciente acude luego de 3 semanas a control sin recidiva.

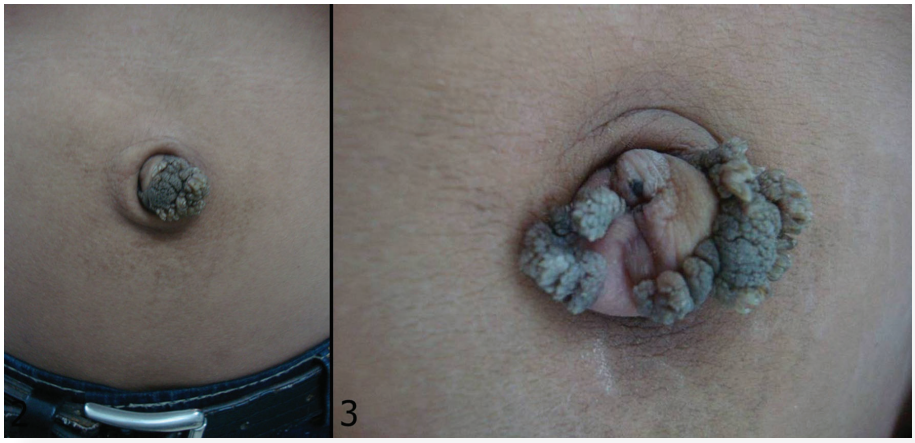

Figura 2 y 3. Caso 2. Clínica. Tumoraciones hiperpigmentadas de entre 5 y 25 mm de diámetro bordes regulares y límite netos, superficie hiperqueratósicas y verrugosas localizadas sobre cicatriz umbilical.

Figure 2 and 3. Case 2. Clinic. Hyperpigmented tumors between 5 and 25 mm diameter with regular margins and net limit, hyperkeratotic and warty surface located on umbilical scar.

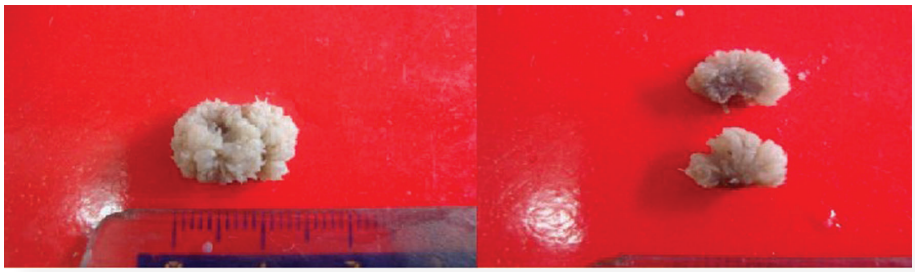

Figura 4. Caso 2. Macroscopía. Lesión papulosa de superficie verrucosa, sólida elástica, de 1.5 cm. de eje mayor.

Figure 4. Case 2. Macroscopy. Papular lesion of verrucous surface, elastic solid, 1.5 cm. major axis.

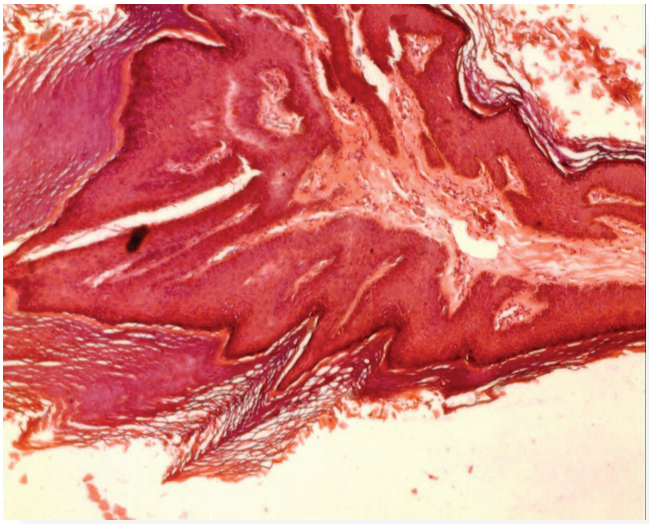

Figura 5. Caso 2. Histopatología, Tinción con Hematoxilina y Eosina. Lesión a menor aumento muestra acantosis, papilomatosis e hiperqueratosis.

Figure 5. Case 2. Histopathology, hematoxylin and eosin staining. Injury to lower magnification shows acanthosis, papillomatosis and hyperkeratosis.

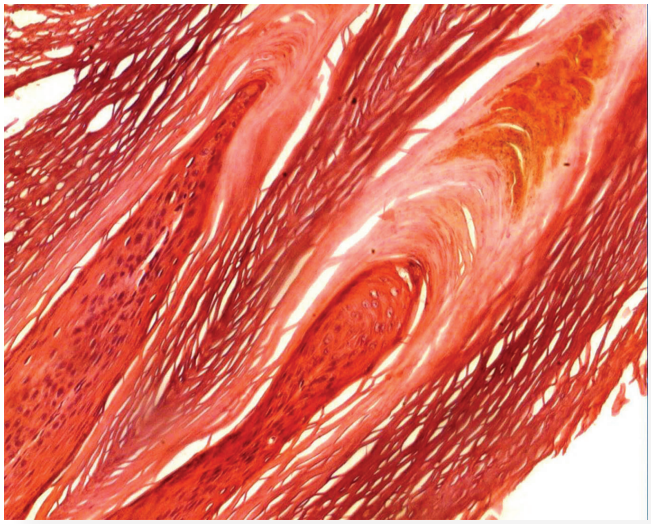

Figura 6. Caso 2. Histopatología, Tinción con Hematoxilina y Eosina. A mayor aumento se observa agranulosis bajo las columnas de paraqueratosis y hemorragia en estas columnas.

Figure 6. Case 2. Histopathology, hematoxylin and eosin staining. Agranulosis under columns of parakeratosis and hemorrhage in these columns.

Comentarios

El conducto onfalomesentérico o vitelino comunica la cavidad celómica con el intestino medio hasta la 5º - 7º semanas de gestación, involucionando luego hasta desaparecer al final del tercer mes de gestación [1,2]. Las anomalías relacionadas con la ausencia total o parcial de dicha involución, se presentan en el 2% de la población. El 6% de estas malformaciones corresponden a conductos onfalomesentéricos persistentes y hasta un 20% de ellos se presentan con complicaciones. El 73% de los casos muestran síntomas dentro de los primeros 28 días de vida y son más frecuentes en pacientes del sexo masculino. Se clasifican en cuatro formas básicas, según la descripción de Trimingham: conducto onfalomesentérico total o parcialmente permeable, pólipo umbilical y banda congénita. De estas malformaciones, la más frecuente es el divertículo de Meckel, divertículo verdadero localizado en el borde antimesentérico del íleon, que se presenta hasta en 3% de la población [3,4,9].

Los pólipos umbilicales forman parte de este grupo de anomalías, son de presentación poco frecuente y se diagnostican generalmente en neonatos, aunque se han encontrado lesiones en niños mayores y aún en adultos, pero siendo en estos últimos excepcionales. Clínicamente se presentan en forma de una pequeña tumefacción redonda, roja, de superficie lisa y de aspecto brilloso por ser mucosa, recubierto de serosidad, localizado en la base del ombligo. Dentro de los diagnósticos diferenciales que se plantean ante la presencia de esta lesión el más importante por su semejanza clínica es el granuloma umbilical, de presentación más frecuente, el cual se diferencia principalmente por su menor tamaño y la buena respuesta que presenta al tratamiento tópico con nitrato de plata, mientras que en el pólipo el tratamiento es quirúrgico. Otras entidades con las que debe diferenciar son: hernia umbilical, persistencia del uraco, onfalocele, angiomas. El estudio histopatológico de la lesión muestra una abrupta transición del epitelio escamoso a un epitelio glandular de tipo gástrico, intestinal o colónico y menos frecuentemente tejido pancreático [4-6].

Nuestro primer caso corresponde a un pólipo umbilical, nódulo rojo cereza, indoloro. La histopatología muestraba un tejido polipoide, constituido por mucosa colónica con glándulas de morfología preservada, musculo liso, folículos linfoides y gruesos vasos centrales.

La persistencia total del conducto onfalomesentérico (fístula entero-umbilical) es extraordinariamente rara y son pocos los casos que aparecen documentados en la bibliografía. La persistencia total del conducto con manifestaciones tempranas en la etapa neonatal, antes de la caída del cordón, puede diagnosticarse por el aspecto dilatado, que deja ver una tumefacción oscura del canal onfalomesentérico. Después de la caída del cordón, el aspecto de este conducto permeable es el de un grueso pólipo umbilical, que puede dar lugar a confusión e interpretarse como un granuloma umbilical. No obstante, en algún momento, y sobre todo con el llanto o los esfuerzos, se podrá observar la salida de gases y líquido intestinal [4-6].

La persistencia parcial puede también adoptar dos aspectos: el de un ombligo exudativo o el de una tumefacción umbilical. La obliteración incompleta del conducto onfalomesentérico recibe el nombre de divertículo de Meckel y es la forma de mayor incidencia clínica [5,6].

La aparición de una formación polipoidea a nivel umbilical de color fresa y generalmente de un tamaño discretamente superior al típico granuloma umbilical, debe hacernos sospechar la existencia de restos de mucosa intestinal no involucionada. Ante dicha lesión es obligada la búsqueda de un estoma en su superficie. El diagnóstico de persistencia del conducto onfalomesentérico se confirma por medio de la ecografía abdominal, que puede mostrar la presencia de una estructura tubular con aire que conecta con el intestino, o por medio de la fistulografía. Las complicaciones que se pueden presentar por un conducto onfalomesentérico permeable incluyen: infección del ombligo, dermatitis periumbilical, sangrado de la mucosa intestinal, estrangulación ileal, potencial de malignización, prolapso e infarto del intestino y obstrucción intestinal. Las complicaciones más graves pueden llevar hasta a un 18% de mortalidad, especialmente en el período neonatal. El tratamiento de este tipo de malformación es quirúrgico debido a que este conducto no involuciona después del nacimiento y a las consecuencias potencialmente graves que puede originar [8-10].

Por lo tanto, la persistencia del conducto onfalomesentérico debe sospecharse en todo neonato que presente secreción umbilical, granuloma umbilical que no responde a la cauterización con nitrato de plata o en presencia de un lumen no vascular adicional en el cordón umbilical. El cuadro clínico de presentación puede ir desde el granuloma umbilical que no se resuelve con las curas habituales, hasta cuadros severos de obstrucción intestinal o hemorragia digestiva asociada a la presencia de mucosa gástrica la cual no ha sido reportada en la fístula onfalomesentérica simple. Dejando de un lado las formas de presentación típicas del Divertículo de Meckel que son la hemorragia digestiva, la obstrucción intestinal y la peritonitis por perforación del mismo, básicamente distinguimos dos formas de presentación clínica: el ombligo húmedo, que sería la forma asociada al pólipo umbilical, el seno umbilical y la fístula enteroumbilical, y por otro lado la obstrucción intestinal, la cual se asocia a cualquier tipo de malformación en que exista una banda de tejido ya sea permeable o no entre el ombligo y la pared intestinal [9-11].

Desde el punto de vista clínico, su principal diagnóstico diferencial es el granuloma umbilical, sin embargo, existen diferencias que nos permiten distinguir entre ambas patologías. Generalmente, el granuloma umbilical es asintomático mientras que la persistencia del conducto onfalomesentérico puede acompañarse de complicaciones como la hemorragia, invaginación, obstrucción y vólvulo intestinal que incluso pueden poner en riesgo la vida del paciente. El granuloma umbilical o la onfalitis responde a los cuidados tópicos con nitrato de plata y antiséptico, mientras que una evolución tórpida, que en la mayoría de casos cursa con trastornos tróficos de la piel periumbilical, requiere una terapia más agresiva, que consiste en la extirpación quirúrgica de la lesión cutánea seguida por una exploración abdominal para descartar la existencia de anomalías y de restos embriológicos [10-13].

Las exploraciones complementarias a parte de la ya referida, fistulografia cuya sensibilidad y especificidad en casos de permeabilidad total es del 100%, pueden aportar información sugestiva de la persistencia de restos del conducto onfalomesentérico.

En casos de presentación como obstrucción intestinal baja, la realización de un enema opaco puede mostrar como signos típicos de vólvulo de intestino delgado sobre una banda onfalomasentérica, una imagen distal en forma de «pico» o un desplazamiento medial del ciego.

La ultrasonografia con ecógrafo de alta resolución es capaz de delimitar la anatomía normal del ombligo y de sus estructuras adyacentes, vainas de los músculos rectos anteriores y peritoneo [11,13].

El diagnóstico en el curso de un abordaje lapároscopico del abdomen es fácil, observándose una banda de tejido que se extiende desde la cara interna del ombligo en profundidad.

El tratamiento de estas malformaciones es quirúrgico dado su prácticamente nulo potencial de involución después del nacimiento, y las molestas implicaciones que producen las formas más sencillas o las consecuencias potencialmente graves de las formas completas. El abordaje del ombligo a través de una minilaparotomía umbilical, es en la mayoría de casos suficiente para un tratamiento cómodo y eficaz de la malformación. Dicho tratamiento en las formas más sencillas consiste en una simple exploración del ombligo que descarte la extensión intraperitoneal de la lesión y una resección de los restos mucosos a nivel umbilical [11,12,14].

Los hematomas del cordón umbilical son entidades poco frecuentes. Se señalan grandes hematomas con repercusión evidente en el feto en uno por cada 5500 embarazos, con una mortalidad inmediata de un 47% [7]. En el momento del parto son vistos pequeños hematomas sin que produzcan necesariamente cambios importantes en la fisiología del neonato. En su etiología no existe una causa definida, aunque algunos autores piensan que son debidos probablemente a la fuerza mecánica que ejerce el feto y que, en tal caso, ocurren por la ruptura de los vasos, principalmente de la vena. Tienen forma fusiforme, cilíndrica y están situados en la periferia del cordón. Pueden ser unidos o múltiples, separados por segmentos de cordón normal. Estos hematomas no presentan histológicamente ninguna característica especial, excepto que en algunos es posible ver los sitios de rotura de los vasos o la compresión de estos por el hematoma. Las consecuencias que se derivan de los hematomas están en dependencia de su tamaño y de la afectación vascular que comprendan, lo cual puede determinar cambios metabólicos importantes en el feto y anoxia aguda progresiva. El diagnóstico diferencial se realiza con otras patologías de tipo vascular y tumoral, entre las cuales destacan la dilatación aneurismática de la vena umbilical [13-16].

Entre otros tumores de ombligo se puede mencionar el angiofibromixoma y el angioma. En ellos, por lo general, existe una mezcla de varios componentes estructurales que no permiten clasificarlos como pertenecientes a un solo tipo; no aparecen con frecuencia y se desarrollan de restos embrionarios. Pueden aparecer a cualquier edad [13,14].

La Hernia Umbilical es un defecto del cierre de la fascia abdominal, que permite la protrusión del contenido intestinal, a través de anillo umbilical. Es la patología umbilical más frecuente en lactantes, se observa el 10% de todos los recién nacidos normales y con mayor frecuencia en pretérminos, el síndrome de Down, hipotiroidismo, etc. Se identifica a partir de la 2ª semana de vida después del desprendimiento del cordón umbilical. Es una pequeña tumoración blanda, del tamaño de una cereza que se reduce fácilmente, que está formada por el peritoneo y la grasa del epiplon que protruye a través del anillo inguinal. Suele aumentar de tamaño al esfuerzo del niño (llanto, defecación, etc.). Suelen ser indoloras y su incarceración excepcional. Con el tiempo el anillo umbilical se contrae espontáneamente y cierra el defecto, siendo 8 de cada 10 hernias umbilicales las que cierran solas, durante los 4 primeros años de vida. Para predecir este cierre espontáneo tiene importancia el diámetro del defecto del anillo umbilical; tamaños superiores a 1,5cm. pueden precisar cierre quirúrgico a partir delos 2 años de edad [16,17].

En cuanto a las patologías infecciosas se describe principalmente la onfalitis, que se presenta con eritema umbilical, edema y secreción maloliente. La edad promedio de presentación es 3º o 4º día de vida. Se presenta en un 0.7% de los RN nacidos en países desarrollados y hasta un 2.3% en países en desarrollo. Las onfalitis pueden ser extremadamente graves, provocando una sepsis, debido a la permeabilidad de los vasos umbilicales que persiste hasta aproximadamente los 20 días de vida, por lo que su tratamiento debe ser tomar muestra para identificar bacteriológicamente el germen y antibiograma e iniciar de inmediato el tratamiento antibiótico. Las fascitis necrotizante, el tétanos neonatal, o la erisipela en zona umbilical, son entidades excepcionalmente raras actualmente en nuestro medio [16,17].

Otra patología infecciosa citada, aunque infrecuente son las verrugas que asientan sobre cicatriz umbilical. Las mismas son tumores epiteliales comunes, contagiosos, causados por el virus del papiloma humano (VPH). La prevalencia de las verrugas cutáneas es de hasta un 10% en niños de 2-12 años de edad, afectando por igual a ambos sexos, comprometiendo frecuentemente manos y rodillas, aunque pueden aparecer en cualquier localización de la piel o superficie mucosa [18-20]. La infección y la inducción de la hiperproliferación se inician cuando el virus entra en células epiteliales basales en proliferación, lo que requiere un traumatismo. Los VPH tienen mecanismos evolucionados para evadir al sistema inmunológico de vigilancia, sin embargo, una respuesta inmune exitosa se genera en la mayoría de los casos, ya que dos tercios de verrugas cutáneas sufren regresión espontánea en el plazo de 2 años y las lesiones multifocales a menudo regresan en forma concomitante. Las verrugas vulgares son típicas de niños y adolescentes. Se cree que hasta un 20% de escolares las presenta. Se desarrollan dentro de unas pocas semanas hasta 18 meses tras la inoculación viral.

En cuanto al tratamiento se describe autoresolución del cuadro en promedio en 2 años, pero cuando la lesiones son múltiples y exuberantes o las mismas provocan en el paciente complejos por estética, deben ser tratadas. No existe un tratamiento 100% eficaz por lo que la elección deberá hacerse según lo requiera cada paciente. Las opciones terapéuticas incluyen: agentes queratolíticos (ácido salicílico o ácido láctico tópico), terapia con ablativos (crioterapia, electrofulguración, extirpación quirúrgica, terapia fotodinámica, láser CO2) [21,22], inmunomoduladores (imiquimod tópico, levamisol o metronidazol vía oral, cantaridina intralesional) [23-26] y citotóxicos (ácido tricloroacético, 5-fluorouracilo tópico o intralesional, interferón intralesional, bleomicina intralesional) [27-29], en muchos de los casos se requieren de terapias combinadas.

La peculiaridad de la lesión presentada radica en su localización. Si bien se han descrito casos de verrugas umbilicales, las mismas se hallaban asociadas a condilomas en localización genital. Nuestro paciente no presentaba lesiones genitales clínicamente discernibles [30].

Conclusion

Toda neo formación umbilical en el niño merece una especial atención por parte de su médico tratante.

Dado el amplio abanico de patologías posibles en dicha región, dónde cada una de las mismas posee distinto nivel de impacto en la vida diaria del niño y una morbimortalidad particular, resulta crucial que el dermatólogo, el neonatólogo y el pediatra general estén familiarizados con las mismas.

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AN INTERESTING CASE OF GIANT MOLLUSCUM WITH FLORID VERRUCA VULGARIS IN AN IMMUNOCOMPETENT PATIENT

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Abstract
Molluscum contagiosum and warts are two fairly common skin infections caused by DNA viruses i.e. poxvirus and human papilloma virus (HPV) respectively. Both the conditions are benign and mostly self-limited. However in immunocompromised individuals, these infections can have varied atypical presentations like larger, more extensive, recalcitrant and refractory lesions. These atypical presentations in a non-immunocompromised individual are, however, quite rare. We present one such case with atypical presentation of molluscum contagiosum and warts (verruca vulgaris).

Key words: molluscum contagiosum; warts; non-immunocompromised

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Introduction

Molluscum contagiosum (MC) is a benign viral infection of the skin caused by a DNA poxvirus (molluscum contagiosum virus). The disease is quite common in young children, though sexually active adults and immunocompromised individuals may also be affected. The incubation period is around 2-3 months [1]. The characteristic lesions are white to pink, dome shaped, waxy, umbilicated papules usually 2-5 mm in size. Most of the lesions are benign and self-limited. In immunocompromised individuals, the infection may, however, assume atypical characteristics, such as large size of lesions (giant molluscum contagiosum when ≥1 cm) [1,2], widespread, chronic and recalcitrant lesions [1,3,4]. Presence of giant molluscum in an immunocompetent host is an uncommon entity.

Warts are a form of skin and mucous membrane infection caused by human papilloma virus (HPV) and have a universal occurrence. Extensive and refractory warts may be seen in immunocompromised individuals [5], thus underlining the role of immune system in eradication of the causative virus from the body.

The occurrence of the atypical MC and verruca vulgaris in a non-immunocompromised individual is not so common, and we are reporting such a case, where excellent response to autoinoculation was found.

Case Report

A 20 year old male presented with multiple, discrete, dome shaped, umbilicated skin coloured papules and nodules ranging in size from 0.5 to 3 cm, mainly localised to the axillae, groins and genitalia (Figs. 1A and B). The first skin lesion had appeared nearly one year back. The lesions were largely asymptomatic except for slight occasional pruritus. Upon compression, some of the nodules expressed white caseous material. Excision biopsy of one lesion revealed characteristic histologic features of large, eosinophilic intracytoplasmic inclusion bodies (molluscum bodies). The patient also presented with multiple hyperkeratotic papules and plaques with a rough, irregular surface ranging in size from 0.5cm to 2cm on the dorsal aspects of hands and feet (Fig. 2). The patient also reported recurrent episodes of tinea corporis and onychomycosis (Fig. 2). His face had diffuse erythema and telangiectasia at places on the malar area and nose. The patient was otherwise mentally and physically healthy with no other systemic complaint. The patient denied current use of any immunosuppressive drugs and the family history was non-contributory.

General physical examination revealed an average built patient with no signs of pallor, icterus, cyanosis or clubbing. There was no significant lymphadenopathy. Systemic examination revealed no abnormality.

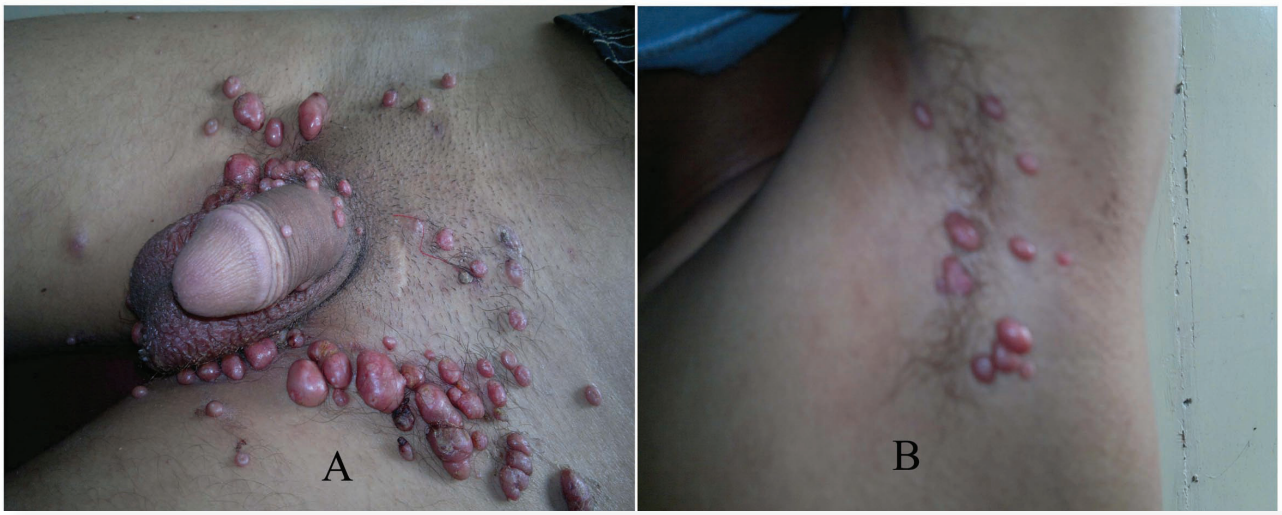

Figure 1A and B. Molluscum contagiosum on groin and genitals (A) and axillae (B).

Several laboratory tests were performed to investigate any underlying primary or secondary immunodeficiency. Human immunodeficiency virus (HIV) 1 and 2 serology was negative. Chest X-ray was normal. Sputum was negative for acid fast bacilli (AFB) and Mantoux test was negative. Erythrocyte sedimentation rate (ESR) was within normal limits. Antinuclear antibody (ANA) was positive at a low titre and anti-ds DNA was negative. Hepatitis B and C serology was negative. Serum cortisol levels were within normal limits.

Measurement of the levels of major immunoglobulin classes: IgG (1234 mg/dl), IgA (735mg/dl), IgM (460mg/dl) and IgE (16.8IU/ml) were non-contributory. The absolute lymphocyte count (2764/mm^3) was within normal limits. The percentage and absolute numbers (in parentheses) for different lymphocyte subsets were determined as follows: CD3 -75% (2076/µl), CD4 – 51% (1404/µl), CD8 – 18% (588/µl). The CD4/CD8 ratio (2.4) was also within normal limits.

Some of the giant molluscum lesions were successfully treated with extirpation followed by cauterisation of the base with potassium hydroxide. The hyperkeratotic lesions over hands and feet, diagnosed as verruca vulgaris, and most of the MC were, however, recalcitrant to treatment. Autoinoculation done for the same resulted in significant improvement in the lesions over a period of 2-3 months (Fig. 3). In addition, the patient also received oral levamisole (150mg twice weekly) and oral zinc sulphate (200mg once daily) for a period of 3 months.

Discussion

Molluscum contagiosum is a common viral infection of the skin caused by a large DNA virus (molluscum contagiosum virus).The infection is usually self-limited with lesions mostly disappearing within 6 to 12 months, but may take as long as 4 years. Giant molluscum contagiosum (>1cm in size) is an uncommon variant usually seen in immunocompromised states. Immunodeficient states are also typified by more widespread and recalcitrant forms of molluscum contagiosum. Occurrence of molluscum contagiosum in these forms is rare in immunocompetent individuals.

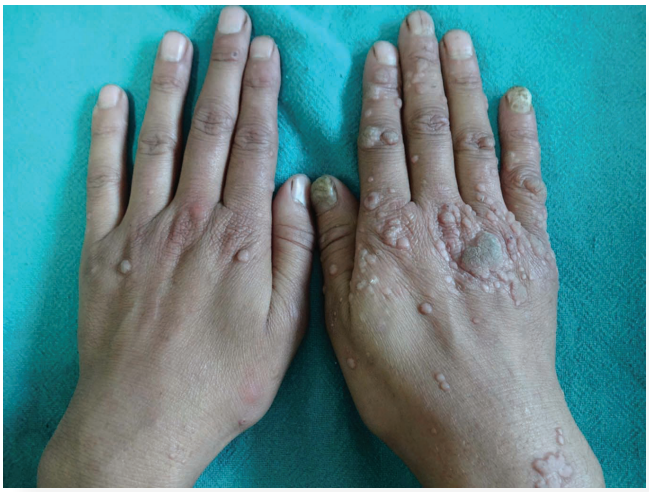
Figure 2. Verrucae and onychomycosis on the hands.

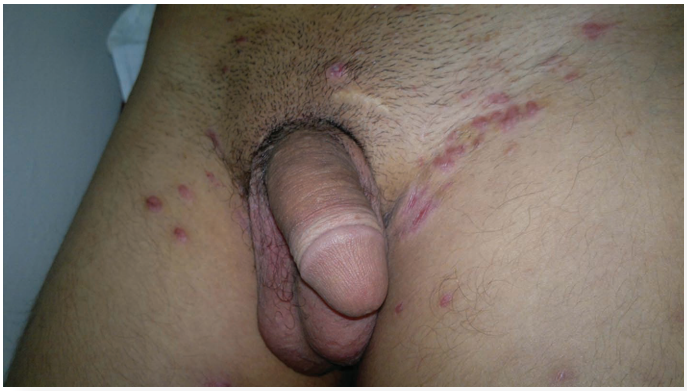
Figure 3. Excellent response to autoinoculation.

Verruca vulgaris caused by human papilloma virus, although quite common, occurs more extensively, are usually recurrent and recalcitrant to treatment in immunocompromised hosts.

Only a few cases of florid giant molluscum contagiosum occurring in immunocompetent patients have been reported. However, complete evaluation of the immune status was not carried out in most of them. Majority of these reported cases involved immunocompetent children. Giant molluscum contagiosum in immunocompetent adults appears to be even rarer. Dickinson A et al [6], Agarwal S et al [7], and Egawa K et al [8], reported cases of giant molluscum in immunocompetent adults. However none of these cases underwent complete evaluation of the immune status. Matsuda M et al [9], reported a case with concomitant giant molluscum contagiosum and verruca vulgaris. The immunocompetent status of the patient, however, could not be fully elucidated.

In our patient, concomitant giant MC and verruca vulgaris, tinea corporis and onychomycosis was found, after ruling out any immunocompromised status.

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CHRONIC ULCERATING GENITAL HERPES SIMPLEX VIRUS INFECTION: A DIAGNOSIS MISLEAD BY HIV INFECTION

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Abstract
We report a case of chronic herpes simplex in a 27 year old lady presenting with a history of persistent verrucous ulcer in the natal cleft of nine months duration. The patient was diagnosed and treated initially as a case of Tuberculosis Verrucosa Cutis (TVC) based on the chronicity of the ulcer, negative HIV serological tests and histopathological findings. The diagnosis had to be revised as the lesion was increasing in size and the patient was not responding to treatment even after completing antituberculous treatment for six months. Repeat histopathological examination and immunohistochemistry showed DNA of herpes simplex. Based on this finding a repeat HIV serology was sent which was positive. The ulcer healed after a course of acyclovir. The case is being reported to highlight the importance of considering chronic herpes simplex infection in a case of chronic genital ulcer. In addition this case reminds us the nature of HIV infection to mislead the diagnosis by altering the natural course of the disease process.

Key words: Herpes; HIV; Verruocous ulcer; Acyclovir; Tuberculosis Verrucosa Cutis; Genitalia

Cite this article:
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Introduction

Herpes simplex virus type 2 (HSV-2) infections is the most common cause of genital ulcerative disease in the developed world. Its etiological agent is herpes simplex virus type 1 (HSV-1) or 2 (HSV-2). The principal route of infection with HSV is asymptomatic viral shedding. The infection is life-long; despite treatment [1]. The clinical polymorphism of Chronic herpes simplex virus (CHSV) and chronic varicella zoster virus (CVZV) makes their recognition difficult [2].

We report a case of chronic ulcerating genital herpes simplex virus infection in a HIV infected patient because of the tendency on part of physician to overlook the diagnosis when HIV infection is not suspected.

Case Report

A 27 year, widow from Palpa district of Nepal presented with a single, asymptomatic, 3x2cm mobile and non indurated verrucous plaque over natal cleft since nine months which was slowly progressing. It was associated with low grade fever that subsided spontaneously. She was diagnosed as Tuberculosis Verrucosa Cutis (TVC) on the basis of clinical, laboratory (Total WBC count: 6310; N48, L45, ESR: 60mm Wintrobes, Mantoux test: induration diameter = 0mm) and histopathological findings (neutrophilic and lymphoplasmacytic infiltrate, necrosis with aggregates of epitheloid cells, Periodic acid Schiff and Ziehl Nelson Stain were negative). She was started with a course of Anti-Tubercular Therapy (ATT) which was followed by decreasing size of the lesion during the initial one month period. Gradually, after two months, the lesion started ulcerating and she also developed new well defined 1x1 cm discrete, punched out, non tender, kissing ulcers over labia minora (Fig. 1). Her serology for HIV was negative. VDRL and pathergy tests were also negative. A repeat biopsy was done and the histopathological findings showed chronic ulcer with vague granulomatous reaction in the dermis; suggestive of healing tuberculous lesion. ATT was continued for 6 months but no improvement was noted and she was also started with oral doxycycline with slight improvement in the first two weeks.

The patient lost follow up for 4 months and had discontinued the medication when she presented to us. The lesions had now coalesced to form two large painful ulcers with sero-purulent discharge involving the peri-anal area and the labia minora. Other mucosal surfaces, hair and nails were spared. There was no lymphadenopathy, no history of night sweats, weight loss, and decreased appetite, joint pain, bleeding manifestations or ophthalmic problems.

There was no history of blood transfusion and extra-marital sexual relationship. Her husband, who worked abroad, expired eight years back because of pulmonary tuberculosis.

The patient was not responding to any of the treatments provided which prompted us to revise the diagnosis. On further histopathological work up, Immunohistochemistry for Herpes Simplex virus type 1/2 was positive with reactivity in the nuclei of enlarged and multinucleated keratinocytes. Also a repeat serology for HIV was sent which to our surprise was positive with CD4 count of 39cells/mm^3. She was then started on Acyclovir 200mg five times a day with improvement after first week of therapy (Fig. 2). She was also started on anti-retroviral drugs.

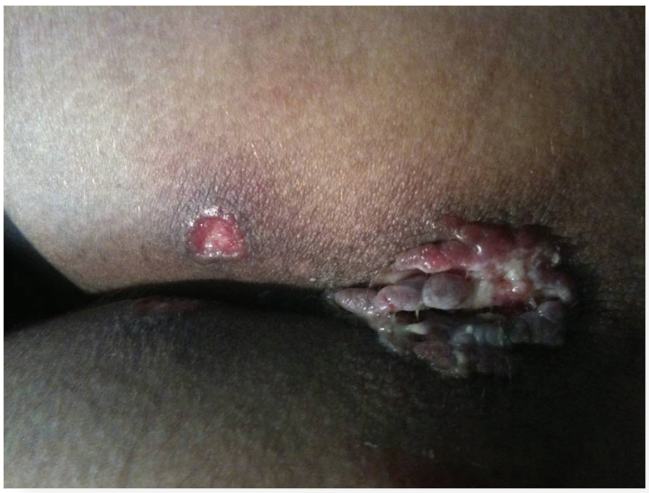

Figure 1. Verrucous ulcer in anogenital area at presentation.

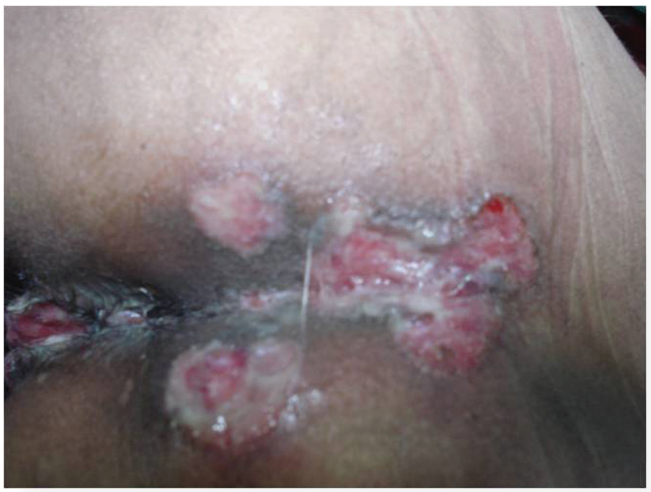

Figure 2. Healing ulcer 7 days post treatment with acyclovir.

Discussion

Genital herpes is the most frequent cause of genital ulcer diseases. Other agents responsible for genital ulceration are *Haemophilus ducreyi*, *Treponema pallidum*, *Kleibsiella granulomatis*, *Chlamydia trachomatis* (LGV strain) [4]. Herpes is the fourth commonest sexually transmitted disease; the first 3 being chancroid, gonorrhoea, and genital warts; genital herpes accounts for 22.4% of the new patients [5]. In the United States of America it is commoner than gonorrhoea and has increased 9 folds in the last 2 decades [6,7]. Also in a study done by Shobhana et al, out of 410 HIV seropositive patients 40% had mucocutaneous involvement and genital herpes was the most common genital ulcer disease [8].

Herpes simplex is known to occur as a manifestation of AIDS, where it is more severe and atypical and perianal lesions are characteristic [9]. In our patient the presentation was a persistent mucocutaneous wart-like and ulcerative infection, which is one of the commonest atypical presentation of chronic herpes simplex virus infetion associated with HIV. It may occasionally present with other types of immunosuppression as well [3]. Low CD4+ counts also act as a marker of HIV disease progression [10].

Conclusion

A high index of suspicion is necessary to pick up a case of HIV positivity from an outpatient department. HIV can lead to bizarre presentation of common conditions like herpes, so awareness of the disease and its various manifestations becomes immensely important for proper diagnosis and treatment of our patients.

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CENTRAL CENTRIFUGAL CICATRICIAL ALOPECIA AMALGAMATED WITH ALOPECIA AREATA: IMMUNOLOGIC FINDINGS

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Abstract
Introduction: Both scarring and non-scarring alopecias exist; however, rare cases demonstrate features of both classes.
Case Report: We describe an interesting alopecia case with amalgamated clinical, histologic and immunopathologic features of scarring and non-scarring alopecia. Specifically, the case displays combined features of alopecia areata (AA) and of central centrifugal cicatricial alopecia (CCCA). A 36 year old female presented with symmetric, round, patchy hair loss on her scalp.
Methods: Biopsies for hematoxylin and eosin (H&E) examination, as well as for special stains, direct immunofluorescence (DIF) and immunohistochemistry (IHC) were performed.
Results: The H&E biopsy revealed focally diminished hair follicular units, and sebaceous gland damage. Perifollicular concentric fibrosis was confirmed by Verhoeff elastin special staining. Antibodies to micelles were noted. Positive IHC staining for CD4, CD8, CD45 and multiple proteases and protease inhibitors was noted around selected follicular unit remnants.
Conclusion: We present a rare alopecia, combining histologic features of CCCA with additional, selected immunologic features of AA.

Key words: Autoimmunity; scarring alopecia; alopecia areata; fibrosing alopecia; CD99

Abbreviations: Alopecia areata (AA), central centrifugal cicatricial alopecia (CCCA), direct immunofluorescence (DIF), immunohistochemistry (IHC), hematoxylin and eosin (H&E).

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Abreu Velez AM, Smoller BR, Howard MS. Central centrifugal cicatricial alopecia amalgamated with alopecia areata: immunologic findings. Our Dermatol Online. 2014; 5(3): 287-291.

Introduction

Scarring alopecias are often syndromic. Many scarring alopecia immunodermatologic findings are not well studied, especially in overlapping syndromes [1-3]. The most common clinical scarring alopecias include lupus erythematosus, lichen planus, pseudopelade of Brocq, follicular mucinosis, severe folliculitis, dissecting cellulitis, folliculitis decalvans, acne kelodalis nuchae, tinea kerion and favus [1-3]. Overall, immunologic findings derived from direct immunofluorescence (DIF) and/or immunohistochemistry (IHC) in scarring and non-scarring alopecias are not well documented in the literature. Alopecia areata (AA) is classically considered a non-scarring alopecia [4]. Although scarring alopecias may clinically present in a similar manner to AA, discernible differences may also be present. In AA, the hairless patches are usually smaller, more symmetric and round. Scarring alopecias may clinically "burn out"; the hairless spots will then stop increasing in diameter, concomitant with cessation of the clinical etiology [1-3]. Overlap syndromes involving alopecias have been described, but often without significant documentation of DIF and IHC data. Previous attempts to confirm autoantibodies directed against hair follicle components in sera from AA patients have met with difficulty [4-6]. In addition, the majority of perilesional inflammatory cells around hair follicles in AA are either CD4 or CD8 positive lymphocytes.

Case Report

A 36 year old African American female presented for alterations in her scalp hair. Clinically, she demonstrated symmetric, round patches of alopecia with some burning sensations. Examination also revealed focal non-symmetric, scarring alopecic areas. Skin biopsies for hematoxylin and eosin (H&E) examination, IHC and multiple fluorochrome DIF were performed.

Initial processing of the biopsies for H&E examination, DIF and IHC stains was performed as previously described [5-7]. Our case was IRB exempt because no patient identifiers were recorded. Skin DIF cryosections were prepared and incubated with multiple fluorochromes as previously reported [7-12]. The H&E sections demonstrated an unremarkable epidermis with no interface inflammation. Within the papillary and reticular dermis, hair follicular unit density was focally diminished. There were 2-3 hairs per follicular unit, and less than four sebaceous glands per follicular unit (Fig. 1). Sebaceous gland morphology varied from normal to complete destruction. The overall anagen:telogen ratio appeared normal. A mild, superficial, perivascular lymphohistiocytic infiltrate was present. No perifollicular inflammation was seen. Lymphocytes were predominantly present around blood vessels surrounding hair follicular units. Mild perifollicular concentric fibrosis was noted. Diffuse scarring was seen in focal regions of the biopsy, and rare follicular stelae scars were seen. A Verhoeff elastin stain confirmed focal dermal scarring, occupying approximately 25% of the biopsy area. A Periodic acid Schiff(PAS) stain displayed positive enhancement along basement membrane zone areas of some hair follicular units and eccrine glands (Figs. 1, 2). Finally, an Alcian blue special stain highlighted follicular remnants, with mucin deposition noted within scarring areas (Fig. 2). By IHC, vimentin defined dermal pilosebaceous gland remnants. TIMP1 was positive on remnants of follicular units, and concentrated on sebaceous glands. CD8 positive cells were noted within the perifollicular lymphocytic infiltrate, and also around blood vessels that supplied piloerector muscles and eccrine glands (Fig. 1). Within the isthmus of hair follicles, we also noted CD8 positive staining. CD4 positive cells displayed a similar pattern to the CD8 positive cells. Strong CD45 and CD99 positivity was noted around perifollicular blood vessels. There was also strong positive staining with IgG and IgD around hair follicular units; IgD was accentuated around follicular remnants. Positive staining for IgG also was noted in focal areas of the epidermal granular cell layer, within dermal endothelial-mesenchymal cell junctions, and in endothelial cells of perifollicular blood vessels. IgM demonstrated a similar, but stronger staining pattern as IgG. Complement/C3c demonstrated a similar pattern to IgG, but with weaker staining within endothelial/mesenchymal dermal cell junctions. By DIF, Complement/C1q showed strong positivity within micelle-like structures near damaged sebaceous glands (Fig. 3). Strongly positive IgD staining was noted within and around hair follicles, and specifically around surrounding blood vessels. Complement/C3c and C1q were also strongly positive within the follicular remnants (Fig. 3 and Tabl. I).

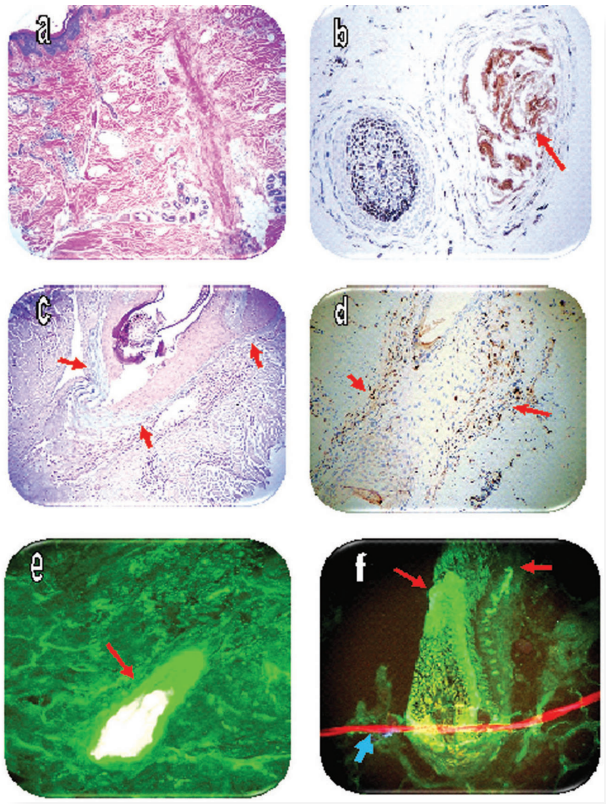

Figure 1. a. A representative H&E section, demonstrating the decrease in hair follicular units. **b.** IHC CD8 positive staining inside remnants of a hair follicle (brown staining; red arrow). **c.** Alcian blue special stain, highlighting reactive mucin deposition in areas of dermal scarring (light blue staining; red arrows). **d.** IHC CD8 positive staining around a hair follicle, and around adjacent blood vessels(brown staining; red arrows). **e.** DIF positive staining of a hair bulb remnant, utilizing FITC conjugated anti-human Complement/C1q (yellow/white staining; red arrow). **f.** DIF positive staining of a hair bulb remnant, utilizing FITC conjugated anti-human IgD; note the staining against several areas within the hair follicle and hair bulb (green staining; red arrows). The thin, horizontal red structure represents a long neurovascular fiber, with its nuclei counterstained with Topro III (red staining; blue arrow).

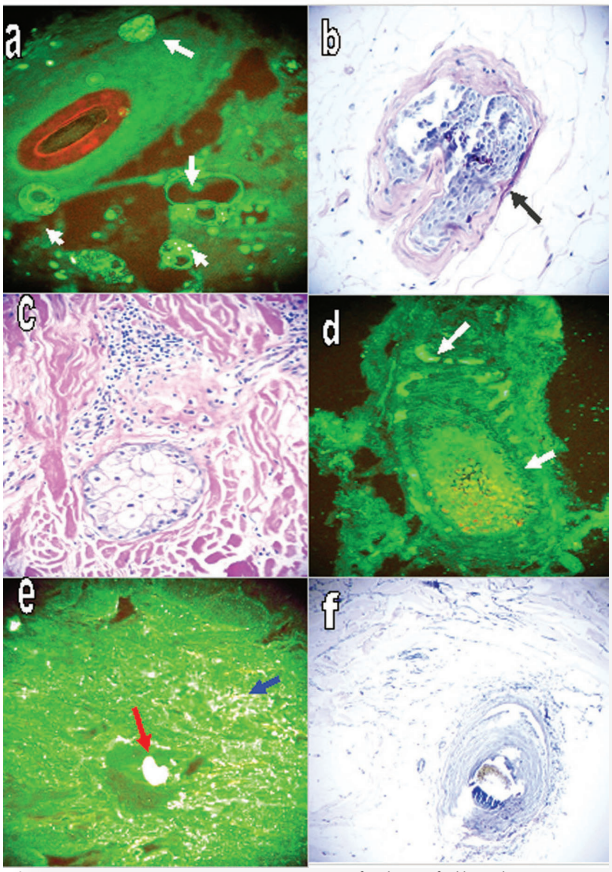

Figure 2. a DIF positive staining of a hair follicular unit remnant, utilizing FITC conjugated anti-human IgD; note the micelles formed at the interface of the aqueous and lipid components (round structures; green staining, white arrows). **b.** Positive PAS special staining along a hair follicle basement membrane (red/purple staining; black arrow). **c.** H&E staining, demonstrating sebaceous gland destruction accompanied by inflammation around the remnants of a hair follicular unit; focal scarring is also present. **d.** Positive DIF staining of a hair bulb remnant and some areas of the hair follicle, utilizing FITC conjugated anti-human Kappa light chains antibody (yellow/green staining; white arrows). **e.** DIF positive staining with FITC conjugated Complement/C1q antibody of a hair bulb remnant (white staining; red arrow), and several dermal blood vessels (white staining; blue arrow). **f.** A clinical picture of the alopecia.

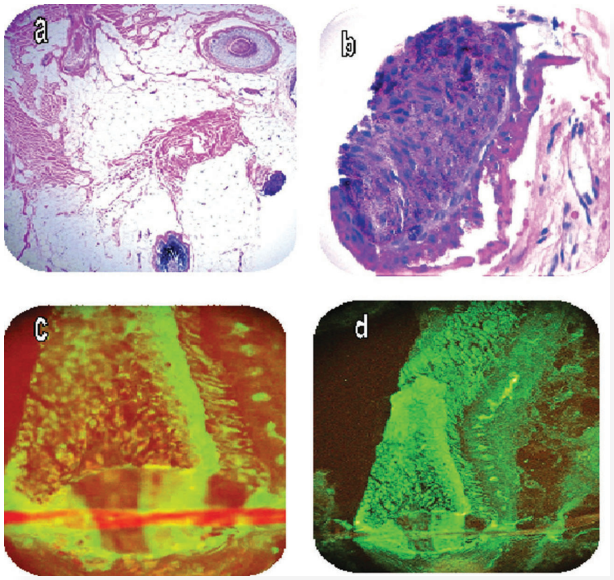

Figure 3. a H&E staining shows a deep dermal and subcutaneous adipose tissue area with some hair remnants, and some alterations of the extracellular matrix. **b.** H&E section highlighting a damaged hair follicle. **c** and **d.** Positive DIF staining in a hair follicle with FITC conjugated anti-human IgD at higher (400x) and lower (200X) magnifications, respectively (green staining).

DIF Antibodies	DIF results	IHC Antibodies (all from Dako)	IHC results
IgG-FITC, Dako.	Positive on hair follicle germinal bulbs (+++) with additional epidermal positivity.	Vimentin	Strong reactivity around hair follicular units, dermal blood vessels and some atrophic eccrine sweat glands and eccrine ducts.
IgM-FITC, Dako.	Positive on hair follicle germinal bulbs, and one focus outside the sebaceous glands.	LAT	Negative.
IgA-FITC, Dako.	Negative.	Metallothionein	Positive in dermal eccrine glands.
Complement/C3--FITC, Dako.	Positive on hair follicle germinal bulbs, and around dermal blood vessels.	TIMP-1	Positive at the bases of a few hair follicles.
Complement/C4-FITC, Dako.	Positive on hair follicle germinal bulbs, and in remnants of damaged hair follicular units.	CD99	Positive on dermal blood vessels and accentuated on blood vessels associated with hair follicle remnants.
Fibrinogen-FITC, Dako.	Positive on hair follicle germinal bulbs.	CD8	Positive around several dermal blood vessels, and eccrine ducts close to damaged follicles.

Table I. Summary of DIF and IHC staining.

DIF Antibodies	DIF results	IHC Antibodies (all from Dako)	IHC results
Albumin-FITC, Dako.	Positive staining of the BMZs of the sebaceous and eccrine glands. Positive epidermal staining within the corneal layer, and some pericytoplasmic staining in keratinocytes of the epidermal granular cell layer. Positive on hair follicle germinal bulbs.	CD45	Positive around dermal blood vessels, close to hair follicles.
IgE –FITC, Goat anti-human ,Vector Laboratories.	Negative.	CD4	Positive around dermal blood vessels, close to hair follicles.
Complement/C1q-FITC, Kent Laboratories.	Positive on hair follicle germinal bulbs, in micelles formed after destruction of sebaceous glands, and in remnants of the sebaceous glands.	Complement/C3c	Positive around hair follicle germinal bulbs, and around blood vessels in the dermis.
IgD-FITC, Goat anti-human, Southern Biotechnology.	Positive on hair follicle germinal bulbs, with focal additional staining in the epidermis. Positive at bases of hair follicle germinal bulbs.	Complement/C1q	Positive around hair follicle germinal bulbs, and around several dermal blood vessels (especially those in proximity to hair follicular units). Positive also on remnants of sebaceous glands.
Kappa light Chains-FITC, Dako.	Focal positivity in the hair follicles.	IgD	Positive in remnants of hair follicular units.
Lambda light Chains-FITC, Dako.	Pericytoplasmic staining in keratinocytes of the epidermis. Also positive in hair follicle germinal bulbs.	IgM	Positive on hair follicle germinal bulbs, and around dermal blood vessels.

Table I. Summary of DIF and IHC staining (continuation).

Discussion

In clinical practice, often one type of alopecia seems to share selected clinical features with others. Examples include lupus erythematosus (LE) and lichen planus (LP) that may present with an overlap syndrome. Other examples that have been described of possible nosologic overlap include fibrosing alopecia in patterned distributions, and/or Graham-Little syndrome. AA does not classically present with scarring, nor has a definitive DIF pattern been clearly identified for this disease. We present a patient with clinical and immunologic features that resembles an overlap between AA and central centrifugal cicatricial alopecia (CCCA). Moreover, our combined histopathologic and immunologic results did not match any previously described alopecia. Our case demonstrates a scarring alopecia (with positive Alcian blue mucin deposition) and the additional presence of IHC CD4, CD8, CD45 and CD99 cell staining in lesional areas. We also observed the presence of multiple immunoglobulins in these areas, including a very strong response with IgD that seemed to amplify the immune response of the other immunoglobulins and complement. Thus, we document a unique combination of immunoreactants that are not routinely evaluated in routine dermatopathology and dermatoimmunology laboratories. Our results demonstrate a complex pattern of reactivity; some immunoreactivity was noted within follicular germinal bulbs and follicular unit remnants, especially with anti-IgG, IgM, IgD, complement/C1q, C3c, C4 and fibrinogen.

We also noticed many micelle-like, immunologically reactive structures that were likely formed by the destruction of sebaceous glands and associated mixing of hydrophilic and hydrophobic tissue components. Previous authors have demonstrated similar findings to these in AA [8-10]. According to some researchers, follicular dropout may occur in nonscarring alopecias, leading to a biphasic histologic pattern. The biphasic pattern has been documented in AA, androgenetic alopecia and traction alopecia, and may be pertinent in our case [8-10]. Our DIF and IHC studies also suggest that an antibody and complement-mediated immune response was part of the disease pathogenesis in this patient, along with a T cell response. Overall, we suggest that our case is best categorized as an overlap syndrome. Specifically, our case demonstrates amalgamated pathologic features of non-scarring and scarring alopecias. Consistent with these findings, the patient improved clinically after the application of intralesional corticosteroids. In summary, we describe a case of clinical and histologic CCCA, with additional immunologic features of an AA immune response mediated by antibodies, complement, T cells and selected proteases. The significance of our findings remains unknown, and warrants further investigation.

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THE DANCER HEEL AND THE ALPINIST HEEL (BLACK HEEL). CASE REPORTS

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Abstract
„Black heel" (calcaneal petechiae) is a lesion affecting the back or posterolateral aspect of the heel. The cause is assumed to be trauma. The patients does not remember when the lesions occurred.
We describe two patients with classical case of black heel (talon noir) (BH).
One man were alpinist and second were dancer. The patients does not remember when the lesions occurred and they noticed it accidentally.
Black heels, characterized by speckled bluish-black areas of macular pigmentation occurring at the border of the heel, have been observed in two young male.

Key words: black heel; talon noir; pigmentation; foot

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Introduction

Black heel (BH) first described by Crissey and Peachey in 1961 (in a group of basketball players) under the name „calcaneal petechiae" has since been called „black heel," „plantar chromhidrosis," and „plantar pseudochromhidrosis." The lesion consists of a number of pinpoint- to millimeter-size dark-red to black dots lying deep in the skin. It is asymptomatic and is usually found on the medial or lateral surfaces of the heel, though lesions on the hands (tache noir) (TN) have been reported. TN has been described on the thenar eminence in weightlifters, gymnasts, golfers, tennis players, and mountain climbers [1,2].
Small linear areas of speckled bluish-black pigmentation appearing at the periphery of the heel slightly above the hyperkeratotic edge of the plantar surface. This condition occurs predominantly in young people [2]. The pigmentation is due to small lakes of intrakeratinous hemorrhage and may clinically resemble a plantar wart or may be mistaken for a malignant melanoma [3]. In the following report two cases of black heel are described.

Case Reports

Case 1

A 16-year-old boy, a dancer, was seen because of an asymptomatic area of pigmentation on his right and left heels of months' duration. On physical examination an area of speckled macular bluish-black pigmentation was seen at the outer border of the right and left heels slightly above the hyperkeratotic edge of the plantar surface (Fig. 1). There was no elevation or thickening in the area.

Case 2

A 28-year-old man, an alpinist, had noticed two spots of pigmentation on his heels one month earlier. The lesions were asymptomatic. On physical examination, he had spots of speckled, macular bluishblack pigmentation, one on the outer surface of his right heel and the other one on the inner surface of his left heel (Fig. 2). There was no elevation or thickening in the area.

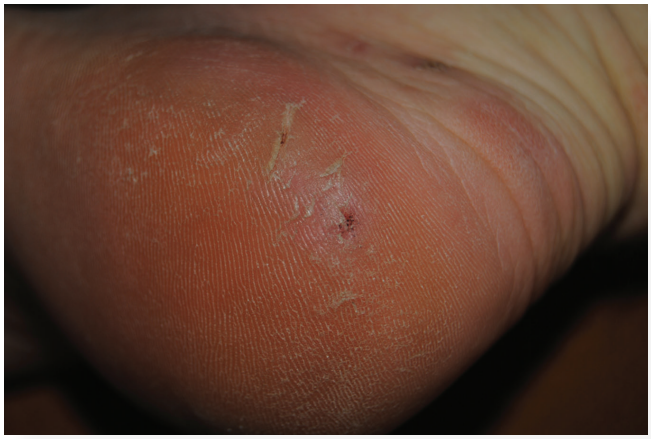

Figure 1. Black heel on the left heel in a 16-year-old boy.

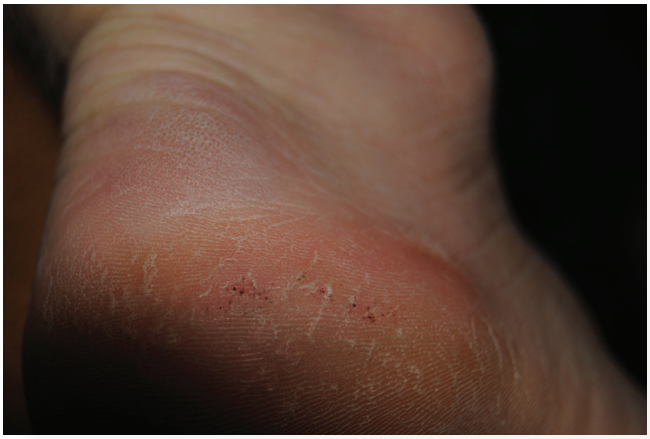

Figure 2. Black heel on the right heel in a 28-year-old man.

Discussion

”Black heel” (calcaneal petechiae) is a lesion affecting the back or posterolateral aspect of the heel. The cause is assumed to be trauma. The patients does not remember when the lesions occurred. It is seen almost exclusively in adolescentes or young adults engaged in active sports: football or tennis (tennis heel) and (as in our patients) mountaineering, dancer.

„Black heel” is probably more common than is realized. It is likely to be cuased by a shearing or pinching stress from abrupt contact of the foot with a floor or hard ground. As it is usually symptomless, it may be disregarded or only observed by chance [1,2].

Black heel (calcaneal petechiae) is caused by a repeated lateral shearing force of the epidermis sliding over the rete pegs of the papillary dermis. This damages the delicate papillary dermal capillaries, resulting in intraepidermal hemorrhage [3].

The exact incidence of black heel (calcaneal petechiae) is unknown. One study involving soldiers showing BH an incidence of 0,09% [4].

The diagnosis of atypical melanocytic hyperplasia should be considered in the differential diagnosis of the black heel.

In the uncertain lesions, to rule out melanoma in such clinical situations, a biopsy is needed to reveal homogeneous eosinophilic masses deposited under the nail plate or within it (transepidermal elimination) [2].

The diagnosis of black heel (calcaneal petechiae) is clinical and can be aided by paring down the lesion with a surgical blade. Melanocytic lesions will not lose their pigmentation with paring, while black heel may clear completely after the stratum corneum is removed.

Treatment is not necessary for black heel (calcaneal petechiae) because the lesion resolves spontaneously with discontinuation of the causative activity.

Skin lubrication, heel cups, a change of footwear, wearing 2 pairs of thick socks, and a break from training may reduce the incidence of black heel (calcaneal petechiae).

Sports participation can be continued without harm to the patient, although the black heel (calcaneal petechiae) will persist unless padding is added to the heel of the athletic shoe [5-7].

Complete clearing is achieved with cessation of the causative activity usually within 2-3 weeks of rest.

Conclusion

Black heels, characterized by speckled bluish-black areas of macular pigmentation occurring at the border of the heel, have been observed in two young male.

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BULLOSIS DIABETICORUM INVOLVING AN UNUSUAL SITE-A DIAGNOSTIC DILEMMA; MANAGED SUCCESSFULLY WITH ANTIDIABETIC DRUGS: A CASE REPORT

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Abstract
A case of Bullosis diabeticorum (BD) affecting unusual sites involving anterior abdominal wall and axilla in a female with newly diagnosed type 2 diabetes mellitus (T2DM) without antecedent trauma and drug intake is being reported for its rarity. Dermatologists must be made aware of this under diagnosed possibility in diabetes whose status is unknown after considering direct immunoflurescence studies to exclude other similar histological and immunological entities.

Key words: Bullosis diabeticorum (BD); type 2 diabetes mellitus (T2DM); Oral hypoglycemic drugs

Cite this article:
Tilak Raj R, Kumar H, Pal Singh S. Bullosis Diabeticorum involving an unusual site-A diagnostic dilemma; managed successfully with antidiabetic drugs: A case report. Our Dermatol Online. 2014; 5(3): 294-296

What is known?
· Occurrence in long standing cases of diabetes as a complication
· Etiology is not well defined.
· Tense clear blisters on normal skin
· Treatment is conservative

Introduction

Bullosis diabeticorum (BD) is a rare, blistering condition of unknown etiology, being unique to long standing cases of diabetes [1]. Its yearly reported incidence is 0.16% in a tertiary diabetes care institute with a male preponderance ratio of 2:1 as compared to female [2]. The hall mark of the diagnosis is by exclusion of other similar entities by clinico-pathological correlation and after ruling out immunological components [3]. Although lack of control of diabetes is a predisposing factor in its causation yet glycemic control does not appear to have a direct correlation with bullae formation [1]. However, we report a rare case of BD with atypical presentation of nonacral haemmorrhagic bullae on anterior abdominal wall and axilla in a female with newly diagnosed T_2DM that responded to the glycaemic control with antidiabetic drugs.

Case Report

A 50 years old housewife reported in outdoor patient unit of Department of Dermatology, Veneralogy and Leprosy of Government Medical College and Rajindra Hospital, Patiala with complaints of multiple, painless, large, haemorraghic blisters of 3 weeks duration developing overnight , involving the anterior abdominal wall and right axilla (Figs. 1, 2) without antecedent trauma, diabetes, photosensitivity or drugs intake. There was neither any medical illness nor family or personal history suggestive of autoimmune and allergic diseases. Cutaneous examination revealed multiple, discrete, large, semiflaccid and nontender bullae, of varying sizes measuring 5cm^2 to 10cm^2 in diameter containing haemoserous fluid. They had asymmetrical distribution along with collapsed blister roof. Some lesions were having red erythematous surface with central and peripheral haemorraghic crusting.

Nikolskys sign was negative and remaining skin was normal, with no involvement of any of the mucous membrane. There was nothing suggestive of neuropathy or symptoms of intermittent claudication. Physical, neurological and mental status examination were normal. The patient was investigated and all other laboratory tests were normal except fasting blood sugar levels which was 320 mg/dl; urine sugar was 4+ with traces of albumin. No ketone bodies were found, HbA1c was 10.8% and had a normal anion gap. Urine for uroporphyrins, smears and cultures for bacteria, fungus were negative. A 4mm incisional skin biopsy of the lesion showed stratified squamous epithelium lining exhibiting hyperplasia, hyperkeratosis and thinning at places of epidermis. Evidence of subcorneal bullae showing many acantholytic cells along with infiltrate consisting predominantly of polymorpho-neutrophils (Figs. 5, 6). Dermis showed collegenized odematous stroma along with skin appendanges. Immunofluroscence and ANA titre studies were negative excluding immunobullous and autoimmune diseases. On the basis of histopathology, immuno-fluroscenece and diabetic status; the patient was diagnosed as a case of Bullosis diabeticorum. The patient was treated with a combination of oral metformin 500mg with glipizide 5mg per day. Patient recovered uneventfully in two weeks with residual dyspigmentation (Figs. 3, 4) but without any scarring and her fasting glucose levels were 110 mg/dl at the time of discharge. The follow-up of patient for 6 months did not show any recurrence of BD, while HbA1c (6.0%) and other routine tests were in normal range.

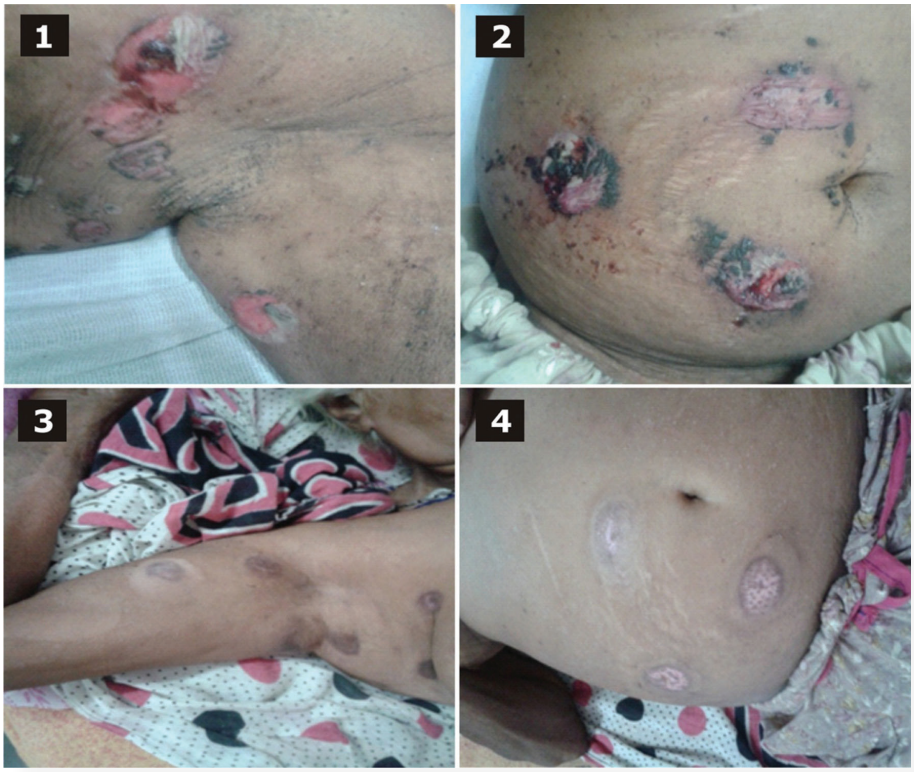

Figure 1 - 4. 1. Multiple, large, collapsed, blister roof over erythematous base at baseline (Day 1); **2.** Multiple, large, collapsed, blister showing haemorrhagic crusting; **3.** Lesions in healing phase after two weeks of oral hypoglycemic treatment; **4.** Lesions in healing phase after six months of follow-up.

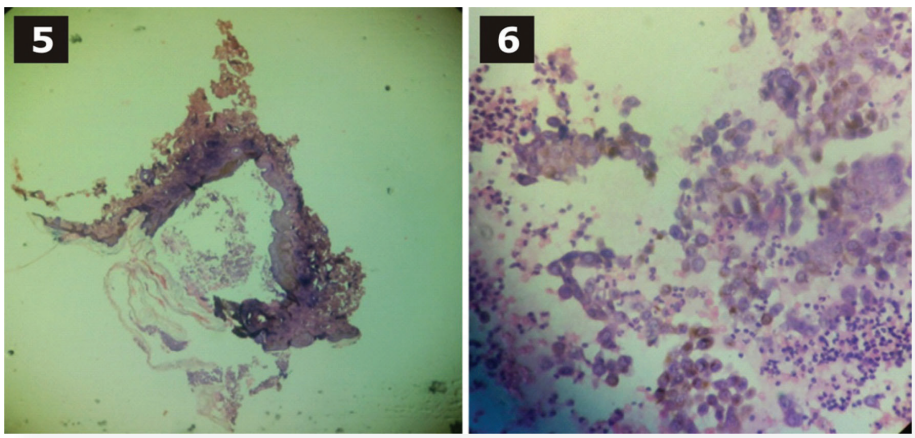

Figure 5 and 6. 5. Histopathology of Bullosis diabeticorum showing subcorneal and focally intraepidermal split (Hematoxylin and eosin stain, X100); **6.** Higher power view of subcorneal bullae showing many acantholytic cells along with infiltrate consisting predominantly of polymorpho-neutrophils (Hematoxylin and eosin stain, X 400).

Discussion

Bullosis diabeticorum (BD) is a rare dermatosis occurring in 0.5% of diabetic patients with 112 cases described in literature [4,5]. It commonly occurs in long standing type 1 diabetes mellitus [T_1DM] with vascular or neurological complications but it may also occur in T2DM [1,4,6]. The common findings of these blisters are that they vary in size from a few milimeter (0.5cm) to several centimeters (10cm), tense, nontender, arising on normal skin, containing clear fluid, involving the acral and distal extremities.They resolve within 2-5 weeks without scarring and most of the cases have recurrences [1,5,6]. Though feet and distal extremites are often effected, blisters can occur rarely on trunk [3,6,7]. In this case, there was non acral presentation which was rare. However, various hypotheses have been proposed regarding the production of bullae i.e., lower threshold for suction that induced blister formation, trauma, ultra violet exposure, nephropathy, alterations in carbohydrate metabolism, immunoglobin mediated vasculitis and ischeamic cationic imbalance due to diabetic nephropathy [1,8]. Larsen et al [1] suggested that poor regulation of blood glucose to be an important factor and Wilson et al [10] confirmed development of new bullae in patients with hyperglycemia when their blood glucose levels varied between 79 mg/dl-340 mg/dl suggesting a correlation between hyperglycemia and bullae formation. Histopathologically, hemorrhagic bullae have the cleavage plane below the derma- epidermal junction and they heal with scarring, atrophy and with destruction of anchoring fibrils [1]. In this case, blisters were multiple, large, semi-flaccid, haemorrhagic, subcorneal bullae with many acantholytic and polymorphic neutrophilic cells that were at variance with cases described earlier in literature i.e., it involved nonacral sites, in a prediabetic female diagnosed as T_2DM without any features of dermatopathy, neuropathy or nephropathy and with a histopathology of acantholytic cell. The Immunofluroscence and anti–nuclear antibody (ANA) titre studies were negative excluding immunobullous and autoimmune diseases. The response to oral hypoglycaemic drugs within two weeks, with dyspigmentation and without having any recurrence or scarring during the six months follow-up suggests the diagnosis of BD, which is a diagnosis of exclusion. It may have occurred spontaneously or as a result of complication of diabetes posing a diagnostic dilemma and needs further research to establish causal relation with diabetes.

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What is new?

- The truncal involvement is a rare presentation of this disease occurring in a newly diagnosed female of T2DM
- No neuropathic, nephropathic, dermatopathic features.
- Haemorrhagic Bullae with acantholytic cell on histopathology.
- Response to antidiabetic drugs.

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NEONATAL OCCIPITAL ALOPECIA IN A NEWBORN

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A newborn, male gender, born at term, APGAR 10, was addressed to us for occipital alopecia observed since birth (Fig. 1). Mother was a young health person of 25 years old, primipara and the birth was non-Caesarian delivery. Alopecia was confirmed in the occipital area, with no signs of inflammation or other dermatological problems on the whole body. A diagnosis of frictional/pressure occipital alopecia was admitted and the family was reassured of the absence of any inquiry. No follow-up was recommended.
Since the alopecia was confirmed during the first days of life of the infant the problem of friction/pressure during sleep was questioned.

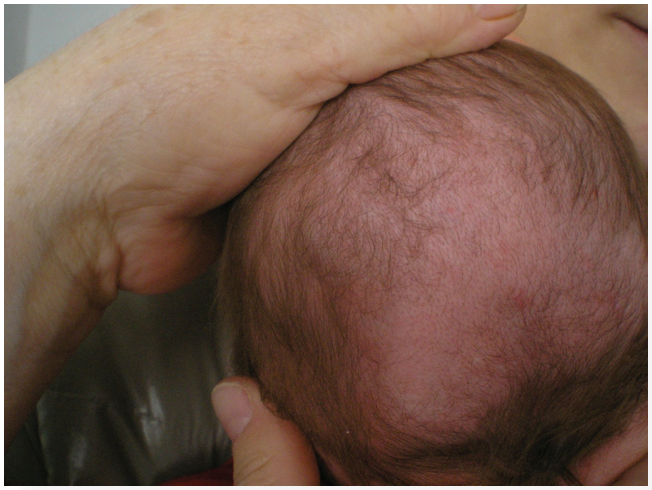

Figure 1. Neonatal occipital alopecia in a newborn.

Looking through the literature: neonatal occipital alopecia was first described by Brocq long time before in 1907 [1]; since then, reports have been published and data showed a prevalence of 9-12 % [2], especially in Caucasian children [3].
It is a non-scarring alopecia, localized-type, described mostly in infants of 2-3 months old [3].
The cause of this type of alopecia remains a subject of debate: induced by pressure/friction during sleeping [4], being an acquired form of alopecia or a physiologic process of hair shedding started during gestation [5]. The present case of neonatal occipital alopecia diagnosed in the first day of life support the second opinion of a physiologic process started in utero. Further opinions and studies are necessary to clarify the question.

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TRANSIENT CUTANEOUS HYPERPIGMENTATION OF EXTREMITIES FOLLOWING DENGUE FEVER

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A 14 year old boy presented with fever and generalized flushing of skin of 1 week duration. His vital signs were normal. Examination revealed generalized blanching macular erythematous rash. Systemic examination was unremarkable except for tender hepatomegaly. Investigations revealed leucopenia, thrombocytopenia and normal hemoglobin with mildly elevated liver transaminases. NS 1 (Non-structural protein-1) antigen and IgM antibody titer for Dengue ELISA was positive suggesting dengue fever. He was managed symptomatically and he recovered. During his follow up after 2 weeks he presented with brownish discoloration of dorsum of both hands and feet. There was no history of intake of any medication. Examination revealed symmetrical striking macular hyperpigmentation involving dorsum of extremities predominantly over the distal interphalangeal joints (Figs. 1, 2). His general physical and systemic examination was normal. His repeat blood counts, renal function tests, liver function tests and serum cortisol levels were normal. Vitamin B12 levels were normal and IgM antibody titre for chikungunya was negative. Workup for HIV and porphyria was negative. Parents were reassured and gradual disappearance of lesions was noticed over next 8 weeks.

Cutaneous hyperpigmentation is known to be associated with a variety of systemic disorders which include endocrinapathies such as Addison's disease, Nelson syndrome, metabolic diseases such as Wilson's disease, Fanconi 's anemia, hemochromatosis and nutritional deficiencies mainly vitamin B12 [1]. Many drugs have been implicated in causing skin pigmentation including non-steroidal anti-inflammatory drugs, antimalarials, amiodarone, cytotoxic drugs, and heavy metals [2]. Viral exanthematous illnesses are also known to cause hyperpigmented lesions, where etiology appears to be post inflammatory. Both diffuse and focal hyperpigmentation predominantly involving centrofacial area has been described in patients with chikungunya fever during the recovery phase [3].

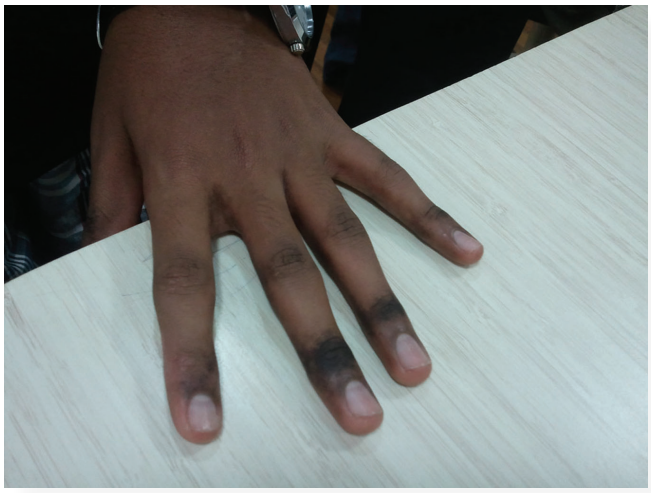

Figure 1. Macular hypermelanosis over dorsum of hand predominantly involving distal interphalangeal joints.

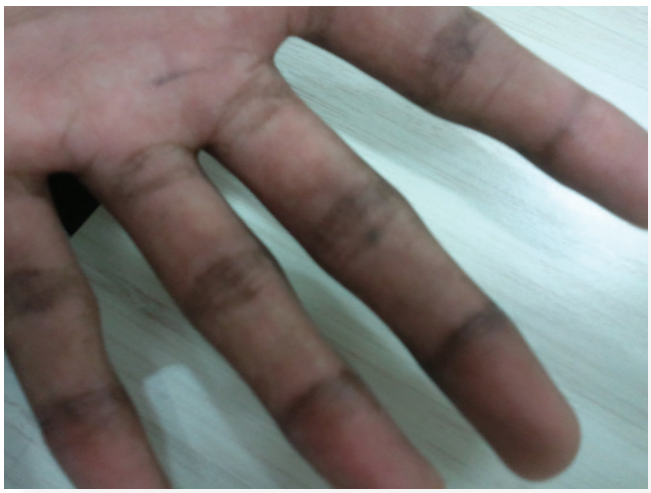

Figure 1. Macular hypermelanosis also involving the palmar aspect of the hand.

Cutaneous pigmentation is also reported in patients with HIV (Human Immuno Deficiency) especially on zidovudine therapy [4,5]. However hypermelanosis associated with dengue fever is very rare. Common cutaneous lesions described in association with dengue fever include a transient generalized macular erythematous rash which blanches upon pressure during the initial phase of illness followed by a generalized confluent petechial rash with sparing of small islands of skin during the convalescent phase [6,7]. Thus occurrence of hyperpigmentation following dengue fever is an extremely rare phenomenon and to the best of our knowledge no such case till now has been reported.

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NEVUS COMEDONICUS

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A 51 years old woman was reffered to our dermatology clinic with one year history of numerous skin coloured papuels which gradually worsened with time.phiysical examination revealed that the papules were follicular with 1-2 mm diameter.some papules had dark black keratinous material on their surface, giving them a comedo like appearance (Fig. 1). The lesion were located in right lower quadrant of abdomen. The patients didn't complain of any symptoms just pruritus before appearance of lesions.we performed elyptical biopsy of the lesions. Histopathologic examination revealed dilated cystic structures filled with lamellar keratin,in accordance with the feature of nevus comedonicus (Fig. 2). The prevalence of nevus comedonicus has been estimated from 1 in 45,000 to 1 in 100,000, with no gender or racial preference. In 50% of patients, the condition develops shortly after birth and in the majority of patients lesions appear before the age of 10. Single cases of delayed development of nevus comedonicus at later age have been reporte [1]. Asymptomatic lesions may be left untreated or therapy may be implemented for cosmetic concerns. Reported treatments include surgical excision, CO2 laser, dermabrasion, extraction, topical retinoic acid, topical tazarotene and calcipotriene and numerous topical keratolytics [2]. In this case,we lost her for follow up.

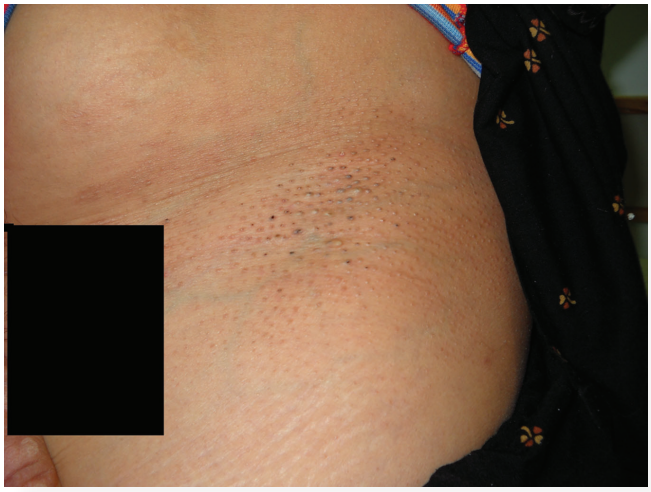

Figure 1. Closely arranged slightly elevated papules that have at their center keratinous plugs resembling comedones.

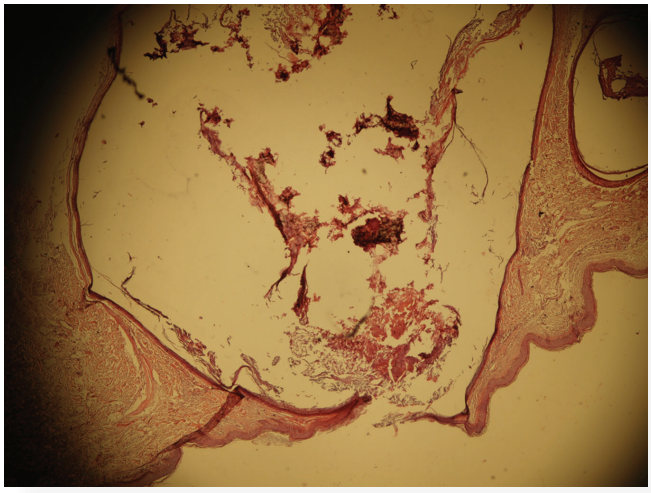

Figure 2. Dilated cystic structures filied with lamellar keratin.

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IS BEAUTY SKIN DEEP – AN APPROACH TO A BEAUTIFUL FACE

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Everyone dreams of a beautiful and flawless face but true beauty is God given gift. Plastic surgery and various filler techniques can just highlight certain features and are just the temporary procedures. Features that further enhance the attractiveness of a beautiful face are the hair, skin, and teeth. These areas are the easiest to routinely enhance. There are many methods of facial sculpting including botulinum toxin, fillers and various other invasive plastic surgery techniques. Whatever the techniques followed by the cosmetic surgeon, certain ethical guidelines should be strictly adhered to. Loss of volume in the face can lead to deepening of the nasolabial folds. Hyaluronic fillers can be used to lift up the fold and restore a natural, youthful contour.

Introduction

The true difference in an individual's face is the positioning, volume, shape and angles of facial fat, skin, skeletal landmarks, and external features such as eyebrows, eyes, cheeks, the nose, etc [1,2]. In evaluating a beautiful face, the features that command the most attention, in order of importance, are:

- Eyes
- Brow
- Cheeks
- Lips
- Nose
- Chin and Jawline

Although covering only approximately 15% of the facial surface area, the brows, eyes and cheeks seem to command over 90% of one's attention. For an artist, this area is the most difficult to capture and recreate since these features differ subtly with each individual, thus creating a "fingerprint" of individuality [3]. These also happen to be the most difficult areas for plastic surgeons to correctly modify. So, how does one determine what the ideal facial structure is. One of the most important, instinctively perceived attributes of beauty is facial symmetry [4]. Along with averageness and youthfulness, this influences the perception of a person as physically attractive or beautiful. All of us are slightly asymmetrical (fluctuating asymmetry) in that one side of the face is slightly different than the other. If a mirror reflection of one side of the face is used to make a whole face, that face will not look like the person him/herself. So if there is an obvious asymmetry to the two halves of the face, that can be corrected to bring them closer in shape to each other.

Discussion

Plastic surgeons have long had the tools and techniques to provide patients with an attractive nose, chin and neckline [5]. The ideal female face is shaped as an inverted egg (Fig. 1) or a heart with the widest area approximately between the eyes and cheekbones. A beautiful nose represents one of the most prominent features of the face that ranges in shape, size, and angle. A beautiful nose must reflect overall harmony and proportion in relation to the other features and the face as a whole (Fig. 2). An attractive nasal contour is represented by a slightly sloped dorsum which blends into a moderate nasal frontal angle located at the supra-pupillary line. The beautiful cheek is one of the most important and attractive facial features. For centuries, this beautiful eminence has been highlighted with make-up and festive painting. The beautiful cheek should be well defined, full, and ovoid, like a definite highlighted "egg". The peak of the highlighted cheekbone, or malar eminence, should be high and full. The full egg volume should be sitting at an angled position, marked from the upper lip to the upper ear with its pointed end toward the ear. The egg apex should lie on the vertical line splitting the lateral canthus and brow, and the horizontal line, from the division of the middle and lower thirds of the nose to the superior auricular tragus or cartilage bump in front of the ear. The fullest portion of the cheek should be centered high over the cheekbone and not down towards the nasolabial fold, as what occurs with aging.

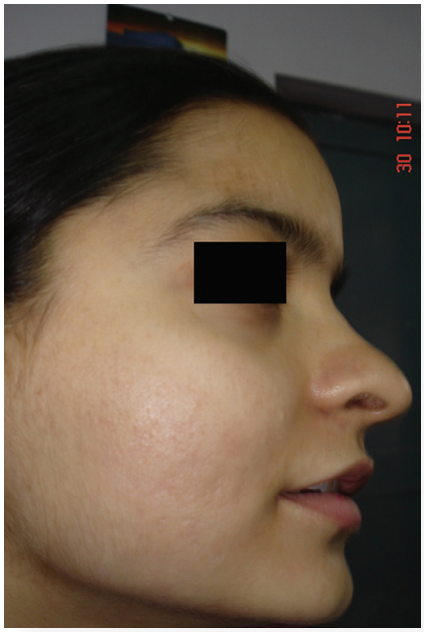

Figure 1. Oval shaped face of a 23 years old female.

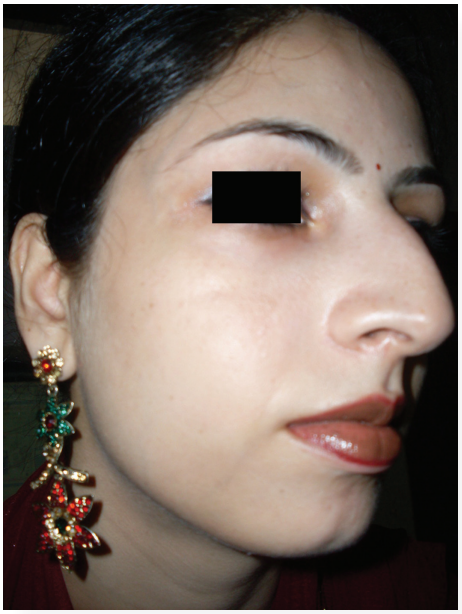

Figure 2. Nose in harmony with other features in a 19 years old girl.

The appearance of the nasolabial fold should be minimal, and the jowl area should be flat or slightly concave. A prominent nasolabial fold occurs due to genetics, aging, the loss of fat and bone volume, or the slipping of the fat pad and skin down against the contracted nasolabial fold. This creates the aged and unattractive cheek folds and jowls.

The lower eyelid should be shaped like a tapered scroll, much like the subtle edge of an English rosebud. The lower lid positioning should be at the level of the iris or slightly below. It should have a slight concavity, but blend smoothly with the cheekbone. The lid margin curves are slightly asymmetric, with slight medial elevation on the upper lid and light depression on the lower lid. The eyelashes, arched and somewhat "full", should be longer and thicker on the upper lid and begin more medially than on the lower lid. A white sclera, with a distinctive color to the iris, is most attractive; hence the popularity of colored contact lenses.

It is possible to change one's facial structure. How difficult or easy it is to do depends on what you want changed. For example, longer, thinner faces can be made fuller with dermal fillers, fat augmentation or implants [6]. Fuller, more round faces are more difficult to change to a thinner, longer one without plastic surgery.

It is absolutely essential that whatever cosmetic procedure you decide on, you choose a board-certified physician in the core cosmetic surgery specialties, like dermatology, plastic surgery or facial plastic surgery, with proper training and experience in that particular procedure. Ask for recommendations, consult with several specialists, make sure you learn as much as you can about the procedure before and after the consultation, look at before and after photos and talk to your doctor about recovery times, risks and possible complications. Of course, in the ideal world, the physicians are ethical, fully trained and are doing what is best for the patient. And in the great majority of cases that is true. However, sometimes that is not the case, and choosing the wrong person to perform the procedure can have tragic consequences.

Non-surgical treatments to rejuvenate and beautify the face and body have come a long way in the last decade, making it possible for patients to achieve a more youthful and attractive appearance with simple walk in procedures and no downtime. Botulinum toxin is a purified protein that is used to eliminate the frown lines between the brows, flatten deep forehead wrinkles, and soften the 'crow's feet' wrinkles next to the eyes. It blocks nerve transmission to the muscles that cause wrinkles of the face [7,8]. After treatment, the muscles relax, and the overlying skin becomes smooth and unwrinkled. Botulinum toxin can be used to decrease the size of hypertrophied or thickened masseter muscles to slim the lower third of the face [9].

More recently a new generation of cosmetic products called dermal fillers have come onto the market that are especially effective in restoring the volume of the face and have rendered many minor plastic surgery procedures unnecessary [10,11]. As we age, we start losing our youthful facial volume, which contributes to the formation of folds and wrinkles. Dermal fillers contain hyaluronic acid, which is a natural substance that binds tightly to water [12,13]. These fillers replace lost volume and restore youthful contours to the skin by smoothing facial wrinkles and folds. They can also help change the shape of the nose or add structure to the jawline or a small/receding chin. The fillers provide natural, immediate results. Common areas include the nasolabial folds (the creases that run from the bottom of your nose to the corners of your mouth), the tear tough (dark shadows under the eyes), and the marionette lines. Full, plump lips are considered feminine and sexy. The 'ideal' lips, according to a survey of Australian women are full, natural-looking and well-defined, with a strong Cupid's bow (the v-shaped area of the upper lip).

Facial implants, a more permanent solution, can be used to do the same for the cheekbones, although if a person loses weight drastically, these implants may become visible.

Facial plastic surgery to change the shape of the nose and chin is also an option. More invasive plastic surgery can be done to shape the bony structure of the face, either increasing (adding implants or bone grafts) or decreasing (shaving down) the size and proportions of cheekbones, chin, etc.

Platelet rich plasma is also used for facial rejuvenation. Also known as "The Vampire Treatment", the use of Platelet Rich Plasma (PRP) is not new [14]. It has long been recognized for its accelerated wound healing properties in such applications as surgery and sports injuries. This technology is now being used for cosmetic enhancement with outstanding results. A small collection of blood (20ml) is taken and processed to give us the PRP required for your treatment. Placing your blood in a centrifuge for 8 minutes separating the plasma and platelets from your red blood cells does this. The concentrated source of autologous platelets within the plasma contains numerous growth factors that stimulate tissue regeneration and remodeling. After application of a topical anaesthetic, the PRP is then injected into your skin, much like having other cosmetic injections [15]. The entire process takes about an hour. Results take around 2-3 weeks to see and a series of up to 3 treatments is recommended 4 weeks apart.

Conclusion

The most important judge of facial attribute is you and your sense of what is attractive. Society's ideas of what is beautiful change [16]. It was not so long ago that women used to remove their lower ribs to make their waists smaller. In my opinion, that's pretty drastic. In addition to that, standards of beauty and attractiveness vary by geography and ethnicity as well. There is no true ideal face. With so many choices of fillers and toxins available, choosing the one that will produce best results is a difficult question to be answered. Answering this question is the key to achieving a result that pleases both the physician and patient. With so many inexperienced injectors currently treating patients, many of them have only been trained to use one or two different filling agents. This usually leads to many dissatisfied patients, as many of the agents are best suited to certain areas of the face. Clinicians are beginning to understand that the ultimate goal of nonsurgical cosmetic dermatology procedures is patient satisfaction, which generally can be defined as the delivery of a natural, relaxed look for most patients.

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NASZA DERMATOLOGIA Online
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LOW-DOSE CICLOSPORIN THERAPY OF ERYTHRODERMIC PSORIASIS

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Introduction

Psoriasis is a chronic, recurrent inflammatory skin disease which affects around 2% of the population and is characterized by erythematous and scaly macules and papules of greatly varying degree of involvement.
Ciclosporin (Cs) is a therapeutic agent rarely used in the treatment of erythrodermic psoriasis as a monotherapy [1].

Case Report

We present a 42-year-old male affected with biopsy-proven vulgar psoriasis admitted to our Department for the appearance of an erythrodermic psoriasis (Fig. 1A). Before admission to the hospital patient suffered from relapsing episodes of diffuse psoriasis, since the age of 19, which responded well to topical emollients and UVB therapy. 5 years ago has suffered from hepatitis C. The laboratory tests did not revealed any abnormalities related to renal and hepatic function. The patient was treated with ciclosporin 2.5 mg/kg per day, doxycycline (2 x 100mg per day) and hydroxyzine tablets for symptomatic relief. The clinical response was not immediate, although at the begining of the third week of the therapy a marked reduction of erythema and scaling was evident. Since week 4 of the treatment, ciclosporin was gradually reduced (0.5 mg/kg per day). Presently patient receives 1.17 mg/kg per day and is under a complete remission (Fig. 1B).

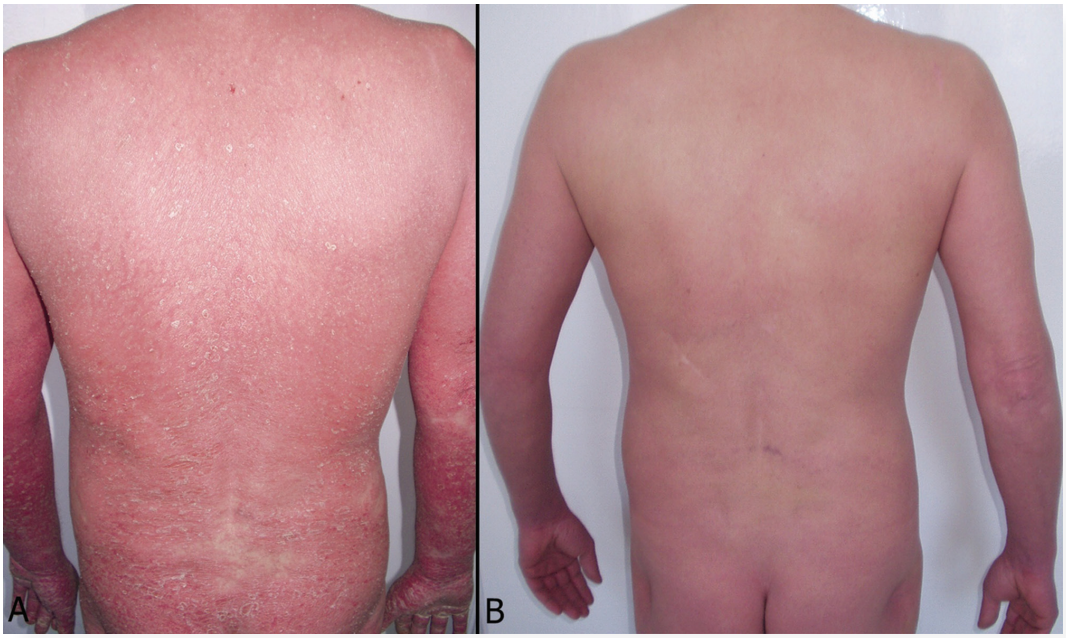

Figure 1. Clinical course of a 42-year-old male with erythrodermic psoriasis before (A) and after 2 month ciclosporin 2.5 – 1.17 mg/kg daily administration. The degree of improvement in PASI scores 85.3 % (B).

Discussion

Because of hepatitis C in the past, we have consciously disqualified treatment with methotrexate, acitretin or with combined therapy, although combined therapy is often used in psoriasis to increase clinical efficacy and to reduce side effects [2]. This case is noteworthy because we have observed clinical improvement at low doses of Cs alone. The degree of improvement in PASI scores was 85.3 % achieved comparatively late, which obtain with relatively low dose of Cs [3]. This case is negatory to papers reporting, that starting with dosages lower than 3.0 mg/kg daily may lead to insuficient efficacy [4] and strengthens reports suggesting minimising potentially harmful side-effects by treatment with initial daily oral dose of 2.5 – 5.0 mg/kg daily, which may be modulated only in a case of insufficient efficacy [5-7].

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NASZA DERMATOLOGIA Online
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HERPES ZOSTER DUPLEX SYMMETRICUS IN AN IMMUNOCOMPETENT 70-YEAR FEMALE

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Introduction

Herpes zoster is a neuroectodermal viral infection which afflicts one or more closely grouped, spinal or cranial nerves, resulting in unilateral radicular pain and vesicular eruption limited to a dermatome innervated by that nerve [1]. Bilateral involvement is rare, bilaterally symmetrical involvement is extremely rare. We hereby report a case of bilaterally symmetrical herpes zoster in an old immunocompetent female.

Case Report

A 70 year old, apparently healthy diabetic female presented with a four day history of multiple vesicular lesions with burning pain over upper back and both upper limbs in a zosteriform pattern. On examination there were grouped vesicles distributed in a dermatomal fashion over the C8, T1, T2 region (Figs. 1 - 3). A clinical diagnosis of bilaterally symmetrical herpes zoster was made. Tzanck smear showed multinucleated giant cells. Routine investigations were within normal limits. Gynaecological examination, chest X-Ray, USG abdomen and pelvis was normal. Serological tests for HIV, Hepatitis B and C were negative. Oral valacyclovir 1g thrice a day, anti-inflammatory drugs were given initially for 7 days followed by 10 days. The lesions remained confined within the original dermatome affected and healed completely within two weeks, with minimal scarring.

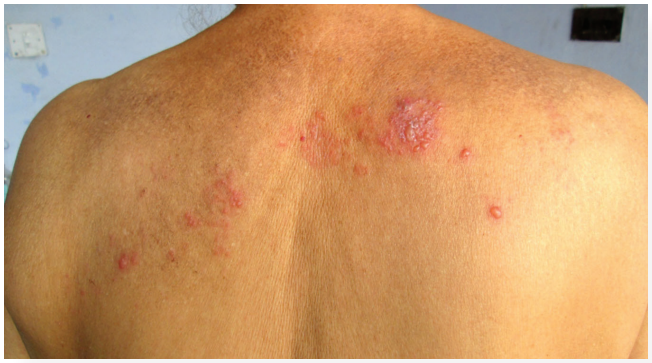

Figure 1. Multiple grouped vesicular lesions in T1, T2 dermatomes.

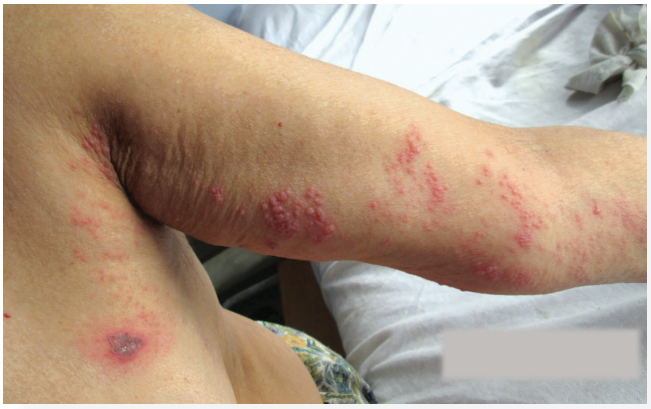

Figure 2. Multiple grouped vesicular lesions in C8, T1 dermatomes of left upper limb.

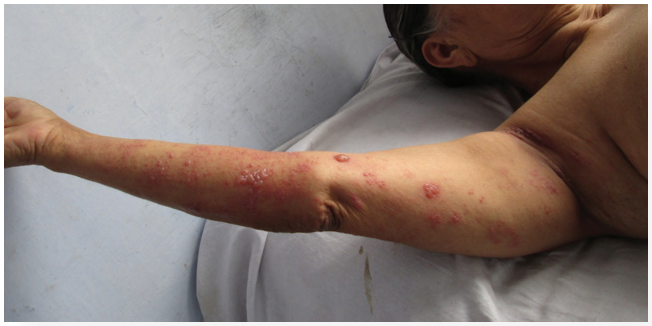

Figure 3. Multiple grouped vesicular lesions in C8, T1 dermatomes of right upper limb.

Discussion

VZV remains dormant in peripheral sensory ganglia following varicella infection but mechanism of reactivation remains elucidated [2]. Cellular immunity plays a key role in localizing the primary varicella infection as well as preventing the reactivation of latent VZV [3]. Blocking of cell mediated defenses by rising levels of specific antibodies after exposure to exogenous varicella zoster virus or by some other mechanism may be a possibility [4].

Herpes zoster is determined by factors that influence host-virus relationship that include old age, immunosuppressive disease or drug therapy, physical trauma in the affected dermatome, local therapeutic X -Ray irradiation, female sex, black race [5].

After prodromal symptoms cutaneous eruption consists of closely grouped red papules, rapidly becoming vesicular and then pustular. They may develop in a continuous or interrupted band in the area of one, occasionally two, or rarely more contiguous dermatomes. Mucous membranes within the affected dermatomes may also be involved. The most distinctive feature of herpes zoster is the localization and distribution of the rash, which is nearly always unilateral [2].

In order of frequency, the dermatomes involved are thoracic (53%), cervical (usually C2 C3; 4-20%), trigeminal, including ophthalmic (15%) and lumbosacral (11%).4 The lesions rarely occur distal to the elbows and knees [5].

Tzanck smear made from the base of the lesion shows the presence of multinucleated giant cells and epithelial cells containing acidophilic intranuclear inclusion bodies which distinguishes the cutaneous lesions produced by VZV from all other vesicular eruptions except those produced by HSV [5,6].

Among neurological complications, Post Herpetic Neuralgia (PHN) is common, seen in 8 to 15 % in cases of herpes zoster in older age group. Risk factors for PHN are people older than 60 years of age, prodromal pain, severe pain in acute phase of herpes zoster, greater rash severity, more extensive sensory abnormalities in affected dermatome and, possibly, ophthalmic herpes zoster.

Herpes zoster may recur in the same or different dermatomes or in several contiguous or non contiguous dermatomes. Multiple recurrences of herpes zoster has been reported in HIV and immunocompromised patients [1].

Although herpes zoster is typically unilateral, there has been only few reports of multiple dermatomal involvement [2,7-9] and bilateral asymmetrical [2,9] distribution of herpes zoster lesions with incidence of approximately less than 1% [10]. This presentation has been referred to a zoster duplex unilateralis or bilateralis depending on whether one or both halves of the body is involved [1]. There have been few case reports of bilaterally symmetrical herpes zoster [7,8]. Herpes zoster is usually unilateral, multiple dermatomal involvement is rare, bilateral involvement is still rarer and bilaterally symmetrical involvement is extremely rare. Bilateral VZV reactivation in absence of systemic immunocompromised condition even makes it an even rarer. This case is being reported here because of its extremely rare bilaterally symmetrical involvement.

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VITILIGINOUS LESIONS DURING CONTACT IMMUNOTHERAPY FOR ALOPECIA IN A PATIENT WITH AUTOIMMUNE THYROIDITIS

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Sir,

Squaric acid dibutylester (SADBE) is frequently used for the treatment of alopecia, but sometimes unwanted side effects occur. Herein we report a case which developed vitiliginous lesions induced by topical SADBE application in a patient with autoimmune thyroiditis.

A 60-year-old female visited our department, complaining of diffuse alopecia of the scalp. She was suffering from chronic autoimmune thyroiditis over several years, and taking thyradin (90mg per day). After obtaining written informed consent, topical application of SADBE solution was started. Two months later, a sufficient effect was obtained for hair regrowth; however, when she was treated with 0.05% SADBE, depigmentation appeared and rapidly spread on the scalp. On physical examination, diffuse depigmentation along with gray hairs was found on the scalp, forehead, and nape (Fig. 1). Laboratory examination showed normal liver and renal function, anti-nuclear antibody (1:160, speckled), anti-thyroid antibody (1:100), anti-microsome antibody (1:6400), anti-thyroid peroxidase antibody (139.6 IU/ml, normal <16), but anti-thyroid stimulating hormone receptor antibody, free T3 and T4 levels were normal. A skin biopsy showed decrease of melanocytes and melanin deposition in the epidermis (Fig. 2A). Results of immunohistochemistry revealed a predominant CD8-positive T-cell infiltration (Fig. 2B). SADBE therapy was stopped, and betamethasone butyrate propionate and carpronium chrolide lotion were applied, which showed a dramatical effect within 9 months (Fig. 3).

Adverse effects of topical immunomodulatory therapy include local irritation, blister formation, persistent dermatitis, lymphadenopathy, generalized eczema, and urticarial reaction. Mechanism of contact immunotherapy is suggested to modulate cytokine gene expression balance, and interferon-γ expression was reduced while interleukin-2 (IL-2), IL-8, IL-10 and tumor necrosis factor-α levels were increased in the lesional skin [1]. Further, recent studies demonstrate that Th17 cells are involved in the pathogenesis of contact hypersensitivity. Skin biopsies of hypersensitivity reactions to contact sensitizers demonstrate the presence of CD8+ T-cells, Th1 CD4+ effector cells and regulatory T-cells [2]. T-cells play an important role in the pathogenesis of vitiligo, and IL-10 is supposed to play a role by inhibiting T-cells. Also, active Th17 cells are increased in vitiligo skin [3], and thus those mediators may play a role in the autoimmune mechanisms of vitiligo.

Our case developed vitiliginous lesions not only on the scalp, but the forehead and nape were also involved beyond the application areas. Three months later from the start of immunotherapy, depigmentation was suddenly induced without prior contact dermatitis, which suggests that our case was not a result of contact leucoderma.

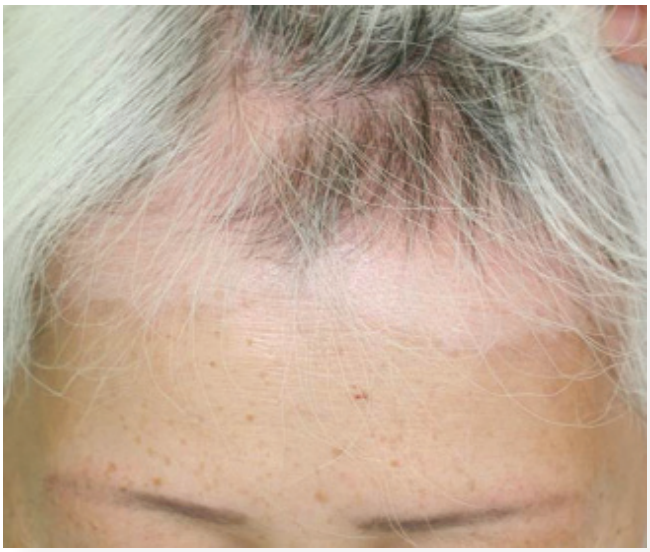

Figure 1. Depigmentation on the forehead and nape developed during contact immunotherapy with SADBE.

However, it is difficult to differentiate contact leukoderma, which arises on the site of application as a consequence of eczematous reaction, or even at the distant areas. Nine months later, depigmentation was recovered by topical corticosteroid ointment. To date, several cases of vitiligo induction during topical immunotherapy have been reported [4-8].

The mechanisms are speculated as a direct cytotoxic effect of SADBE on the melanocytes, or as a result of Köbner phenomenon. Thyroiditis is a representative disorder associated with not only alopecia but also vitiligo. In our case, autoimmune condition may be associated with the development of vitiligo, and SADBE may have a triggering role. Careful attention should be paid when we carry out contact immunotherapies for patients with autoimmune thyroiditis.

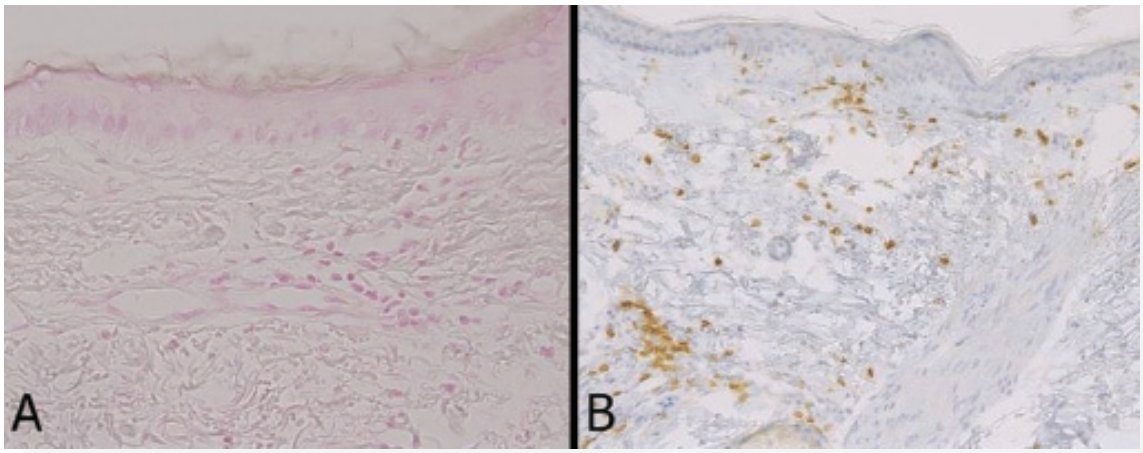

Figure 2. (a) Histology showing decrease of melanocytes in the epidermis (Fontana-Masson stain, ×200) (b) Cellular infiltrates were positive for CD8 (×100).

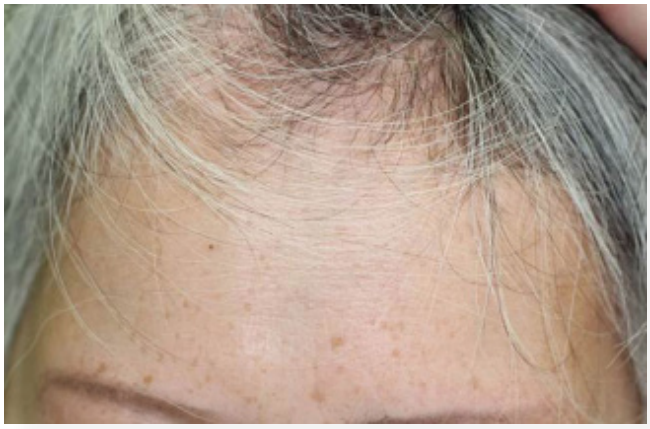

Figure 3. Depigmentation was much improved by topical steroid ointment 9 months later.

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NASZA DERMATOLOGIA Online
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BULLOUS PYODERMA GANGRENOSUM IN PATIENTS WITH ULCERATIVE COLITIS AND MULTIPLE MYELOMA

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Sir,

Bullous pyoderma gangrenosum (PG) is a rare subtype of PG, which frequently involves extremities. We herein report two cases of bullous PG in association with other systemic diseases, such as hematological malignancy and inflammatory bowel disease.

Case 1

A 52-year-old man suffered from stomachache, diarrhea, and bloody stools for some months, and was diagnosed with ulcerative colitis (UC) by colonoscopy examination. Biopsy specimens showed inflammatory cell infiltration in the mucosal epithelium. Almost simultaneously, he developed bullous lesions on the lower legs. Physical examination showed rounded, edematous bloody bullous lesions on the bilateral shin (Fig. 1). Laboratory examination showed increased levels of C-reactive protein (CRP; 3.12 mg/dl) and erythrocyte sedimentation rate (53 mm/h), and white blood cell counts (8900/mm3) with 70% neutrophils. Histological examination showed subepidermal bulla and neutrophil and mononuclear cell infiltration in the mid- to lower dermis. After admission, systemic prednisolone (30 mg/day) was administered for intestinal lesions, which also improved skin lesions.

Case 2

A 76-year-old man was suffering from multiple myeloma for 8 years. He had been treated with chemotherapies (ranimustine, vincristine, melphalan, dexamethasone), which however could not lead to remission induction. During the course, he was hospitalized and consulted to dermatology department, as for the skin lesions on his forearm. Physical examination revealed hemorrhagic bullae on the left forearm (Fig. 2). Laboratory examination showed increased levels of CRP (14.7 mg/dl). A biopsy specimen revealed prominent red blood cells, diffuse neutrophil infiltration in the entire dermis (Fig. 3). There were no atypical cells. He was initially treated with antibiotics without effects, but successfully treated with oral prednisolone (30 mg/day).

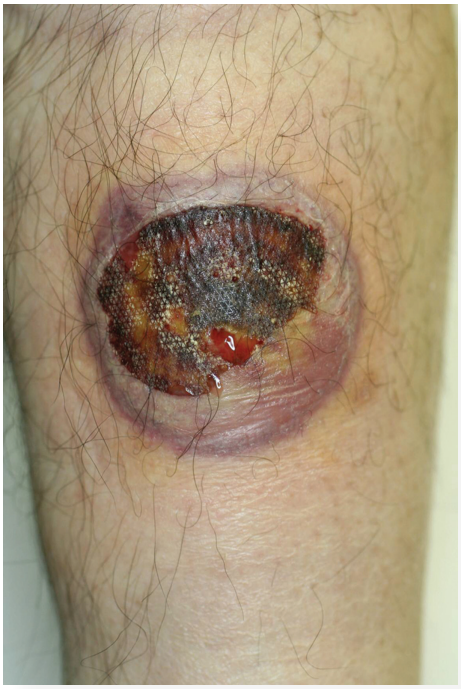

Figure 1. Hemorrhagic shallow bullae on the shin of Case 1.

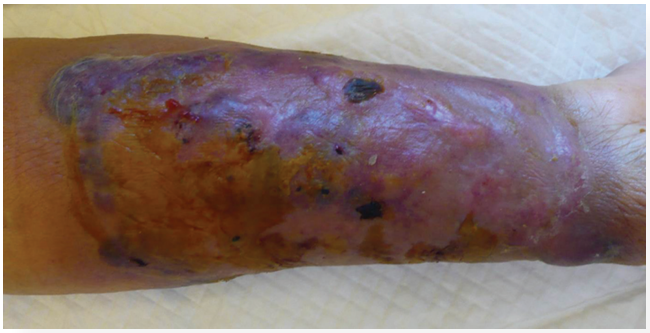

Figure 2. Bullous hemorrhagic lesions on the forearm of Case 2.

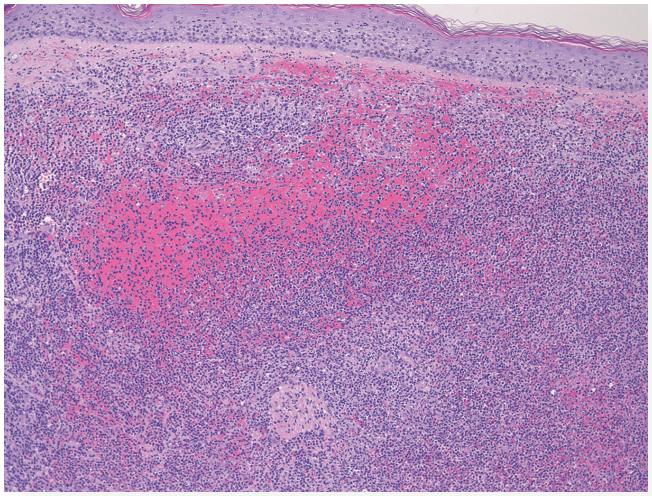

Figure 3. Skin biopsy specimen showing numerous neutrophils infiltration with a number of erythrocytes in the dermis.

PG is clinically classified into 4 types, i.e. ulcerative, bullous, pustular and vegetative type. Bullous PG is relatively rare, and to date, more than 30 cases of bullous PG have been reported [1,2]. This type is characterized by rapid development of vesicles and enlarging bullae with central necrosis and shallow erosions. Previous reports indicate that extremities are the most frequently involved, and hematological malignancies, i.e. preleukemic conditions and leukemia, are mostly associated [2]. We describe herein 2 cases of bullous PG occurred on the upper and lower extremities. Case 1 had UC, and Case 2 had multiple myeloma. In both cases, development of bullous PG was related with the activity of gastrointestinal and hematological conditions, respectively. Case 1 presented with typical clinical features of bullous PG. In Case 2, we at first suspected myeloma cells infiltration in the skin, because previous reports showed that leukemia cells recruited to the sites of leakage of a drip infusion on the forearm [3]. However, histological features denied atypical cells and demonstrated PG.

In the lesional skin of PG, not only neutrophils but also a number of CD3-positive T cells are infiltrated [4], which is implicated to play an important role in the induction of PG, via T cell-derived cytokines and chemokines. IL-8 has been implicated to play an important role in neutrophil recruitment in the lesional skin. Tumor necrosis factor-α (TNF-α) induces IL-8 production by peripheral mononuclear cells [5]. Also, therapies targeting TNF-α result in beneficial effects on refractory PG [6,7], suggesting a crucial role of TNF-α in the pathogenesis of PG. TNF-a enhances vascular permeability in endothelial cells [8] as well as endothelial barrier dysfunction, which may be relevant to bullous formation of PG. TNF-a plays an important role in inflammatory bowel disease, whereas role of TNF-a in hematological malignancy is unclear. The etiology of bullous PG in hematological conditions needs further studies.

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DERMATOLOGY EPONYMS – SIGN – LEXICON – (M)

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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 (M) and other. The symptoms and their synonyms, and those who have described this symptom or phenomenon.

Key words: eponyms; skin diseases; sign; phenomenon

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MACHUPO SIGN, [South America]

Fever and bleeding caused by the zoonotic Bolivian hemorrhagic fever Arenavirdae virus. Machupo virus is spread from its primary hosts, rodents, to humans via aerosol and vector-borne (infected ticks and mosquitoes) transmissions. Aerosol transmission occurs when an infected rodent secretes any bodily fluids, such as urine or saliva, on an area where it's highly used by humans. Upon contact, a human becomes infected with the virus through inhalation of just a few organisms. From there, the machupo virus is able to produce a disease within the site of infection particularly in the lungs. The virus uses hilar lymph nodes and parenchymal organs for viral growth purposes.
Machupo virus outbreak has been reported mostly in the country of Bolivia – agriculture remote area – and Bolivia's surrounding countries. The reservoir hosts of this virus are rodents particularly in the family of Calomys callosus – the vesper mice. The recent major outbreak in Bolivia occurred during the 1962-1964 because of an increase population of the vesper rodents which resulted in over 1000 human cases of machupo virus infection [1,2].

MACLEAD'S SIGN
Rheumatoid arthritis with joint effusion [3,4].

RODERICK MACLEOD
Scotch physician, 1795-1852.

MADAGASCAR SIGN
Eosinophilia and seizures from the ingestion of infected arthropods containing eggs from the zoonotic Inermicapsifer cestoda [5].

MADURA FOOT SIGN
Chronic fungi caused disease, most common form in the foot, pus contains red, black and yellow granules [6-8].

MAGNAN'S SIGN
A frightening illusory sensation of a foreign body under the skin. A sign seen in cases of cocaine addiction [9].

VALENTIN JACQUES JOSEPH MAGNAN
French psychiatrist, 1835-1916 (Fig. 1). A pivotal figure in the historical classification of mental diseases. He studied medicine in Lyon and Paris. From 1867 to the end of his career he was associated with the Hôpital Sainte-Anne in Paris.

Figure 1. Valentin Jacques Joseph Magnan.

Magnan was an influential figure in French psychiatry in the latter half of the 19th century. He is remembered for expanding the concept of degeneration that was first introduced into psychiatry by Bénédict Augustin Morel (1809-1873). Magnan's theory of degeneration was a form of „evolutionary biology" that was based on an hereditary precept. He used terms such as bouffée délirante (transitory delusional psychosis) and délire chronique évolution systématique (chronic systemized delusional disorder) as descriptive categories of mental illness. [2] In 1892 with psychiatrist Paul Sérieux (1864-1947), he published a monograph on the latter mental state titled Le délire chronique a évolution systématique.
Magnan believed that the prodiguous use of alcohol, particularly absinthe, was a major factor in what he perceived was a decline of French culture. In his investigations of absinthe he tried to establish a particular „absinthe effect" that wasn't present in other forms of alcohol, and suggested that the delirium of absinthe was different from delirium tremens experienced in alcoholism. In his research with laboratory animals, Magnan used essence of absinthe (wormwood), rather than the beverage itself, which contains only a small percentage of wormwood. From his experiments he observed that animals experienced epileptiform convulsions when exposed to concentrated levels of wormwood [10].

MAJOCCHI'S SIGN
Purpura annularis telangieciodes [11].

DOMENICO MAJOCCHI
Italian dermatologist, (1849–1929) (Fig. 2). He characterized Majocchi's disease and Fungal folliculitis (also known as „Majocchi granuloma"). Born in Rome Roccalvecce, he completed his studies in Rome, where he graduated on 11, August, 1873. He entered the competition for the Hospital of St. Galligano and began his career as a dermatologist. In fact while passing other hospitals and doing extensive practice in operative surgery it had always been an object of his to study particularly the various branches of dermatology. His sifilografia of Venereology, lying today in the hospital of St. James, is an extensive treatise on syphilis of the nose and palate which remains vital and valuable still, along with other minor but noteworthy contributions. He became, in 1880, the first Chair of the University Clinic Dermosifilopatica Parma, a position which he help until 1892. During this period he made nu- Merosi disciples, he published valuable studies among which stand out in particular that of the granuloma tricofitico, a hitherto undescribed form that brought him great fame. In 1892 he was unanimously called to the chair of dermosifilopatia of Bologna, held it up to his retirement, that is, 1924, and in this golden age of his career, he published many works among which the most famous is the one on purpura annnlaris teleangectodes, dermatosis new linked perpetually to his name. He continued to bring new contributions to the study of granuloma tricofitico, published highly valuable memoirs on the rupee foliacea, various forms of ringworm, on ,acariosis from wheat, etc.., also dealing with skin abnormalities (duplicatio supercilii, supernumerary frenulum, etc..) and more still of the History of Medicine (Syphilis in Bologna at the descent of Charles VIII, Jerome Mercuriale Marcello Malpighi, etc..).

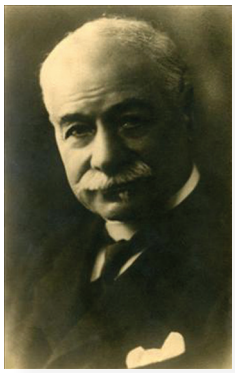

Figure 2. Domenico Majocchi.

He retained to the last his activity as evidenced by its latest publication, left incomplete, that he was dictating to his niece a few hours before his death, on the teaching of dermatology in Bologna. A gentle and good person devoted to his clinic, his disciples, to his patients; complex shape of humanist, scientist, dermatologist, of sifilografo, a historian of medicine; appassionatissimo of music and the arts, lover of conversation with scholars and scholars (and in his time in Bologna and learned scholars did not defect) whose friendship kept in a special way, in his tireless activity found time to devote to all his favorite activities. Admirer and follower of the work of Ferdinand Hebra [12].

MALIGNANT MILITARY SIGN

A term referring to the fact that many more British soldiers died from dysentery during the Crimean War (1854-56) and the Boer War (1899-1902) than from enemy action. History reveals disease has proven to be more lethal than the enemy weapons in most military campaigns [13].

MAO'S SIGN (China)

Green teeth and the most extremely foul breath associated with the practice of cleaning the mouth by only rinsing with green tea.

".....Eccentric, at any rate. In matters of personal care, for instance, Mao was strictly a minimalist. When Li first started treating him, he was startled to discover that the chairman had apparently never brushed his teeth. Instead, as with many Chinese peasants, he rinsed his mouth with tea, then chewed the leaves. The result was that Mao's teeth were green and his gums oozed pus from infections. Li encouraged the Great Helmsman to brush, without much success. „Does a tiger brush his teeth?" Mao demanded....." [14].

MAP SIGN

Zoonotic *Mycobacterium avium subspecies paratubetrculosis*. Causes chronic diarrhea, sometimes fatal. The bacterium is found in cattle, sheep, giraifes, wildebeest, antelope, and other ruminants [15].

HEINRICH ALBERT JOHNE (pronounced YOH-ne)

Figure 3. Heinrich Albert Johne.

German pathologist (1839-1910) (Fig. 3). He contributed to the literature of actinomycosis and trichinosis and discovered a method of staining bacterial capsules. He was instrumental in the introduction of meat inspection. Johne's disease, a paratuberculosis disease of cattle he described in 1895, is named for him [16].

MARBURG SIGN (Africa)

Rapid fever, muscle pain, vomiting, maculopapular rash with desquamation, liver involvement and bleeding. Moriality can be 30 percent, caused by the zoonotic Marburg hemorrhagic fever Filoviridae virus [17].

MARFAN'S SIGN

A red triangle on the tip of a furred or coated tongue. A sign of typhoid fever [18].

ANTOINE BERNARD-JEAN MARFAN

French paediatrician, 1858-1942 (Fig. 4). Marfan entered the medical school in Toulouse. After two years he went to Paris in 1879, became externe in 1880 and started an internship in 1882. After taking time out to do his military service, he graduated with a silver medal in 1886 and received his doctorate in 1887.

Figure 4. Antoine Bernard-Jean Marfan.

He was Chef de clinique medicale 1889-1891, agrégé of paediatrics to the Faculté de Médecine de l'Université de Paris in 1892 and until 1901 deputised for Grancher in the Hôpital des Enfants Malades during the winter terms. It was here he became interested in pediatrics. In 1892 he was appointed assistant professor of paediatrics in the Paris faculty.

Marfan was made head of the diphteria service at the Hospital for Sick Children and in 1910 professor of therapy. In 1914, at the age of 56 years, he was appointed as the first professor of infantile hygiene at the newly established pediatric clinic at the University of Paris.

His career was spent at the Hôpital des Enfants Malades in the Rue des Sèvres, where he remained until his retirement in 1928. He was a member of the Académie de Médecine from 1914. In 1920 his chair was moved to the Hospice des Enfants-Assistés. The writing of his doctoral thesis, „Troubles and gastric lesions in pulmonary tuberculosis", prompted Marfan's interest in pulmonary tuberculosis.

This paper gave rise to the concept known as the Marfan law, which noted the rarity of pulmonary tuberculosis following the healing of local tuberculous lesions because of the development of immunity. Marfan wrote: „One rarely records pulmonary tuberculosis in people who, during their childhood, had been attacked by the disease and in whom lesions had healed before the age of 15 years". Research such as this led to the development of the BCG vaccine.

Marfan was one of the first to recognise the importance of skin reactions and when von Pirquet developed his technique for skin testing for tuberculosis he immediately employed this in his clinical studies which became classics.

Marfan published extensively on pediatric themes and in 1897 was co-author of Treatise of Children's Diseases which was awarded the prize of the French Academy of Sciences. He investigated the harmful effects of feeding infants goat's milk and made extensive researches on rachitis. He was undoubtedly the pioneer in paediratrics in France and one of the most outstanding figures in his time.

He stated: «In medicine it is always necessary to start with the observation of the sick and to always return to this as this is the paramount means of verification. Observe methodically and vigorously without neglecting any exploratory procedure using all that can be provided by physical examination, chemical studies, bacteriological findings and experiment, one must compare the facts observed during life and the lesions revealed by autopsy.» [19].

In 1896 Marfan, presented the case of a 5-year-old girl, Gabrielle P, to the Société Médicale des Hôpitaux de Paris. Marfan pointed out Gabrielle's disproportionately long limbs. and asthenic physique. Her mother had noticed the abnormalities already at birth. The fingers and toes were exceptionally long and slender, making a spider-like impression. Marfan used the term „pattes d'araignée", spider's legs, and called the condition dolicostenomely (Greek: stenos = narrow, slender; melos = limb). Gabrielle P's striking abnormalities of the skeletal system progressed to the time of her death in early adolescence, probably from tuberculosis [Marfan, 1938].

The first to use the term Marfan's syndrome was Henricus Jacobus Marie Weve (1888-1962) of Utrecht in 1931.

MARIE'S DISEASE SIGN

Akromegaly [20].

PIERRE MARIE

French neurologist, 1853-1940 (Fig. 5). After finishing medical school, he served as an interne (1878), working as an assistant to neurologist Jean-Martin Charcot (1825–1893) at the Salpêtrière and Bicêtre Hospitals in Paris. In 1883 he received his medical doctorate with a graduate thesis on Basedow's disease, being promoted to médecin des hôpitaux several years later (1888). In 1907 he attained the chair of pathological anatomy at the Faculty of Medicine, and in 1917 was appointed to the chair of neurology, a position he held until 1925. In 1911 Marie became a member of the Académie de Médecine.

One of Marie's earlier contributions was a description of a disorder of the pituitary gland known as acromegaly. His analysis of the disease was an important contribution in the emerging field of endocrinology. Marie is also credited as the first to describe pulmonary hypertrophic osteoarthropathy, cleidocranial dysostosis and rhizomelic spondylosis. In his extensive research of aphasia, his views concerning language disorders sharply contrasted the generally accepted views of Paul Broca (1824–1880). In 1907, he was the first person to describe the speech production disorder of foreign accent syndrome.

Marie was the first general secretary of the Société Française de Neurologie, and with Édouard Brissaud (1852–1909), he was co-founder of the journal Revue neurologique. His name is associated with the eponymous Charcot–Marie–Tooth disease, being named along with Jean-Martin Charcot and Howard Henry Tooth (1856–1925) [21].

Associated eponyms:

„Marie's ataxia": an hereditary disease of the nervous system, with cerebellar ataxia.

„Marie-Foix-Alajouanine syndrome": cerebellar ataxia of the cerebellum in the elderly; usually due to alcohol abuse.

„Marie's anarthria": inability to articulate words due to cerebral lesions.

„Marie–Strümpel Disease": also known as Ankylosing spondylitis; a severe arthritic spinal deformity.

„Marie-Léri syndrome": hand deformity caused by osteolysis of the articular surfaces of the fingers.

„Bamberger-Marie disease": also known as Hypertrophic pulmonary osteoarthropathy.

Figure 5. Pierre Marie.

MARINER'S SIGN

A sign of religious mutilation in which Tonga natives cut off a portion of the little finger.

"……amongst an earlier generation of Tongans it was comparatively rare to find anyone who lived a long life with both little fingers intact….." [22].

MARSHALL'S SIGN

Bagginess of the eyelids and bloated facies that give the patient an appearance of a wax doll. A sign of myxoedema. Also known as wax doll sign [23].

GEOFFREY MARSHALL

British physician.

MARTIN'S SIGN
Martin described a remarkable variety of ichthyosis in which the skin was covered with strong hairs like the bristles of a boar. When numerous and thick the scales sometimes assumed a greenish-black hue. An example of this condition was the individual who exhibited under the name of the „alligator-boy." The skin affected in this case resembled in color and consistency that of a young alligator (Fig. 6). Also called Alligator's sign (Martin and Taylor) [24].

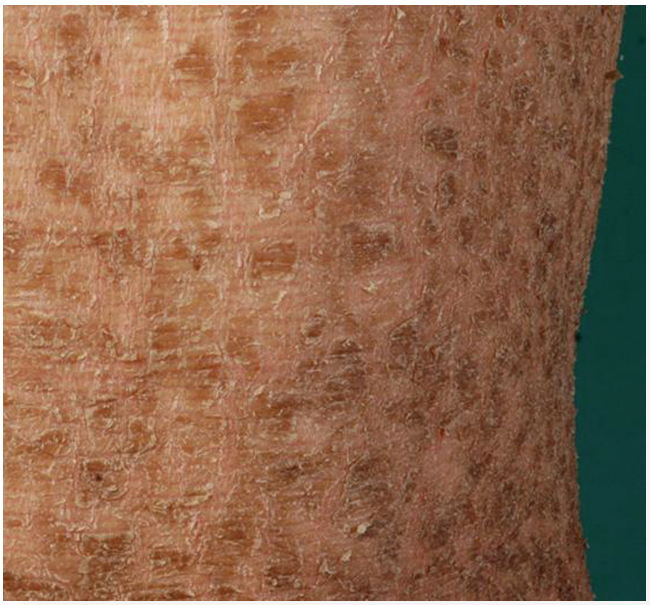

Figure 6. Martin's sign.

MATCHBOX SIGN
Patient having delusions of parasitosis (acarophobia, entomophobia) collects skin debris with mistaken belief that such collected material contains alleged parasite in a matchbox, tissue paper, or small container (Fig. 7). This whole exercise executed by the patient is referred to as „matchbox sign." [25,26].

Figure 7. Different containers in which patients bring „Evidence of parasites".

MATHIEU'S SIGN
Severe leptospirosis [27,28].

ALBERT MATHIEU
French physician, 1855-1917 (Fig. 8). He studied in Paris and became an interne in 1878. He was particularly influenced by Ernest-Charles Lasègue (1816-1883) and Charles Lailler (1822-1893), and in 1883 received his doctorate with a remarkable thesis on purpura haemorrhagica. He first mainly concerned himself with dermatology, but after having been chef de clinique with Germain Sée (1818-1896) in 1883, he turned to the study of digestive diseases, in which field he made important contributions. He worked at the Hôpital St.-Andral 1896, and then worked in the Hôpital St.-Antoine [29].

Figure 8. Albert Mathieu.

MCDOUGALL'S POWDER SIGN
The presence of a white stain around the mouth and brown stains, known as eschars on the skin of the face. Indicating suicide from the intake of McDougall powder, a sewage deodorant and parasitc insecticide made from carbolic acid [30]. Sign described by Alexander Mcdougall and Robert Angus Smith.

ROBERT ANGUS SMITH
British chemist, (1817–1884) [30].

MEAL TAG SIGN
Tattoos containing clear names and registration numbers on military personnel to be used if needed for post mortem identification. Often located on the ribs.

MECCA SIGN (c. 1831)
Epidemic marking cholera's first devastating invasion of Mecca, site of Islam's holiest shrine.
Cholera epidemics appeared more than 40 times between 1831 and 1912 during the Muslim pilgrimage. The disease was then widely dispersed as the followers of Muhammad returned home and the term Mecca of disease came into use, meaning: The place where diseases come from. Today in the 21st century, pilgrims to Saudi Arabia are especially at risk of contracting a meningococcal infection which causes fatal meningitis and fatal septicaemia blood poisoning. Vaccination requirements are now in place for the multiple sub groups of the meningococcus bacterium. The modern Mecca sign would now be defined as infections relating to the meningococeus bacterium instead the cholera bacillus [31].

MEFFERT'S SIGN
It is described in Fordyce's disease, characterized by presence of ectopically located sebaceous glands on the lips, oral mucosa and less commonly on gums. Prominent lip involvement can result in a lipstick like mark left on the rim of a glass mug after consuming a hot beverage (Meffert's sign) [32].

MEIGE'S SIGN
A form of hereditary edema of the legs. Also called Milroy's sign [33].

HENRI MEIGE
French physician, 1866-1940 (Fig. 9). He studied medicine in Paris under Jean Charcot (1825–1893), earning his doctorate in 1893. Afterwards he worked at the Salpêtrière and the École des Beaux-Arts, where in the 1920s he was appointed professor.
With Édouard Brissaud he researched skeletal changes in acromegaly, concluding that gigantism in adolescents is fundamentally the same disease as acromegaly in adults. During World War I he conducted studies of neuropathy with Pierre Marie.
Meige is best known for his work with extrapyramidal lesions. In 1902, with Eugene Feindel, he published an important work on motor disturbances, blepharospasms and tics. In contrast to Charcot, Meige asserted that disturbances of the extrapyramidal system were manifestations of pathological changes outside the pyramidal system.
He was editor of the journals Nouvelle iconographie de la Salpêtrière and Schriftleiter of the Revue Neurologique [34].
Related eponyms: Meige's syndrome I; Meige's syndrome II; Nonne-Milroy-Meige disease.

Figure 9. Henri Meige.

MEIROWSKY SIGN
Darkening of existing melanin, perhaps by oxidation, beginning within seconds and complete within minutes to a few hours after exposure to ultraviolet radiation [35].

EMIL MEIROWSKY
German-American dermatologist, 1876-1960. Meirowsky studied at the universities of Berlin and Königsberg, where he received his doctorate in 1901. He spent his hospital service and time as an assistant at the Berlin Polyclinic at Oscar Werl, in Wroclaw in Albert Neisser, Paul Gerson Unna and in Paris. In 1919 he received the title of professor. In 1920 he was habilitated at the University of Cologne, a year later he was appointed extraordinary professor. He was chairman of the Cologne Chamber of Physicians and a member of the German Democratic Party. In 1939 he emigrated to England. In 1947 he emigrated to the United States.
Meirowsky conducted research on the origins of melanin. In 1906 he proved (in Unna's laboratory) that the epidermis can produce melanin. According to him, the Meirowsky phenomenon (1909), the tanning of the skin, is produced by high temperatures.
His daughter Lisa Maria Meirowsky was also a doctor and was murdered in the concentration camp Auschwitz-Birkenau. His brother was the entrepreneur and art collector Max Meirowsky [36].

MELTING SIGN
The gingival tissues turn from normal pink to purple-black and appear to melt away. Awash in a flow of haemorrhage and the eyes may weep tears of blood. An indication of envenomation by the Dispholidus typus—Boomslang viper (Fig. 10). Also referred to as the Sahara plague [37].


Figure 10. Dispholidus typus – Boomslang viper.

E. A. WHILE
American historian-archaeologist.

MENANGLE SIGN (New South Wales, Australia)
Fever from exposure to infected fruit bats or pigs carrying the zoonotic Menangle virus [38].

MENDEL'S SIGN
The patient experiences anesthesia of the popliteal space. A sign of tabes dorsalis. Also known as Mendel-Bekhterev sign [39].

VALDIMIR MIKHAILOVICH VON BEKHTEREV
Russian neurologist and psychiatrist, 1857-1927 (Fig. 11). To the lay public Vladimir Bekhterev is known for Bekhterev's disease, pelvospondylitis. Bekhterev's most important work, however, was in the study of reflexes and the morphology of the brain. He is the founder of psycho reflexology, transmitting to humans the same pattern of thinking that Pavlov had developed in his work on conditioned reflexes in dogs, and he used similar experiments.

He enrolled at the Military Medical and Surgical Academy in St. Petersburg in 1873, at 16 years of age. After graduating in 1878 he held a position at the psychiatric clinic in St. Petersburg. It was here that he turned to the field that would make him famous: the anatomy and the physiology of the brain. In 1881 Bekhterev defended his dissertation for the medical doctorate that dealt with the possible relation between body temperature and some forms of mental illness. He was habilitated for Privatdozent of neurology and psychiatry in 1881 and was appointed associate professor - Dozent - that year. In 1895 he returned to Russia to become professor of psychiatric diseases at the University of Kazan. In 1913 he founded the State Institute for the Study of the Brain, which today bears his name. Independently of Pavlov Bekhterev developed a theory of conditioned reflexes, studying both inherited an acquired reflexes in the laboratory. He also accumulated a considerable volume of data on skeletal reflexes that was later applied in neurology. Bekhterev's most lasting work was his research on brain morphology and his original description of several nervous symptoms and illnesses. He discovered the superior vestibular nucleus (Bekhterev nucleus) as well as several previously unknown brain formations. He also described numbness of the spine (Bekhterev's disease) and new forms of syphilitic-sclerosis, motor ataxia and spondylitis. [40].

Figure 11. Valdimir Mikhailovich von Bekhterev.

KURT MENDEL

German neurologist, 1874-1946 (Fig. 12). In 1897 he received his doctorate from Kiel, and in 1899 went to work at the policlinic of Emanuel Mendel in Berlin. Kurt Mendel was an editor of Neurologisches Zentralblatt. With Russian neurophysiologist Vladimir Bekhterev (1857-1927), the eponymous Mendel-Bekhterev reflex is named, which is flexion of the toes caused by percussion of the upper surface of the foot, a sign of lesions of the pyramidal tract [41].

Figure 12. Kurt Mendel.

MENDEL-BEKHTEREV SIGN

See Mendel's sign.

METAL LINE SIGN

A line on the gums nearly identical to the lead line, but is caused by mercury. A sign of treatment for venereal disease [42].

METCHNIKOFF'S SIGN

In Pfeiffer's phenomenon, if the animals are given an intraperitoneal injection of bouiIlon or other material. Twelve hours before the test, lytic phenomena are replaced by phagocytosis [43].

ELIE METCHNIKOFF

Nobel laureate, Russian zoologist, 1845-1916 (Fig. 13). Best known for his pioneering research into the immune system. Mechnikov received the Nobel Prize in Medicine in 1908, shared with Paul Ehrlich, for his work on phagocytosis.

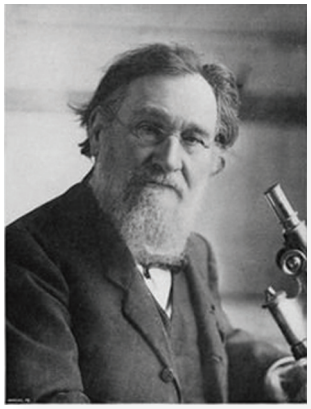

Figure 13. Elie Metchnikoff.

He is also credited by some sources with coining the term gerontology in 1903, for the emerging study of aging and longevity. He attended Kharkiv University where he studied natural sciences, completing his four-year degree in two years. He then went to Germany to study marine fauna on the small North Sea island of Heligoland and then at the University of Giessen, University of Göttingen and then at Munich Academy. While he was at Giessen, he discovered, in 1865, intracellular digestion in one of the flatworms, an observation which was to influence his later discoveries. Travelling on to Naples he prepared a thesis for his Doctorate on the embryonic development of the cuttle-fish Sepiola and the Crustacean Nelalia. In 1867 he returned to Russia to the appointment of docent at the newly established Imperial Novorossiya University (now Odessa University), followed by an appointment at the University of St. Petersburg. In 1870 he returned to Odessa to take up the appointment of Titular Professor of Zoology and Comparative Anatomy. Mechnikov became interested in the study of microbes, and especially the immune system. In 1882 he resigned his position at Odessa University and set up a private laboratory at Messina to study comparative embryology, where he discovered phagocytosis after experimenting on the larvae of starfish.

He realized that the process of digestion in micro-organisms was essentially the same as that carried out by white blood cells. His theory, that certain white blood cells could engulf and destroy harmful bodies such as bacteria, met with scepticism from leading specialists including Louis Pasteur, Behring and others. At the time most bacteriologists believed that white blood cells ingested pathogens and then spread them further through the body.
He worked with Émile Roux on calomel, an ointment to prevent people from contracting syphilis, a sexually transmitted disease. Mechnikov also developed a theory that aging is caused by toxic bacteria in the gut and that lactic acid could prolong life. Based on this theory, he drank sour milk every day. He wrote three books: Immunity in Infectious Diseases, The Nature of Man, and The Prolongation of Life: Optimistic Studies, the last of which, along with Metchnikoff's studies into the potential life-lengthening properties of lactic acid bacteria (Lactobacillus delbrueckii subsp. bulgaricus), inspired Japanese scientist Minoru Shirota to begin investigating a causal relationship between bacteria and good intestinal health, which eventually led to the worldwide marketing of kefir and other fermented milk drinks, or probiotics.
In honor of this great and illustrious researcher, The Russian Empire created the prestigious Mechnikov Medical Academy in St. Petersburg. One of the most prestigious institutions in the training of physicians and senior professionals in Russia [43].

METH MOUTH SIGN
The front teeth are often missing or black and broken down, due to the heat and dry mouth associated with smoking methamphetamine. Also known as Crack Teeth sign [44].

MEYERSON PHENOMENON
Meyerson phenomenon is an uncommon clinical condition that is characterized by an eczematous halo surrounding a preexisting melanocytic nevus and numerous other lesions (Fig. 14a, b) [45].

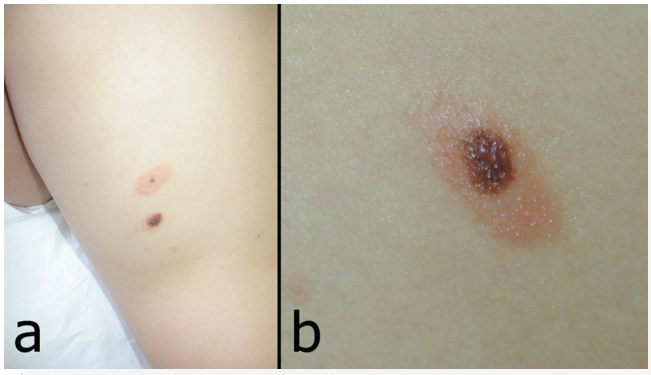

Figure 14a and b. Meyerson phenomenon.

In 1971, Meyerson described two patients that presented erythema, desquamation and pruritus concerning exclusively nevi, localized on the trunk and close extremities and that improved after therapeutics with topical corticosteroids. Since then, this phenomenon has been described in various pigmented lesions including junctional nevi , Sutton nevi, atypical nevi and congenital ones. It was even documented in non-melanocytic lesions such as basal cells carcinomas, spinocellular carcinomas, seborrheic keratosis, keloids, histiocytofibromas and insect bites [46].

ÉMILE MEYERSON
Polish-born French epistemologist, chemist, and philosopher of science, 1859-1933 (Fig. 15). Meyerson was educated in Germany and studied chemistry under Robert Wilhelm Bunsen. In 1882 Meyerson settled in Paris. He served as foreign editor of the Havas news agency, and later as the director of the Jewish Colonization Association for Europe and Asia Minor. He became a naturalized French citizen after World War I [47].


Figure 15. Émile Meyerson.

MIASMATIC SIGN
One due to malaria poisoning [48].

MIBELLI'S SIGN
Porokeratosis with yellow brown patches and red and white dike like borders (Fig. 16). Also called keratodermia [49-51].

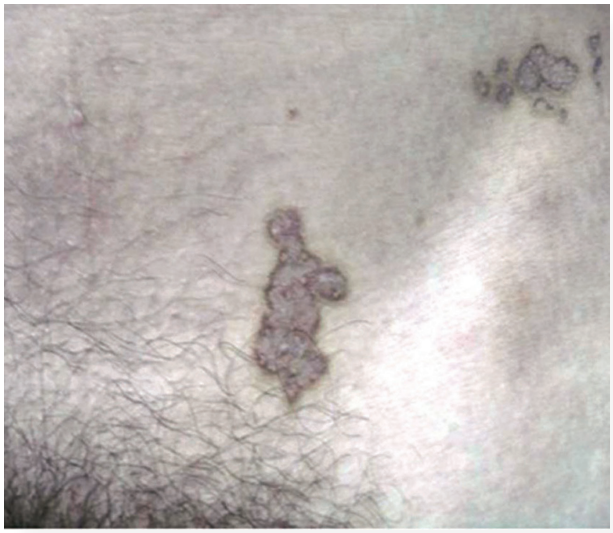
Figure 16. Mibelli's sign.

VITTORIO MIBELLI
Italian dermatologist, 1860-1910 (Fig. 17). He studied in Siena and, following further education in Florence, became prosector in the anatomical institute in Siena, and subsequently assistant in the dermatological clinic in that town. He was habilitated in 1888, from 1889 worked with Paul Gerson Unna in Hamburg and 1890 came to the University of Cagliary as extraordinary professor and director of the skin clinic. In 1892 he was called to Parma, where he was appointed ordinarius in 1900 and was active until his death in 1910 [52].

Figure 17. Vittorio Mibelli.

MICKEY SIGN
Giddiness, blueness of the face, coldness of extremities and unconsciousness. A sign of chloral hydrate or chloralamide poisoning [53].

MIKULICZ'S SIGN
Chronic enlargement of the lacrimal and salivary glands, due to replacement of the glandular tissue by lymph-cells: called also achroacytosis [54].

JOHANN VON MIKULICZ-RADECKI
Polish-Austrian surgeon, 1850-1905 (Fig. 18). He was professor in Kraków, Wrocław, and Królewiec (Königsberg). Inventor of new operating techniques and tools, one of the pioneers of antiseptics and aseptic techniques. In Poland he is regarded as one of the founders of the Kraków school of surgery. After finishing studies at the University of Vienna under Theodor Billroth he was a director of surgery at the Jagiellonian University in Kraków, the University of Königsberg (Królewiec, Kaliningrad) and from 1890 at the University of Wrocław.
Mikulicz-Radecki's innovations in operative technique for a wide variety of diseases helped develop modern surgery. He contributed prodigiously to cancer surgery, especially on organs of the digestive system. He was first to suture a perforated gastric ulcer (1885), surgically restore part of the oesophagus (1886), remove a malignant part of the colon (1903), and describe what is now known as Mikulicz' disease.
In 1881 he developed improved models of the esophagoscope and gastroscope. As an ardent advocate of antiseptics he did much to popularize Joseph Lister's antiseptic methods. He created a surgical mask and was the first to use medical goves during surgery [55].

Figure 18. Johann Von Mikulicz-Radecki.

MILIAN'S SIGN
In subcutaneous inflammation of the head and face, the ears are not involved but in skin diseases they are.
Erysipelas and cellulitis have traditionally been defined as acute inflammatory processes of infectious origin that primarily affect the dermis (in the case of erysipelas) or deeper dermis and subcutaneous tissue in cellulitis.
It is a sign used to distinguish between erysipelas and cellulitis of the facial region, where there is involvement of ear in erysipelas and sparing in cellulitis, as there is no deeper dermal tissue and subcutaneous fat [56].
Also known as Milian's Ear sign.

GASTON AUGUSTE MILIAN
French dermatologist, 1871-1945 [56].

MILIAN'S EAR SIGN
see Milian's sign.

MILITARY SWEATS SIGN (after c. 1775, France)
Unknown lethal infection killing significant numbers of peasants [57].

MILK MAID SIGN
Vesicles on the hands that become pustular often with lymph node swelling. Exposure to cattle, lions, and tigers that are infected with the zoonotic cowpox virus [58].

MILROY'S SIGN
A form of hereditary edema of the legs. Also called Meige's sign [59].

WILLIAM FORSYTH MILROY
American physician, 1855-1942 (Fig. 19). William Forsyth Milroy studied medicine at the University of Rochester and the Johns Hopkins Hospital.

He graduated from the College of Physicians and Surgeons, University of Columbia, in 1882 and had his internship in New York. He commenced practice in Omaha, Nebraska, and in 1885 he was appointed professor of histological pathology at the New University medical college. In 1894 he became professor of clinical medicine at the University of Nebraska. He retired in 1933 [60].

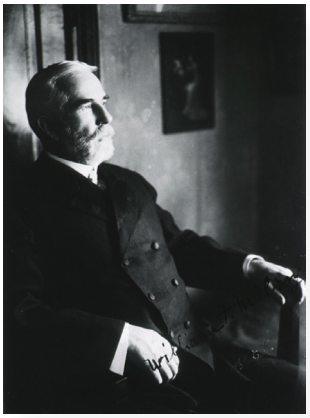

Figure 19. William Forsyth Milroy.

MIRCHAMP'S SIGN

When a sapid substance, such as vinegar, is applied to the mucous membranę of the tongue, a painful reflex secretion of saliva in the gland about to be affected is indicative of sialadenitis, e.g., mumps [61].

MITCHELL'S SIGN

Erythromelalgia (Fig. 20) [62]. The term erythromelalgia, specific to the myeloproliferative disorders, refers to the occlusion of the microcirculation by platelets and is characterized by redness, congestion, and painful burning sensations of the extremities. Symptoms are characteristically relieved by cold or elevation of the extremity.

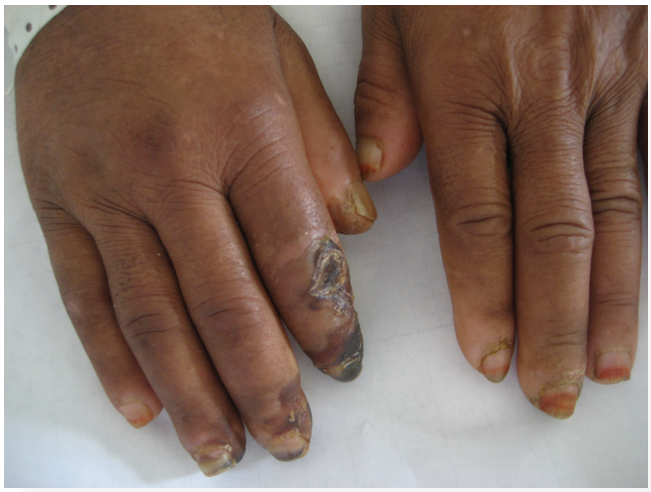

Figure 20. Erythromelalgia.

SILAS WEIR MITCHELL

American neurologist and writer known for his discovery of causalgia, 1829-1914 (Fig. 21). He studied at the University of Pennsylvania in that city, and received the degree of M.D. at Jefferson Medical College in 1850. During the Civil War he had charge of nervous injuries and maladies at Turners Lane Hospital, Philadelphia, and at the close of the war became a specialist in neurology. In this field Mitchell's name became prominently associated with his introduction of the rest cure, subsequently taken up by the medical world, for nervous diseases, particularly neurasthenia and hysteria. His medical texts include Injuries of Nerves and Their Consequences (1872) and Fat and Blood (1877). Mitchell's disease (erythromelalgia) is named after him. He also coined the term phantom limb during his study of an amputee.

Silas Weir Mitchell discovered and treated causalgia (today known as CRPS/RSD), a condition most often encountered by hand surgeons. He is considered the father of neurology as well as an early pioneer in scientific medicine. He was also a psychiatrist, toxicologist, author, poet, and a celebrity in America and Europe. His many skills and interests led his contemporaries to consider him a genius on par with Benjamin Franklin. His contributions to medicine and particularly hand surgery continue to resonate today [63].

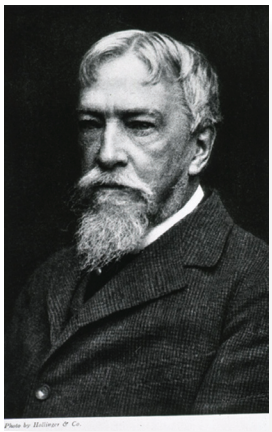

Figure 21. Silas Weir Mitchell.

MIZUTANI'S SIGN (Round finger pad sign)

It is seen in Raynaud's phenomenon associated with systemic sclerosis. This sign refers to the disappearance of the peaked contour on fingerpads and replacement with a hemisphere-like fingertip contour especially on ring fingers (Figs. 22a, b) [64]. Sign was described by Hitoshi Mizutani and Tomoko Mizutani.

MOELIER-BARLOW'S SIGN

Subperiosteal hematoma in rickets [65].

"Under this name, and under the name of MÖLLER-BARLOW'S disease, a condition has been described in which a hemorrhagic effusion takes place under the periosteum, which is quite rare, but nevertheless interesting. Six cases of this rare disease have recently been recorded by BRUN andRENAULT, of Paris, in La Presse Médicale, Jan. 12, 1898.

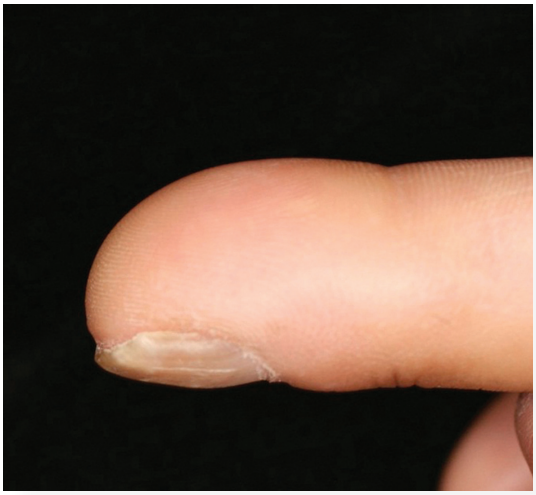

Figure 22a. Finger tip of a patient with systemic scleroderma with positive for round finger pad sign.

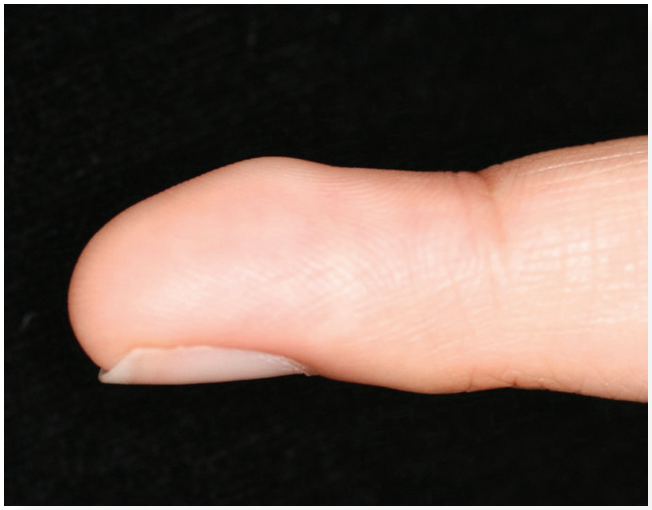

Figure 22b. Finer tip of a healthy control subject with the peaked contour.

MOELIER-BARLOW'S SIGN

Subperiosteal hematoma in rickets [65].

"Under this name, and under the name of MÖLLER-BARLOW'S disease, a condition has been described in which a hemorrhagic effusion takes place under the periosteum, which is quite rare, but nevertheless interesting. Six cases of this rare disease have recently been recorded by BRUN andRENAULT, of Paris, in La Presse Médicale, Jan. 12, 1898.

These six cases were observed in the Hospital for Children's Diseases during the past two years. The first case was that of a girl of three months. The father and mother were healthy, but a younger brother had died in convulsions. The child was born at term after a normal labor and had been nursed for six months. It was brought to the Hospital because of the swelling of the right thigh. The general appearance of the child was good..."

JULIUS OTTO LUDWIG MÖLLER

German surgeon, 1819-1887. He studied in Königsberg, Halle and Vienna, receiving his doctorate in 1840. He was physician in Königsberg from 1841, until 1863 extraordinary professor of practical medicine, director of the medical policlinic and Medcinalrath. In 1863 he was «politisch gemassregelt» and laid down the named positions. From 1845 to 1863 he wrote a number of treatises in various journals [66].

SIR THOMAS BARLOW

English physician, 1845-1945 (Fig. 23); known for his research on infantile scurvy. He studied as an undergraduate at Manchester and London. University College London (UCL) Bachelor of Medicine (BM) in 1873 and Doctor of Medicine (MD) 1874. He became a registrar at Great Ormond Street Hospital, and later a physician and in 1899 a consultant. He was professor at the UCL from 1895 to 1907, initially of paediatrics and later of clinical medicine. Barlow's disease – infantile scurvy – is named after him.

He was Royal Physician to Queen Victoria and attended her on her death, and to King Edward VII and King George V. He was knighted as a Knight Commander of the Royal Victorian Order in March 1901, and in February 1902 he was created a Baronet, of Wimpole Street in St Marylebone in the County of London. [4] He was President of the Royal College of Physicians from 1910–1914 and delivered their Harveian Oration in 1916 on the subject of Harvey, The Man and the Physician. He was elected a Foreign Honorary Member of the American Academy of Arts and Sciences in 1918 [67].

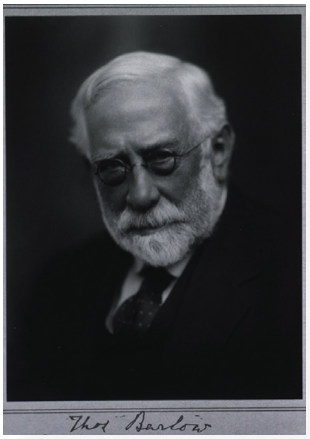

Figure 23. Thomas Barlow.

MOELLER'S TONGUE SIGN

Generalized loss of filiform papillae of the tongue in pernicious and other anemias. Early cases present as enlargement and tenderness of the papillae, a form of chronic lingual papillitis (CLP) (Figs. 24a - c) [68]. CLP is an innocuous entity represented by focal or diffuse enlargement of numerous lingual papillae, primarily the filiform papillae. It appears to usually have an adult onset and most likely represents papillary reaction to very low-grade, chronic irritation or desiccation. Some cases with childhood onset, however, seem to be variations of normal anatomy. No treatment or biopsy is required, but a number of systemic disorders and syndromes must be ruled out before applying the CLP diagnosis. Also called Moeller's glossitis.

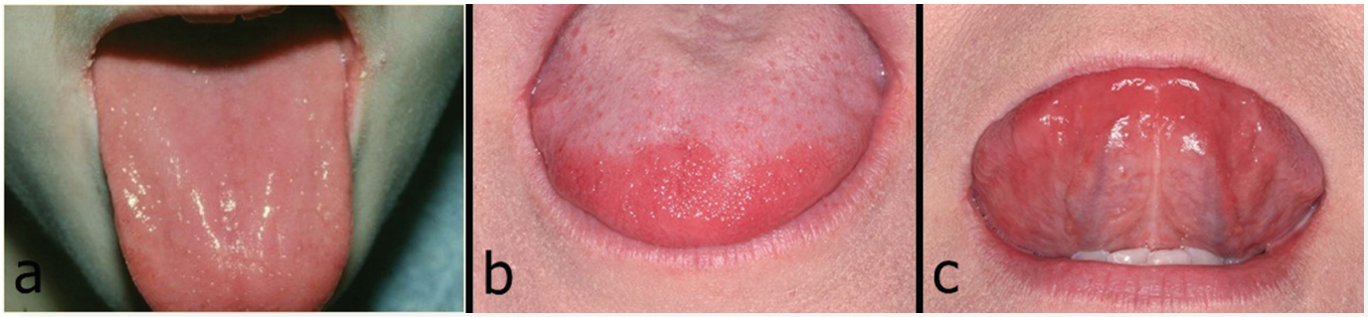

Figure 24a - c. a) Moeller's glossitis in Vitamin B12 deficiency (pernicious anemia) presenting as a diffuse loss of filiform papillae on the tongue, with remaining nodules representing unaffected fungiform papillae; b and c) early Moeller's glossitis in Vitamin B12 affecting only the tip of the tongue, with an area of enlarged, tender papillae, sometimes referred to as chronic lingual papulosis.

MÖLLER
German surgeon, 1829-1862

MOKOLA FEVER SIGN (Africa)
Fatal encephalitis caused by a zoonotic rabies lyssavirus. The disease course does not have the classic rabies signs [69].

MONGOL SPOT SIGN
A birthmark on the lower back of Peruvian children with Asian lineage which later disappears (Fig. 25). Also known as „Mongolian blue spot" [70].

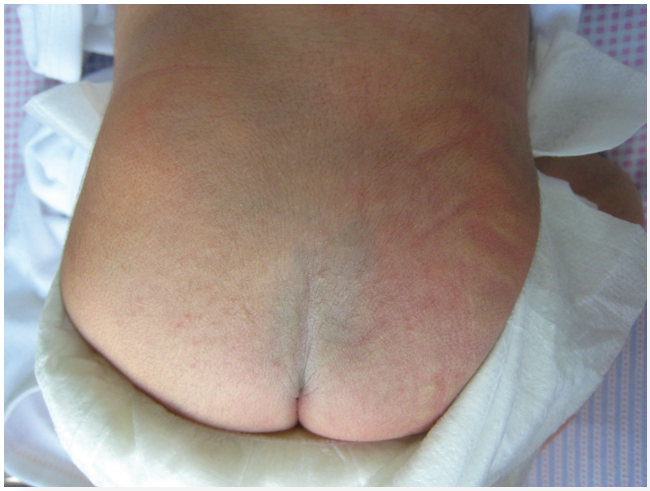

Figure 25. Mongol Spot sign.

MONGOLISM SIGN
Down syndrome [71].

JOHN LANGDON HAYDON DOWN
English physician, 1828-1896 (Fig. 26). At the age of 18 he was supporting himself as an assistant to a surgeon in private practice on White Chapel Road, where he had the opportunity to concern himself with blood-letting, tooth extraction etc.
A few months later, in 1847, he was allowed to commence work at the laboratory of The Pharmaceutical Society in Bloomsbury Square, London, where he made great progress and concentrated his efforts in organic chemistry. In 1849 he became assistant to professor Redwood and subsequently became research assistant to Michael Faraday.
Down was predicted a brilliant career at the university hospital, but surprised his teacher when he, in 1858, became resident physician and subsequently medical superintendent at the Earlswood Asylum for Idiots in Surrey. He was elected assistant physician to the London Hospital in 1859 shortly after Mr. Jonathan Hutchison had been elected assistant surgeon. He was conferred doctor of medicine in London in 1859.
Down wanted to work for the then hitherto gravely neglected mentally retarded children, and for a period of ten years (1858-1868) he shared his time between the Earlswood institution for the mentally retarded and his London practice.
Down became a lecturer on materia medica and therapeutics at the London Hospital Medical College and afterwards lecturer in the principles and practice of medicine. For the first 9 years following this appointment he continued to live at the Earlswood Asylum and to work there and superintend the asylum's organisation and development. This resulted in a model for the care of the mentally ill in the UK. Down described mongolism in his Letsom lectures entitled «On some of the mental afflictions of childhood an youth» delivered in 1887. He published relatively little, but was awarded several medals for his publications on psychiatry.
Down's monograph Mental Affections of Childhood and Youth, published in 1887, contained the classic description of the condition which now bears his name. He also mentioned adrenogenital dystrophy, which gained recognition more than 40 years later as Fröhlich's syndrome (adiposogenital syndrome, entered as Babinski-Fröhlich syndrome or disease, under Joseph François Félix Babinski, French Neurologist,) [71].

Figure 26. John Langdon Haydon Down.

MONKEY BITE SIGN
Vesicular blisters and encephalitis, including seizures and coma. Very high mortality caused by the bites or scratches of Old World monkeys infected with the zoonotic ceropithecine herpesvirus-simiae type B [72].

MONKEY PANCREATITIS SIGN
Acute panereatitis caused by a tapeworm infection in the biliary tract. The zoonotic infection is usually associated with consumption of raw pork viscera, but can also be found in monkeys. Also called Asian taeniasis disease [73].

MONKSHOOD SIGN
Prickling and tingling sensations with giddiness and possible numbness in the mouth. The prickling feeling spreads on to the face and then to the whole body. A sign of aconite or aconitine poisoning [74]. Also known as Aconite sign.

MONTEVERDE'S SIGN
Failure of any response to the subcutaneous injection of ammonia. A sign of death [75].

N. N. MONTEVERDE
1885-1952 [75].

MOON'S SIGN
Domed-topped first molars seen in congenital syphilis [76].

HENRY MOON
English dental surgeon, 1845-1892 (Fig. 27) [77]. Henry Moon qualified in London in medicine and dentistry, emigrated to New Zealand, eventually returning to London. He is known for his observations of the malformation of tooth cusps in children with congenital syphilis.

Figure 27. Henry Moon.

MORPHEA SIGN
Circumscribed scleroderma presenting in patches and bands (Fig. 28) [78].

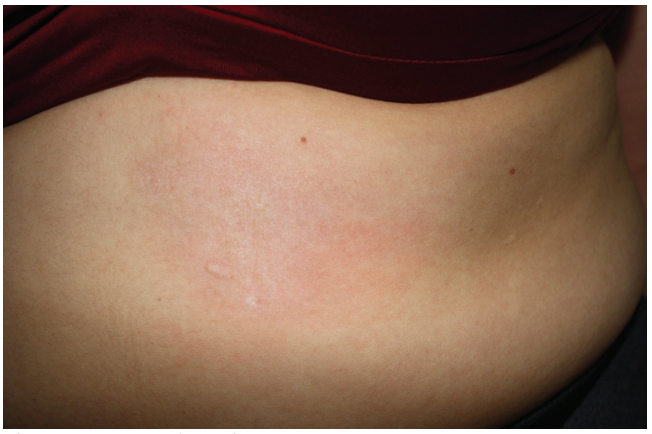

Figure 28. Morphea sign.

MORQUIO SIGN
Mucopolysaccharidosis IV or Morquio's [79].

LUIS MORQUIO
Uruguayan physician and professor, (1867–1935) (Fig. 29). He graduated in 1890 and obtained his doctorate two years later for a thesis on the treatment of typhoid fever.
In 1893 Morquio paid his first visit to Europe, spending a year as intern broadening his experience, especially in Paris, where he pursued his chosen field of paediatrics at Jacques-Joseph Grancher's clinic for sick children. He worked with Antoine Bernard-Jean Marfan and was present at the clinics of Jean Martin Charcot, Pierre Charles Édouard Potain and Paul Georges Dieulafoy as well as Georges Hayem (1841-1933) and Étienne Lanceraux.
He returned to Uruguay in 1894 and opened practice as a paediatrician. During his absence, his faculty had created a chair of paediatrics and on his return Morquio was appointed second in command, succeeding to the professorship in 1900.

He was professor of internal pathology 1895-1900. In 1915 he was a founder of the Sociedad uruguaya de pediatría.
Morquio maintained links with his colleagues in France, where he was elected to membership of several academic societies. The French government conferred upon him the rank of officer of the Légion d'Honneur and in 1930, in Geneva, he was elected president of the international Save the Children Society. In 1930 he was appointed director of Clínica Pediátrica y Puericultura - the Institute of Clinical Pediatrics in Montevideo. Morquio's academic activities extended to many aspects of congenital and acquired disorders of childhood and he was the author of numerous publications in the field of pathology and hygiene of paediatrics, and two paediatric textbooks.
Morquio was an amicable man who was esteemed by his colleagues throughout the world. He died suddenly in 1935 at the age of 68 years, and after his death a bust was erected in his honour at the institute of paediatrics, Montevideo [80].

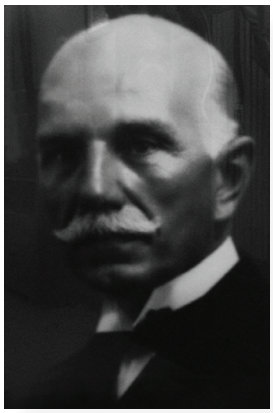

Figure 29. Luis Morquio.

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From Figures:
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Figure 16. - Prof. Beatriz Di Martino Ortiz - Cátedra de Dermatología. Hospital de Clínicas. Facultad de Ciencias Médicas. Universidad Nacional de Asunción. Paraguay
Figure 17. - Dr Khalid Al Aboud - Department of Public Health, King Faisal Hospital, Makkah, Saudi Arabia

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