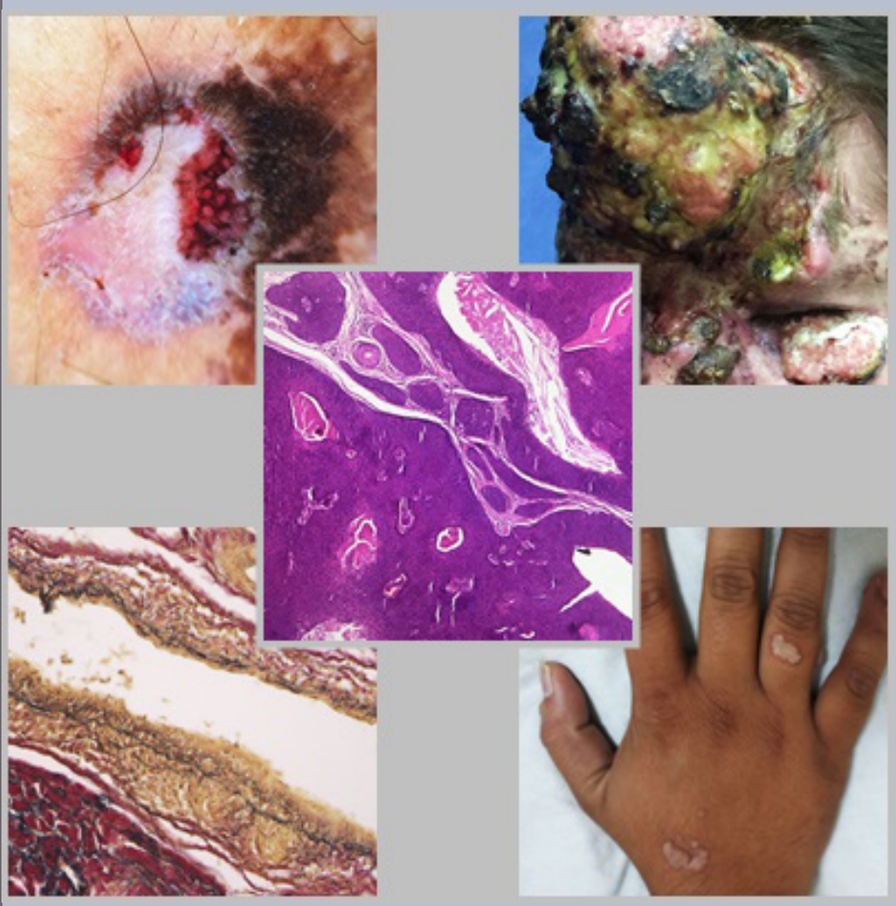
Volume 14, Number 1 January 2023
p. 1- 120
Issue online since Monday January 02 2023

ISSN: 2081-9390
DOI: 10.7241/ourd

Our Dermatology Online

www.odermatol.cowm



- Evaluation of the efficacy and safety of the intralesional purified protein derivative of tuberculin versus intralesional vitamin D3 for the management of recalcitrant warts;

- Comparative study on the effectiveness of intralesional Measles, Mumps, and Rubella vaccine and intralesional vitamin D3 injection in the treatment of verruca;

- Intralesional measles-mumps-rubella vaccine in recurrent common warts: A placebo-controlled study;

- Prevalence of anemia among HIV-infected individuals and the associated factors: A single-center, retrospective review of 513 cases;

- Dermatological manifestations during HIV infection in children in Dakar, Senegal;

- Pregnancy and cutaneous changes;

- Topical steroid menace: A case series of severe debilitating infections during the COVID-19 pandemic;

- Erythrodermic psoriasis eruption following COVID-19 vaccination

Issue 1.2023

Editorial Pages

e-ISSN: 2081-9390
DOI: 10.7241/ourd

Quarterly
Our Dermatol Online

published since 01/06/2010 years

www.odermatol.com

Indexed in:

Universal Impact Factor for year 2012 is = 0.7319
system of opinion of scientific periodicals INDEX COPERNICUS (8,69)
(Academic Search) EBSCO
(Academic Search Premier) EBSCO
MNiSW (kbn)-Ministerstwo Nauki i Szkolnictwa Wyższego (7.00)
DOAJ (Directory of Open Acces Journals)
Geneva Foundation for Medical Education and Research (GFMER), Google Scholar, Open J-Gate, NewJour,
International Committee of Medical Journal Editors (ICMJE), Genamics JournalSeek, Hinari,
Bielefeld Academic Search Engine (BASE), WorldCat, e -journal, WorldWideScience.org, National Science Library,
LibSearch, Sciencegate, Virtual Science Library (VSL), Wanfang Data, COnnecting REpositories (CORE),
CAB Abstracts, Global Health, Journal Indexed in Directory of Research Journals Indexing,
OAIster: The Open Access Initiative, OAJSE - Open Access Journals Search Engine, Scirus

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

Editorial Board

Contents

Original Articles

Brief Reports

Contents

Contents

Our Dermatology Online

Original Article

Evaluation of the efficacy and safety of the intralesional purified protein derivative of tuberculin versus intralesional vitamin D_3 for the management of recalcitrant warts

Manoj Kumar Sharma[1], Alpana Mohta[2], Kapil Vyas[3], Atul Vijay[1]

[1]Department of Dermatology, Venerology and Leprosy, Jhalawar Medical College, Jhalawar, Rajasthan, India, [2]Department of Dermatology, Venerology and Leprosy, Sardar Patel Medical College, Bikaner, Rajasthan, India, [3]Department of Dermatology, Venerology and Leprosy, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India

Corresponding author: Prof. Atul Vijay, MD, E-mail: drvijayatul11@gmail.com

ABSTRACT

Introduction: Warts are caused by the human papillomavirus (HPV), which infects the epidermal cell layers leading to their hyperproliferation. The concept of immunotherapy has recently come to light. It acts by mounting delayed cell-mediated and humoral immunity against the HPV in the host. **Objective:** This study aimed to evaluate the efficacy and safety of the intralesional PPD versus intralesional vitamin D_3 for the management of recalcitrant warts. **Materials and Methods:** This prospective randomized trial was conducted on patients between the ages of 12 and 65 years with two or more recalcitrant extragenital warts. The subjects were randomly divided into two groups, namely, group A (PPD) and group B (vitamin D_3). In group A, a purified protein derivative (PPD) of tuberculin was employed without any prior pre-sensitization testing. Each patient in group I received 0.1–0.2 mL of antigen at the base of the largest wart. In group B, the patients received 0.1–0.2 mL in a similar manner. **Results:** In group A, 39 (78%) patients had complete clearance while, in group B, 38 (76%) had complete clearance in injected warts ($p = 0.8$). As far as distant warts were concerned, in group A, 35 (70%) had a complete response while, in group B, 29 (48%) had a complete response. There was a statistically significant difference between the two groups with a greater degree of clearance in distant warts with the tuberculin PPD ($p = 0.04$). **Conclusion:** Both the tuberculin PPD and vitamin D_3 are reliable and safe management options for recalcitrant, treatment-resistant, and extensive warts.

Key words: Warts; PPD; Vitamin D_3; Immunotherapy

INTRODUCTION

Warts are caused by the human papillomavirus (HPV), which infects the epidermal cell layers leading to their hyperproliferation [1]. Although asymptomatic in most cases, warts tend to spread from one person to another and often pose cosmetic discomfort for the patient. Although a plethora of destructive modalities such as radiofrequency ablation, chemical cauterization, surgical excision, etc., are conventionally utilized for their management, most of these therapies only partially help in extensive and recalcitrant warts. Due to the inherent inability of these management options to mount antiviral immunity in the patient's body, the risk of recurrence and relapse is high [2,3].

Recently, the concept of immunotherapy has come to light. It acts by mounting delayed cell-mediated and humoral immunity against the HPV in the host. The commonly utilized immunotherapeutic antigens are MMR, BCG, and *M. w.* vaccines, *Candida*, *Trichophyton*, and PPD of tuberculin antigens, vitamin D_3, etc. [2,4-8].

How to cite this article: Sharma MK, Mohta A, Vyas K, Vijay A. Evaluation of the efficacy and safety of the intralesional purified protein derivative of tuberculin versus intralesional vitamin D_3 for the management of recalcitrant warts. Our Dermatol Online. 2023;14(1):1-5.

Submission: 29.01.2022; **Acceptance:** 09.10.2022

DOI: 10.7241/ourd.20231.1

The mechanism of action of the PPD vaccine as an immunotherapeutic antigen is the mounting of a Th1-mediated immune response, leading to the upregulation of IL-2,4,5, TNF-α, along with the stimulation of a delayed hypersensitivity reaction [9].

Vitamin D_3, on the other hand, has multiple mechanisms of action, namely, increased epidermal cell maturation, reduced cell proliferation, and cytokine production. It acts by downregulating IL-1α and IL-6, upregulating toll-like receptors of human macrophages, and stimulating the formation of the antimicrobial peptide at local and distant sites [10,11].

This study aimed to evaluate the efficacy and safety of intralesional PPD versus intralesional vitamin D_3 for the management of recalcitrant warts.

MATERIALS AND METHODS

This prospective randomized trial was conducted after obtaining due approval from the institutional ethics board. The study was conducted between June 2019 and June 2021 in two centers. Immunocompetent patients with recalcitrant verruca were recruited for the dermatology outpatient department.

Inclusion Criteria

Included were patients between the ages of 12 and 65 years with two or more extragenital warts, recalcitrant to at least two conventional modalities attempted in the past. Only patients who had not received any other treatment in the previous two months were included.

Exclusion Criteria

Subjects with both genital and extragenital warts were excluded. Additionally, subjects with any form of congenital, acquired, or iatrogenic immunosuppression, patients with systemic illness, those with a history of hypersensitivity reaction to a PPD, vitamin D_3, or any of the additive inactive agents, pregnant or lactating females, and patients with an active infection were excluded.

Detailed records of the patients along with a history of any treatment received in the past were recorded. After explaining the procedure and obtaining written informed consent, the subjects were randomly divided into two groups, namely, group A (PPD) and group B (vitamin D_3).

Sample Size

For each group, the sample size was calculated with the probability at 90% and the significant result at 5%. The sample size was fifty per group.

Randomization

In this single-blinded trial, unstratified randomization was performed by an open list of simple, random number tables.

In group A, the purified protein derivation (PPD) of tuberculin was employed without any prior pre-sensitization testing. Each patient in group A received 0.1–0.2 mL of antigen at the base of the largest wart.

In group B, the patients received 0.1–0.2 mL (600,000 IU; 15 mg/mL) of intralesional vitamin D_3 (Arachitol-6L®; Akums Drugs and Pharmaceuticals Ltd.) at the base of the largest wart.

In both groups, 0.1–0.2 mL of lignocaine (20 mg/mL) was injected perilesionally beforehand.

Injections were applied every four weeks to the same wart up to four injections or until there was a complete clearance in all warts, whichever happened first. After every session, the results were assessed. Follow-up was performed at six and twelve weeks after the last injection.

Treatment Response

The response to treatment was graded as:

- Complete response: clearance in all warts with the appearance of normal skin markings.
- Partial response: a 50–99% reduction in the size and number of warts.
- No response: a less than 50% reduction in size and number.

Statistical Analysis

Descriptive statistics were performed by calculating the mean and standard deviation for the continuous variables. Categorical variables were presented in the form of absolute numbers and percentages. Nominal categorical data was compared with the chi-square test.

RESULTS

Out of the 115 patients, a hundred completed the study, with fifty patients in each group. Table 1 shows the baseline demographic data of the patients.

In group A, 39 (78%) patients had complete clearance, 5 (10%) had partial clearance, and the remaining 6 (12%) had no clearance in the injected warts (Figs. 1a and 1b). In group B, 38 (76%) subjects had complete clearance, 4 (8%) had partial clearance, and the remaining 8 (16%) had no clearance in the injected warts (Table 2) (Figs. 2a and 2b). There was no significant difference between the two groups ($p = 0.81$).

As far as distant warts are concerned, in group A, 35 (70%) had a complete response, 9 (18%) had a partial response, while the remaining 6 had no response. Similarly, in group B, 29 (48%) had a complete response, 5 (10%) had a partial response, while the remaining 16 (32%) had no response (Table 3). There was a statistically significant difference between the two groups, with a greater degree of clearance in distant warts with the tuberculin PPD ($p = 0.04$) (Table 3).

The mean number of injections required for complete clearance in all warts was 3.1 in group A and 3.7 in group B. In the ensuing twelve weeks of follow-up after the last session, none of the patients experienced a recurrence of their warts.

The side effects were minimal in both groups. The most common adverse event in groups A and B was transient pain on the injection site lasting for 24 hours. Other adverse events were seen only rarely, as transient fever in group A and pruritus on the injection site in group B. No significant correlation could be drawn between the duration of the disease and the treatment response.

DISCUSSION

The treatment of warts is often a therapeutic challenge for the treating dermatologist due to the suboptimal response of the available therapies. Since none of these agents show total effectiveness against HPV, the chances of recurrence are exceedingly high. Due to the presence of HPV in the basal layers of the epidermis, where they often escape the immune system of the body, warts tend to run a chronic and recalcitrant course.

Table 1: Baseline demographic data of the two groups.

Parameter	Group A	Group B	*p* value
Mean age	29.7±5.3 yrs.	30.2±6.1 yrs.	> 0.05
Male: female ratio	31:19	29:21	> 0.05
Mean number of warts at baseline	5.9±3.1	6.1±2.9	> 0.05
Duration of warts	8.7±2.2 months	8.9±2.6 months	> 0.05

Table 2: Rate of clearance of the injected warts in the two groups

Rate of Clearance	Group A	Group B
Complete response	39	38
Partial response	5	4
No response	6	8
	Chi-squared value: 0.41 *p* value: 0.81	

Table 3: Rate of clearance of the distant warts in the two groups.

Rate of Clearance	Group A	Group B
Complete response	35	29
Partial response	9	5
No response	6	16
	Chi-squared value: 6.25 *p* value: 0.04	

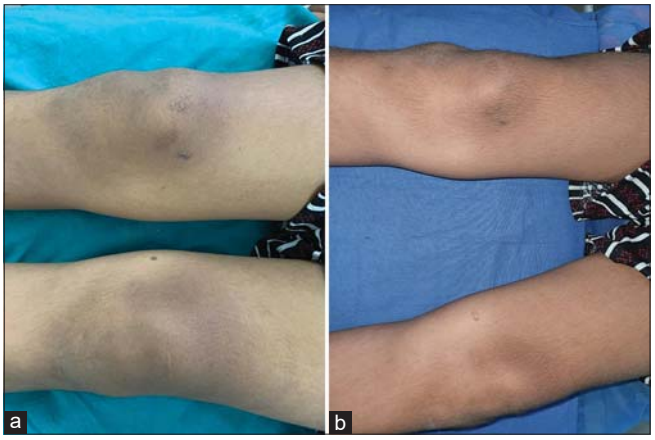


Figure 1: (a) Multiple verrucae on the knee at baseline (b) Complete clearance after three sessions of the PPD.

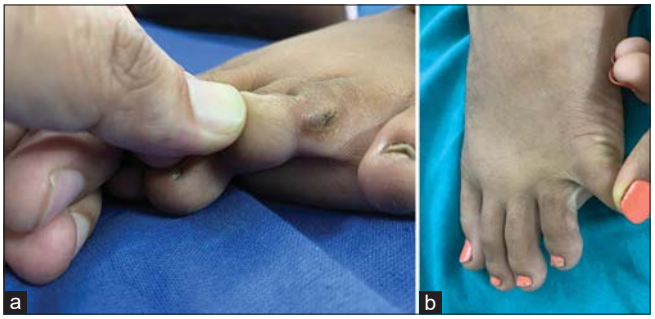


Figure 2: (a)Plantar wart at baseline. (b) Complete clearance after three sessions of vitamin D_3.

Immunotherapy overcomes the limitation of conventional therapies by stimulating the host's immunity against HPV. This ability makes this a potent

management option for multiple, recalcitrant warts or warts on sites that are difficult to treat, such as genital and periungual [12-14].

Both the PPD of tuberculin and vitamin D_3 are widely and easily available and hold promising prospects for managing recalcitrant and multiple warts.

In group A, as far as the injected warts are concerned, a complete response was observed in 39 patients. Due to the obligatory immunization programs of BCG vaccination in India, a majority of the population is already sensitized to mycobacterial antigens. Therefore, there is high PPD immunity in the population. Lahti et al. employed tuberculin jelly as a form of topical immunotherapy for verruca in the year 1982 with a 60% rate of clearance [15]. Abd-Elazeim et al. conducted a study similar to ours and found a 75% clearance rate with the PPD of tuberculin [16]. However, unlike our study, the average number of sessions required for complete clearance was 5.8. A study by Wananukul et al. assessed the efficacy of an intralesional PPD on palmoplantar and periungual warts [17]. They reported complete clearance in 93% of the patients. Kush et al. conducted a similar trial and found a 58.8% improvement in warts [18].

In group B, treated with vitamin D_3, among the injected warts, complete clearance was seen in 33 patients and, in distant warts, 29 patients showed complete clearance. There are only a handful of studies on the efficacy of vitamin D_3 on warts. The rate of response was reported to range from 40% to 90% [19-26]. The findings of our study were similar to the first study published on the role of intralesional vitamin D_3, which was conducted by Aktaş et al. [21]. They reported a complete response in 80% of the patients.

The first studies employing vitamin D_3 for managing warts were conducted by Kavya et al. [22] and Raghukumar et al. [23]. They reported a complete response in 78.57% and 90%, respectively. Various authors in the past conducted similar studies to compare the response of intralesional vitamin D_3 versus various other immunogens, such as MMR, *Candida*, and the PPD [19-26]. A study fairly similar to ours was done by Singh et al. [24], who compared the effectiveness of vitamin D_3 and the PPD of tuberculin on warts. They found a 72.5% response with vitamin D_3. Kareem et al. [26] compared vitamin D_3 versus *Candida* antigen and found a 70% response rate.

The adverse event profile of our patients was minimal, with only slight pain, pruritus, and transient fever reported by less than half of the study subjects. One rare adverse event from vitamin D_3 was the formation of granuloma, which resolved on its own in three months. None of the patients treated with the PPD developed flu-like symptoms, vasovagal syncope, or post-inflammatory pigmentation. Similarly, none of the patients in group B developed hypercalcemia. Due to the prior use of local anesthetic, none of the patients developed discomfort while intralesional injections of the antigens were given. Although, in the case of acral sites, vitamin D_3 injections tend to cause pruritus and pain more frequently.

Our study was limited by a small sample size, a short follow-up period, and a lack of immunological analysis.

CONCLUSION

Both the PPD of tuberculin and vitamin D_3 are reliable and safe management options for recalcitrant, treatment-resistant, and extensive warts. We advocate for these antigens to be employed as the first-line management options for warts.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Mohta A, Kushwaha RK, Agrawal A, Sharma MK, Gautam U, Jain SK. Evaluation of the efficacy of intralesional measles, mumps, and rubella vaccine with intralesional Vitamin D3 as immunotherapies in the treatment of recalcitrant cutaneous warts in adult: A randomized placebo-controlled study. Indian Dermatol Online J. 2021;12:879-87
2. Clifton MM, Johnson SM, Roberson PK, Kincannon J, Horn TD. Immunotherapy for recalcitrant warts in children using intralesional mumps or Candida antigens. Pediatr Dermatol. 2003;20:268-71.
3. Braaten KP, Laufer MR. Human papillomavirus (HPV), HPV-related disease, and the HPV vaccine. Rev Obstet Gynecol. 2008;1:2-10.
4. Lipke MM. An armamentarium of wart treatments. Clin Med Res. 2006;4:273-93.
5. Gupta S, Malhotra AK, Verma KK, Sharma VK. Intralesional immunotherapy with killed Mycobacterium w vaccine for the

treatment of ano-genital warts: An open label pilot study. J Eur Acad Dermatol Venereol. 2008;22:1089-93.
6. Scott M, Nakagawa M, Moscicki AB. Cell-mediated immune response to human papillomavirus infection. Clin Diagn Lab Immunol. 2001;8:209-20.
7. Nofal A, Nofal E. Intralesional immunotherapy of common warts: Successful treatment with mumps, measles and rubella vaccine. J Eur Acad Dermatol Venereol. 2010;24:1166-70.
8. Maronn M, Salm C, Lyon V, Galbraith S. One-year experience with candida antigen immunotherapy for warts and molluscum. Pediatr Dermatol. 2008;25:189-92.
9. Fathia M. Khattab, Mohamed M. Nasr. A comparative study of topical cantharidin and intralesional PPD to treat molluscum contagiosum. J Dermatol Treat. 2020;31:850-4.
10. Moscarelli L, Annunziata F, Mjeshtri A, Paudice N, Tsalouchos A, Zanazzi M, et al. Successful treatment of refractory wart with a topical activated vitamin D in a renal transplant recipient. Case Rep Transplant. 2011;2011:368623.
11. Liu PT, Stenger S, Li H, Wenzel L, Tan BH, Krutzik SR. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. Science. 2006;311:1770-3.
12. Shaldoum DR, Hassan GFR, El-Maadawy EH, El-Maghraby GM. Comparative clinical study of the efficacy of intralesional MMR vaccine vs intralesional vitamin D injection in treatment of warts. J Cosmet Dermatol. 2020;19:2033-40.
13. Fathy G, Sharara MA, Khafagy AH. Intralesional vitamin D3 versus Candida antigen immunotherapy in the treatment of multiple recalcitrant plantar warts: A comparative case-control study. Dermatol Ther. 2019;32:e12997.
14. Garg S, Baveja S. Intralesional immunotherapy for difficult to treat warts with Mycobacterium w vaccine. J Cutan Aesthet Surg. 2014;7:203-8.
15. Lahti A, Hannuksela M. Topical immunotherapy with tuberculin jelly for common warts. Arch Dermatol Res. 1982;273:153-4.
16. Abd-Elazeim FM, Mohammed GF, Fathy A, Mohamed RW. Evaluation of IL-12 serum level in patients with recalcitrant multiple common warts, treated by intralesional tuberculin antigen. J Dermatolog Treat. 2014;25:264-7.
17. Wananukul S, Chatproedprai S, Kittiratsacha P. Intralesional immunotherapy using tuberculin PPD in the treatment of palmoplantar and periungual warts. Asian Biomedicine. 2009;3:739-43.
18. Kus S, Ergun T, Gun D, Akin O. Intralesional tuberculin for treatment of refractory warts. J Eur Acad Dermatol Venereol. 2005; 19:515-6.
19. Mohta A, Kushwaha RK, Gautam U, Sharma P, Nyati A, Jain SK. A comparative study of the efficacy and safety of intralesional measles, mumps, and rubella vaccine versus intralesional vitamin D3 for the treatment of warts in children. Pediatr Dermatol. 2020;37:853-9.
20. Shaldoum DR, Hassan GFR, El-Maadawy EH, El-Maghraby GM. Comparative clinical study of the efficacy of intralesional MMR vaccine vs intralesional vitamin D injection in treatment of warts. J Cosmet Dermatol. 2020;19:2033-40.
21. Aktaş H, Ergin C, Demir B, Ekiz Ö. Intralesional vitamin D injection may be effective treatment option for warts. J Cutan Med Surg. 2016;20:118-22.
22. Kavya M, Shashikumar BM, Harish MR, Shweta BP. Safety and efficacy of intralesional vitamin D3 in cutaneous warts: An open uncontrolled trial. J Cutan Aesthet Surg. 2017;10:90-4.
23. Raghukumar S, Ravikumar BC, Vinay KN, Suresh MR, Aggarwal A, Yashovardhan DP. Intralesional vitamin D3 injection in treatment of recalcitrant warts: A novel proposition. J Cutan Med Surg. 2017;21:320-4.
24. Singh SK, Mohan A, Gupta AK, Pandey AK. A comparative study between intralesional PPD and vitamin D3 in treatment of viral warts. Int J Res Dermatol. 2018;4:197-201.
25. Abou-Taleb DAE, Abou-Taleb HA, El-Badawy O, Ahmed AO, Hassan AET, Awad SM. Intralesional vitamin D3 versus intralesional purified protein derivative (PPD) in treatment of multiple warts: A comparative clinical and immunological study. Dermatol Ther. 2019;29:e13034.
26. Kareem IMA, Ibrahim IM, Mohammed SFF, Ahmed AA. Effectiveness of intralesional vitamin D3 injection in the treatment of common warts: Single-blinded placebo-controlled study. Dermatol Ther.2019;32:e12882.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Comparative study on the effectiveness of intralesional Measles, Mumps, and Rubella vaccine and intralesional vitamin D3 injection in the treatment of verruca

Thambisetti Naresh Babu, Kota Sneha, Birudala Ramadevi, Bangaru Bhavani Pujitha, Kuna Ramadas

Department of Dermatology Venereology and Leprosy, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad-500068, India

Corresponding author: Kota Sneha, MD, E-mail: snehakota3@gmail.com

ABSTRACT

Background: Human papillomavirus (HPV) is the causative agent of verruca and is contagious, recurrent, and recalcitrant due to defects in cell-mediated immunity. No single mode of treatment is completely effective. The most commonly used treatment options are destructive and lead to scarring. The emerging new modality of treatment is immunotherapy, which acts by enhancing cell-mediated immunity (CMI) against HPV to clear treated as well as remote warts. **Objectives**: The objective was to compare the efficacy of intralesional Measles, Mumps, and Rubella (MMR) vaccine and intralesional vitamin D_3 in cutaneous warts. **Materials and Methods**: A randomized, hospital-based, single-blind study on forty patients divided into two groups (groups A and B), comprising twenty patients each, was conducted. In group A, intralesional MMR vaccine 0.5 mL was injected into the base of warts. In group B, intralesional vitamin D_3 0.5 mL was injected into the base of warts after achieving local anesthesia. Sessions were performed in two-week intervals for a maximum number of five sessions. The patients were followed for sixteen weeks. **Results**: In group A (MMR vaccine), a complete response was seen in 75% (15/20) of the patients, a moderate response in 15% (3/20), a partial response in 5% (1/20), and no response in 5% (1/20). In group B (vitamin D_3), a complete response was seen in 65% (13/20) of the patients, a moderate response in 15% (3/20), a partial response in 10% (2/20), and no response in 10% (2/20). No recurrence was noticed after follow-up in either of the two groups. **Conclusion**: Immunotherapy is an option that is easy, safe, cost-effective, and well-tolerated with minimal side effects.

Key words: Verruca; Intralesional MMR; Intralesional vitamin D_3; Immunotherapy

INTRODUCTION

Verrucae, or warts, are the benign epidermal growths of skin or mucosae caused by HPV with no envelope, containing double-stranded DNA (ds-DNA) [1].

HPVs are divided into various genotypes. Different HPV types infect either the cornified squamous epithelium of the skin or the non-cornified mucosa [2]. Some warts remit spontaneously, while others remain and may spread to other parts of the body [3]. Not all warts need treatment as many give little inconvenience and resolve spontaneously.

The available treatment options include topical salicylic acid, glutaraldehyde, formalin, imiquimod, 5-flurouracil, cantharidin, podophyllotoxin, and vitamin D analogs [4]. The systemic treatments include oral H2-receptor antagonists, oral zinc, oral retinoids, and IV cidofovir. The different agents employed in immunotherapy are *Candida* antigen, *Trichophyton* antigen, BCG vaccine, PPD, MMR vaccine, vitamin

How to cite this article: Babu TN, Sneha K, Ramadevi B, Pujitha BB, Ramadas K. Comparative study on the effectiveness of intralesional Measles, Mumps, and Rubella vaccine and intralesional vitamin D3 injection in the treatment of verruca. Our Dermatol Online. 2023;14(1):6-10.

Submission: 27.07.2022; **Acceptance:** 30.09.2022

DOI: 10.7241/ourd.20231.2

D_3, bleomycin, and interferons. Destructive procedures such as cryotherapy, electrosurgery, and laser lead to destructive scarring or dyspigmentation [5]. No single treatment is considered completely efficient.

A major role is played by cell-mediated immunity (CMI) in the clearance of warts. The principle of immunotherapy is by enhancing CMI, thereby clearing warts. Nowadays, immunotherapy is the preferred treatment option as it is safe and overcomes other complications. Its mechanism of action is by mounting a type IV hypersensitivity reaction and the production of Th1 cytokines, which activate cytotoxic and natural killer cells, thus eliminating the infection. Because of sensitization, we have an added benefit in the clearance of remote warts along with treated warts [6].

MATERIALS AND METHODS

This hospital-based, prospective, comparative, interventional study was conducted at the Department of DVL of Kamineni Academy of Medical Sciences and Research Centre in Hyderabad, India, after obtaining ethics committee approval on a total of forty patients. The patients were randomly divided into two groups (groups A and B) comprising twenty patients each. Group A was given intralesional MMR, whereas group B was given intralesional vitamin D_3.

Inclusion Criteria

Included were patients of both sexes suffering from verruca, aged between 12 and 70 years, consenting, and not having taken any treatment for their verruca in the past three months.

Exclusion Criteria

Excluded were patients not consenting, younger than twelve years or older than seventy years, pregnant and lactating females, patients with immunosuppression such as HIV and chronic renal, hepatic, and cardiovascular disorders, patients on immunomodulatory drugs, patients allergic to MMR vaccine, patients with a history of keloidal, hypertrophic scar tendency, and patients who had taken treatment in the past three months.

Methods

After detailed history taking and clinical examination, the patients were divided into two groups, twenty patients each.

In group A, under aseptic conditions, after reconstitution with distilled water, 0.5 mL of MMR vaccine was given with an insulin syringe to the base of the largest warts to a maximum of five warts in each session.

In group B, under aseptic conditions, under local anesthesia with 2% lignocaine, 0.5 mL of vitamin D_3 (600,000 IU) was given to the base of the largest warts with an insulin syringe to a maximum of five warts in each session.

The procedure was repeated every other week for a maximum number of five sessions. In each session, the response was noted (size, number, new lesions). Follow-up was performed up to sixteen weeks.

Treatment responses were classified as complete, moderate, partial, and no response (Table 1).

Ethics Statement

An institutional ethical committee certificate was taken.

RESULTS

All forty patients completed the study and their clinical and demographic data was recorded (Table 2).

In group A, the mean age was 24.4 years, ranging from 12 to 33 years. In group B, the mean age was

Table 1: Response grading.

Response	Definition
Complete response	100% clearance (of local and distant warts)
Moderate response	> 50% clearance
Partial response	< 50% clearance
No response	No clearance

Table 2: Demographic data of the patients in the two groups.

Data	Group A	Group B
Age range	12–33	14–52
Mean	24.4	29.6
Sex ratio (M:F)	4:1	4:1
Type of warts		
Verruca vulgaris	8	10
Palmo-plantar warts	8	6
Periungual warts	4	4
Number of warts		
Mean	5.4	6.4
Range	1–10	1–15
Duration of warts		
Mean	17.6 months	16.6 months
Range	6–36 months	5–35 months
Number of sessions		
Mean	4	3.2
Range	3–5	2–5

29.6 years, ranging from 14 to 52 years. The sex ratio (male-to-female) in both groups was 4:1. In group A, verruca vulgaris and palmoplantar warts were the most common types (40%), with periungual warts being 20%. In group B, the most common type was verruca vulgaris (50%), with palmoplantar and periungual warts being 30% and 20%, respectively.

In group A, the mean duration of warts was 17.6 months, ranging from 6 to 36 months. In group B, the mean duration of warts was 16.6 months, ranging from 5 to 35 months. In group A, the mean number of sessions performed was four, ranging from three to five. In group B, the mean number of sessions performed was 3.2, ranging from two to five.

In group A, a complete response was seen in 75% (15/20) of the patients, a moderate response in 15% (3/20), a partial response in 5% (1/20), and no response in 5% (1/20) (Fig. 1).

In group A, 25% (5/20) of the patients achieved a complete response in three sessions, 30% (6/20) achieved a complete response in four sessions, and 20% (4/20) achieved a complete response in five sessions.

In group A, the side effects observed were pain during the injection of MMR vaccine. No new lesions were noted in the follow-up period.

In group B, a complete response was seen in 65% (13/20) of the patients, a moderate response in 15% (3/20), a partial response in 10% (2/20), and no response in 10% (2/20) (Fig. 2).

In group B, 25% (5/20) of the patients achieved a complete response in two sessions, 25% (5/20) achieved a complete response in three sessions, and 15% (3/20) achieved a complete response in four sessions (Figs. 3 and 4).

In group B, the side effects observed were pain during injection and erythema on the injection site present for one week, which resolved spontaneously. No new lesions were noted in the follow-up period.

Figs. 5 and 6 show photographs of the improvements. Table 3 shows improvements in both groups.

DISCUSSION

Immunotherapy is the preferred option nowadays as it acts on cell-mediated immunity in the individual

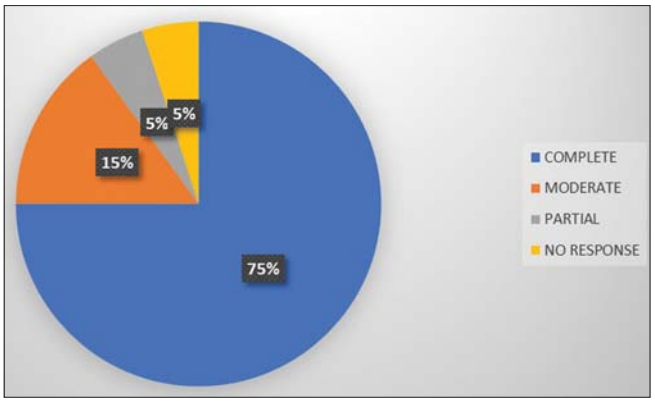


Figure 1: Pie diagram showing response rates in group A.

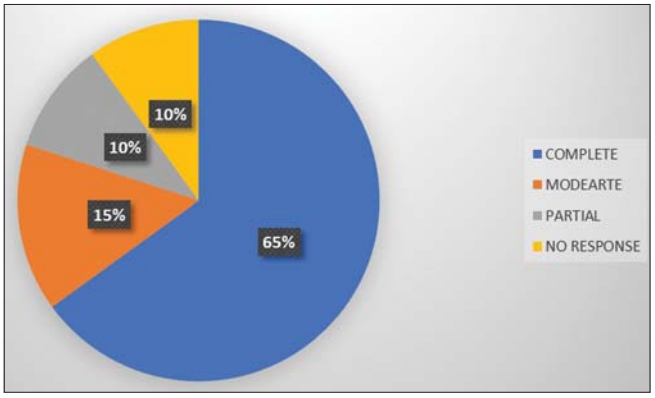


Figure 2: Pie diagram showing response rate in group B.

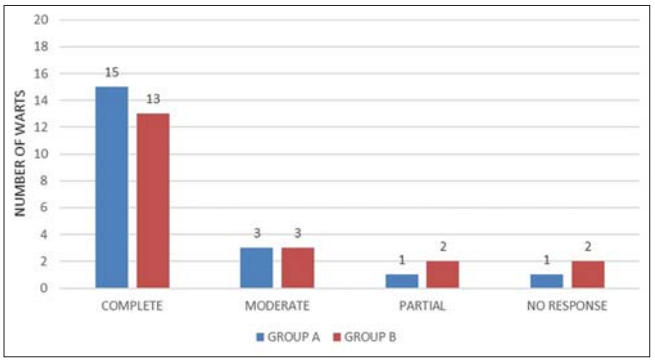


Figure 3: Graph showing clinical improvements in the two groups.

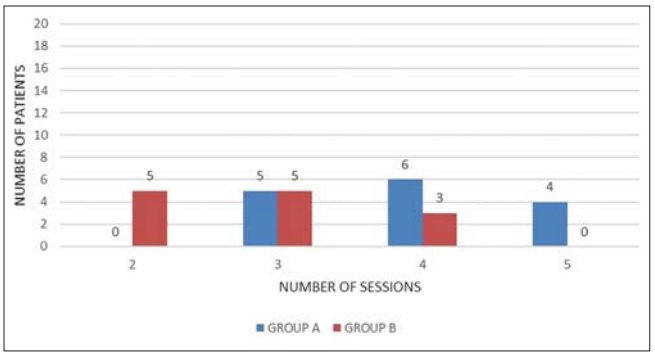


Figure 4: Graph showing patients achieving a complete response with respect to the number of sessions.

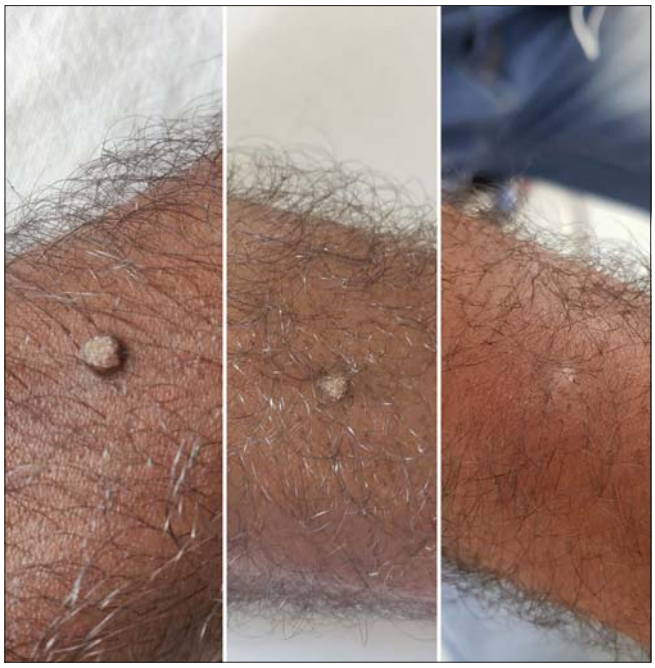


Figure 5: Before-and-after photographs of intralesional MMR vaccine.

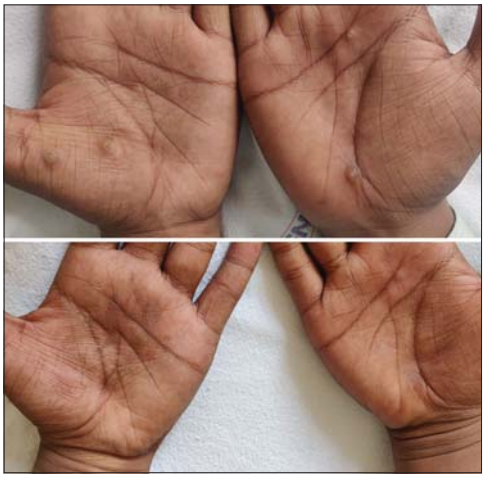


Figure 6: Before-and-after photographs of intralesional vitamin D_3.

Table 3: Percentages of responses in the two groups.

Response	Group A	Group B
Complete response	15 (75%)	13 (65%)
Moderate response	3 (15%)	3 (15%)
Partial response	1 (5%)	2 (10%)
No response	1 (5%)	2 (10%)

unlike other options, which usually concentrate on local clearance. Immunotherapy helps in the clearance of local and remote warts due to sensitization [7].

Various antigens are employed for immunotherapy, thus we chose two antigens in our study.

Injecting the MMR antigen causes the proliferation of peripheral blood mononuclear cells, stimulating a delayed, Th1-mediated hypersensitivity reaction and a release of interferon-gamma and interleukins 2 and 4. These cytokines activate cytotoxic T cells, which in turn stimulate tumor necrosis factor-alpha and IL1. This stimulation helps in the destruction of the HPV virus in both local and remote warts [8,9].

Vitamin D_3 regulates cell proliferation and the differentiation of keratinocytes, which inhibit hyperkeratosis by inhibiting cell replication. It also has immunoregulatory activity with the release of IL21, 42, IFN-γ, and TNF-α [10]. The mechanism of action of vitamin D_3 is by activating Toll-like receptors (TLRs) on macrophages, which stimulates the expression of vitamin D receptor (VDR) and vitamin D 1α hydroxylase leading to the activation of antimicrobial peptides. This activation contributes to the anti-inflammatory action of vitamin D_3 [11,12].

In our study, in group A (MMR vaccine), 75% showed a complete response, 15% showed a moderate response, 5% showed a partial response, and 5% showed no response. In a study by Hassan et al. [13], a complete response was seen in 80%, whereas a partial response, minimal response, and no response was seen in 6.67% each, which was in agreement with our study. Our study findings were also consistent with studies by Malhotra et al. [14] and Kadnur et al. [15], in which a complete response was noted in 76% and 70% of patients, respectively.

The mean number of sessions required in our study was four, with an average of two to five, which was consistent with other studies. There was no statistically significant relationship between age and sex with a treatment response as in other studies. Similarly to other studies, the most common complication noted in group A was pain on at the site of injection.

In our study, in group B (vitamin D_3), 65% showed a complete response, 15% showed a moderate response, 10% showed a partial response, and 10% showed no response. This was in agreement with a study by Hassan et al. [13], which showed a complete response in 66.7% of patients, a partial response in 6.67%, a minimal response in 20%, and no response in 6.67%. Our study findings were also consistent with studies conducted by Malhotra et al. [14] and Kadnur et al. [15], in which a complete response was noted in 60% and 52%, respectively.

The mean number of sessions required was 3.2, with an average of two to five, which was in agreement

Table 4: References with numbers of sessions and response rates.

Study	Vaccines	No. of Sessions	Response Rate
Hassan et al. [13]	MMR	6	80%
	vitamin D_3	6	66.7%
Bhadbhade et al. [16]	vitamin D_3	3	73.3%
	MR	5	66.7%
	PPD	5	30.7%
Kadnur et al. [15]	vitamin D_3	4	52%
	MMR	4	70%
Malhotra et al. [14]	MMR	3	76%
	vitamin D_3	3	60%
Our study	MMR	5	75%
	vitamin D_3	5	65%

with other studies. The most common complications noted were pain and persistent erythema, which faded spontaneously within a week, similarly to other studies [14-16].

Comparing intralesional MMR vaccine with intralesional vitamin D_3, no statistical significance was seen regarding the response. Yet, the number of sessions required was less in the case of vitamin D_3 when compared to MMR vaccine, which was consistent with a study by Hassan et al. [13]. Side effects were more pronounced in the case of vitamin D_3 when compared to MMR vaccine, which was in agreement with a study by Malhotra et al. [14].

Table 4 shows the various studies revealing comparative groups and treatment responses correlating with ours.

CONCLUSION

Immunotherapeutic treatment options are easy, safe, cost-effective, and well-tolerated with minimal side effects. The administration of vaccines in OPD itself is the advantage of immunotherapy. Both modalities of treatment are now preferred due to a decrease in recurrence, which is the significant problem with verruca.

The limitations of our study was a small sample size and a short follow-up period.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Lowy DR, Androphy EJ, Warts D. Warts. In: Freedberg I, Wolff K, et al., editors. Fitzpatrick's Dermatology in General Medicine, 5th edn. New York: McGraw Hill; 2003. p. 2119-31.
2. Sterling JC, Gibbs S, Haque Hussain SS, Hudson PM. British Association of Dermatologists' guidelines for the management of cutaneous warts 2014. Br J Dermatol. 2014;171:696-712.
3. Choi JW, Cho S, Lee JH. Does immunotherapy of viral warts provide beneficial effects when it is combined with conventional therapy? Ann Dermatol. 2011;23:282-7.
4. López-López D, Agrasar-Cruz C, Bautista-Casasnovas A, Carlos J Alvarez-Castro. Application of cantharidin, podophyllotoxin, and salicylic acid in recalcitrant plantar warts: A preliminary study. Gac Med Mex. 2015;151:14-8.
5. Dhakar AK, Dogra S, Vinay K, Sarangal R. Intralesional Mycobacterium w vaccine versus cryotherapy in treatment of refractory extragenital warts: A randomized, open-label, Comparative Study. J Cutan Med Surg. 2016;20:123-9.
6. Alikhan A, Griffin JR, Newman CC. Use of Candida antigen injections for the treatment of verruca vulgaris: A two-year mayo clinic experience. J Dermatolog Treat. 2016;27:355-8.
7. Goihman-Yahr M, Goldblum OM. Immunotherapy and warts: A point of view. Clin Dermatol. 2008;26:223-5.
8. Na CH, Choi H, Song SH, Kim MS, Shin BS. Two-year experience of using the measles, mumps and rubella vaccine as intralesional immunotherapy for warts. Clin Exp Dermatol. 2014;39:583-9.
9. Saini S, Dogra N, Dogra D. A prospective randomized open label comparative study of efficacy and safety of intralesional measles, mumps, rubella vaccine versus 100% trichloroacetic acid application in the treatment of common warts. Int J Res Med Sci. 2016;4:1529-33.
10. Aktaş H, Ergin C, Demir B, Ekiz O. Intralesional vitamin D injection may be an effective treatment option for warts. J Cutan Med Surg. 2016;20:118-22.
11. Kareem IMA, Ibrahim IM, Mohammed SFF, Ahmed AB. Effectiveness of intralesional vitamin D3 injection in the treatment of common warts: Single-blinded placebo-controlled study. Dermatol Ther. 2019;32:12882.
12. Hagaman JT, Panos RJ, McCormack FX, Thakar CV. Vitamin D deficiency and reduced lung function in connective tissue-associated interstitial lung diseases. CHEST J. 2011;139:353-60.
13. Shaldoum DR, Hassan GFR, El Maadawy EH, El-Maghraby GM. Comparative clinical study of the efficacy of intralesional MMR vaccine vs intralesional vitamin D injection in the treatment of warts. J Cosmet Dermatol. 2020;00:1-8.
14. Mittal N, Malhotra SK, Singh NR. Relative efficacy and safety of intralesional measles mumps rubella vaccine (MMR) and intralesional vitamin D in multiple and recalcitrant verrucae vulgaris. IP Indian J Clin Exp Dermatol. 2021;7:158-63.
15. Jartarkar SR, Kadnur M, Mamatha P, Mishra SS, Spoorthy B. A comparative study of therapeutic efficacy of intralesional measles, mumps, and rubella vaccine and intralesional Vitamin D3 in the treatment of recurrent warts. J Dermatol Dermatol Surg. 2021;25:14-7
16. Ahmed R, Bhadbhade SP, Noojibail B, Shetty SM, Varghese A. Comparative study in efficacy and safety of intralesional injections of vitamin D3, measles-rubella (MR) vaccine, and purified protein derivative (PPD) in the management of cutaneous warts. J Cutan Aesthet Surg. 2020;13:326-32.

Source of Support: This article has no funding source, **Conflict of Interest:** The authors have no conflict of interest to declare.

Our Dermatology Online

Original Article

Intralesional measles-mumps-rubella vaccine in recurrent common warts: A placebo-controlled study

Shishira R Jartarkar, Manjunath Kadnur, Spoorthy Babu, Swayamsidda Mishra

Department of Dermatology, Venereology, and Leprosy, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, India

Corresponding author: Spoorthy Babu, MD, E-mail: bspoorthy94@gmail.com

ABSTRACT

Background: Cutaneous warts cause immense an burden to patients as well as physicians. Although most resolve spontaneously within two years, treatment is sought for pain alleviating and cosmetic reasons. Various modalities of treatment are known. The destructive methods are unsuitable for multiple warts and are associated with chances of recurrence, scarring, and pain. In contrast, immunotherapy boosts the host immune response against the virus and helps in clearance, even in distant warts, without scars or physical change. This study was undertaken to assess the efficacy of intralesional MMR vaccine in multiple recurrent common warts. **Materials and Methods:** Sixty-six patients with recurrent common warts were divided equally into two groups. In group one, 0.5 mL of the MMR vaccine and, in group two, 0.5 mL of normal saline were injected intralesionally into the base of the largest wart. The sessions were repeated once in two weeks for a maximum of four sessions. The patients were followed up for twelve months to detect recurrences. **Results:** Complete clearance of warts was noted in 75.76% ($n = 25$) of the patients in the study group, whereas, in the control group, 78.79% ($n = 26$) patients showed no response. The result was statistically significant ($p < 0.01$). **Conclusion**: Intralesional MMR is a safe and effective treatment option for recurrent common warts with minimal side effects.

Key words: viral warts; intralesional MMR vaccine; immunotherapy

INTRODUCTION

Warts are common epidermal proliferations caused by human papilloma virus (HPV) [1]. There are around 180 strains of HPV known to infect epithelial cells with a predilection toward cutaneous and mucosal surfaces [2]. Morphologically, they are classified as verruca vulgaris, plane, filiform, myrmecia, and mosaic warts. Meanwhile, based on their location, they are divided into plantar, palmar, periungual, and anogenital warts [3]. Despite the availability of a wide range of treatment options ranging from medical agents to surgical excision, they pose a therapeutic challenge because of their recurrent nature [4]. These modalities also carry some drawbacks, such as discomfort, scarring, and inefficiency to treat multiple warts [4,5]. However, immunotherapeutic modalities stimulate the host immune system, mainly cell-mediated immunity, which helps in removing the virus without scars or physical change. Various antigens have been attempted both intralesionally and orally, such as vitamin D, interferon, purified protein derivative (PPD), candida antigen, and oral drugs such as levamisole, zinc, and cimetidine [6].

The MMR vaccine is a live attenuated vaccine that provides protection against measles, mumps, and rubella. The intralesional MMR vaccine aids in the clearance of warts via its immunomodulatory action and the stimulation of both humoral and cell-mediated immunity [7].

The aim of this study was to evaluate the safety and efficacy of intralesional MMR injection in multiple recurrent common warts.

How to cite this article: Jartarkar SR, Kadnur M, Spoorthy B, Mishra S. Intralesional measles-mumps-rubella vaccine in recurrent common warts: A placebo-controlled study. Our Dermatol Online. 2023;14(1):11-15.

Submission: 25.05.2022; **Acceptance:** 17.08.2022

DOI: 10.7241/ourd.20231.3

MATERIALS AND METHODS

Study Design

This was a hospital-based, single-blind, placebo-controlled, interventional study conducted in the outpatient department of dermatology from June 2018 to January 2020 after obtaining clearance from our institutional ethics committee.

Patients

Sixty-six patients with multiple recurrent common warts were enrolled in the study after obtaining an informed written consent. The patients were divided randomly into two groups with the "chit in the box" method, each containing 33 patients.

Inclusion Criteria

Included were patients with multiple recurrent common warts of different sizes and duration with or without distant warts, willing to provide informed written consent.

Exclusion Criteria

Excluded were the following: children younger than twelve years old, pregnant and lactating females, patients with a keloidal tendency, anogenital warts, patients who had received treatment in the prior four weeks, patients with immunosuppression, a systemic or dermatological disorder, or hypersensitivity to the MMR vaccine.

Method

All patients underwent a protocol of complete history taking and systemic and cutaneous examination.

Complete history taking included the demographic details and present history (disease duration, presence or absence of distant warts, drug intake, systemic illnesses).

The cutaneous examination included the assessment of the common warts, their number, sizes, and the presence or absence of distant warts.

Thorough general and systemic examinations were performed to exclude systemic diseases.

All patients were subjected to HIV testing, with pre- and post-test counseling; those who tested negative were included in the study.

Photographs were taken prior to treatment (baseline) and on each visit.

Group One (Study Group)

Tresivac (freeze-dried MMR vaccine) in single-use vials stored at 2–8°C was employed. It was reconstituted with 0.5 mL of distilled water. Under aseptic precautions, 0.5 mL of MMR vaccine was injected intralesionally into the base of the largest wart with a 30G insulin syringe.

Group Two (Control Group)

Under aseptic precautions, 0.5 mL of normal saline was injected into the base of the largest wart.

Procedure

After cleaning the lesions with povidone-iodine and spirit, injections were given only into the base of the largest wart with a 40-U insulin syringe. The syringe was held parallel to the skin surface and the needle was held with the bevel facing upwards while injecting in all patients. In both groups, the injections were repeated every two weeks until complete clearance or for a maximum of four sessions.

The patients were followed up for twelve months after the last dose to detect recurrences. The patients were evaluated for clearance of warts and adverse effects.

Post-Treatment Care

No other treatments for cutaneous warts were employed concurrently or during the follow-up period.

Assessment of Improvement

The clinical improvement was assessed with color photographs taken at baseline, on each session, and twelve months after the last session.

The clinical improvement was graded as:

- complete clearance: the disappearance of warts with normal-looking skin;
- partial response: a reduction in size and/or number of the warts;
- no response: no change in size or number.

Statistical Analysis

The statistical analysis was performed with the SPSS software, version 22. Frequencies and percentages were

employed for categorical variables, whereas means were employed for quantitative variables. The Chi-squared test and *t*-test were performed. A p value below 0.05 was considered significant.

RESULTS

All 66 patients completed the study. The patients were comparable with respect to age and sex ($p > 0.05$). The number and location of warts observed in our study were noted (Table 1 and Graph 1). The mean age in the study group (group one) was 29.1 ± 6.46 and, in the control group (group two), it was 28.7 ± 6.72. In our study, we noticed a male predominance in both groups: in the study group, 18 patients (54.55%) and, in the control group, 17 patients (51.52%) (Table 2).

In the study group, complete clearance was noted in 75.76% ($n = 25$) (Fig. 1), and partial clearance was noted in 15.5% ($n = 5$) of the patients. No improvement was noted in 9.1% ($n = 3$) of the patients (Fig. 2). The mean number of injections required for complete clearance of warts was 3.24.

In the control group, 78.79% ($n = 26$) of the patients showed no improvement and 15.15% ($n = 5$) showed partial improvement. Only 6.06% ($n = 2$) of the patients showed complete response (Graph 2). The difference in improvement was statistically highly significant ($p < 0.01$. The complete resolution of distant warts was noted in all patients who had a complete response (Table 3).

Table 1: Numbers and sites of the warts

Site	Number of Warts
Dorsum of the foot	4
Dorsum of the hand	4
Palms	22
Palm and dorsum of the hand	12
Palmoplantar	8
Periungual	8
Extensive	8

Table 2: Demographic data of the participants

Clinical Parameter	Group One	Group Two
Age (mean ± SD) (yrs.)	29.1 ± 6.46	28.7 ± 6.72
Sex		
Male	18 (54.55%)	17 (51.52%)
Female	15 (45.46%)	16 (48.49%)
Duration		
< 6 months	6 (18.19%)	7 (21.21%)
6–12 months	12 (36.37%)	13 (39.4%)
>12 months	15 (45.46%)	13 (39.4%)
Number of warts (mean ± SD)	7.8 ± 5.42	8.1 ± 5.20

Side Effects

Pain during injection was noted in 81.82% ($n = 27$) of the patients in the study group and in 21.21% ($n = 7$) in the controls. Flu-like symptoms were noted in 12.12% ($n = 4$) of the patients, which subsided spontaneously within 48–72 hours. The patients were followed up for twelve months and there was no recurrence in patients with the complete resolution of warts.

DISCUSSION

Recurrent multiple warts bring social stigma to the patient as well as a challenge to the dermatologist. No single therapy had proven to be completely effective, especially if numerous and distant lesions are considered.

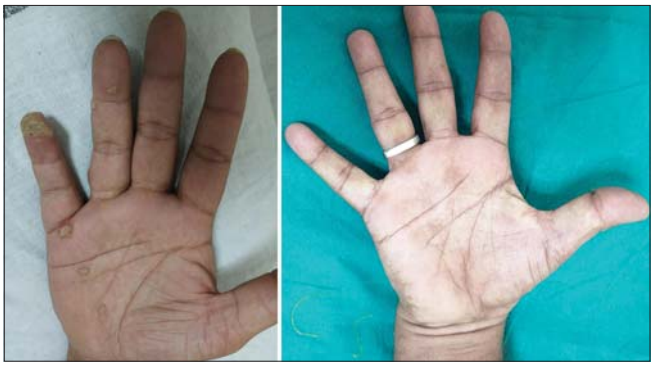


Figure 1: A 30-year-old male with warts on the palms and periungual area, showing complete improvement after three sessions of intralesional MMR vaccine.

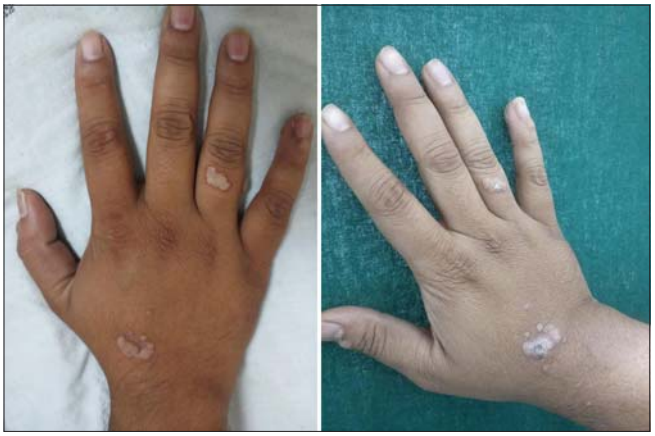
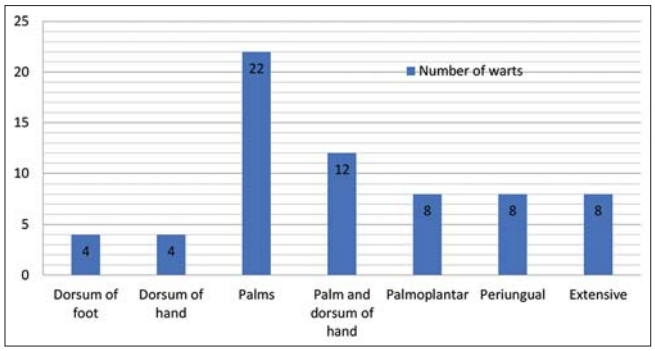


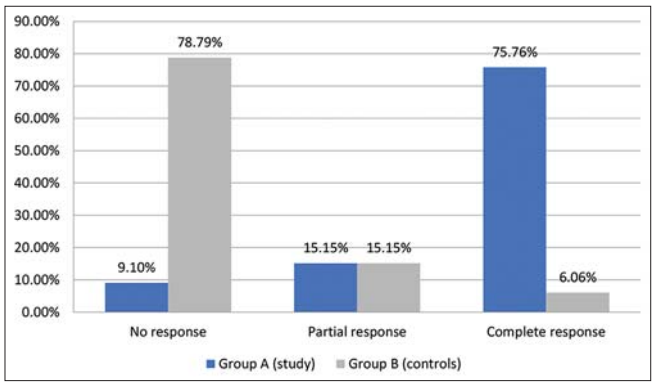
Figure 2: A 30-year-old male with multiple common warts on the dorsum of the hand, showing no improvement after four sessions of intralesional MMR vaccine.

Table 3: Clinical improvement in the cases and controls

Clinical Improvement	Group One: % (*n*)	Group Two: % (*n*)
No response	9.1% (3)	78.79% (26)
Partial response	15.15% (5)	15.15% (5)
Complete response	75.76% (25)	6.06% (2)



Graph 1: Numbers and sites of the warts.



Graph 2: Clinical improvement in the cases and controls.

Immunotherapy is a type of biological therapy that employs substances to modify the immune response to help the body to fight an infection, cancer, or autoimmune disease [8].

It is a preferred treatment option due to its effect on both treated and distant warts by inducing HPV-targeted immunity. Intralesional MMR stimulates the adaptive immune system and activates natural killer (NK) cells. It induces a type 1 helper T-cell mediated delayed-hypersensitivity reaction against the antigen and the HPV-infected cells. This causes the destruction of the virus and infected host cells, not only in the treated warts yet also the distant warts [9,10]. The MMR vaccine is more immunogenic than other skin test antigens. Due to the presence of three synergistic viral antigens, a stronger immune response against HPV is generated via the production of cytokines such as interleukin (IL)-2,4,5 and TNF-α [11,12].

Our study revealed that intralesional MMR vaccine is an effective therapy for multiple recurrent common warts. Twenty-five out of the thirty-three patients (75.76%) showed the complete clearance of warts. Comparable results were reported by Chauhan et al., with 82.4% (42/51) of patients showing complete clearance [13]. Similar results were also observed by Nofal et al., with 81.4% of patients achieving complete healing [14]. Intralesional MMR vaccine was found to be safer and more effective than cryotherapy in a study conducted by Abd El-Magiud et al. [15].

During the follow-up period of twelve months, no recurrence was noted in our study group, which was in concordance with Nofal et al., who reported no recurrence in the MMR group after six months [14].

A placebo-controlled study by Awal and Kaur using 0.5 mL of intralesional MMR vaccine every two weeks for a maximum of five sessions showed complete clearance in 68% of patients [12].

A prospective, randomized study by Saini et al. comparing the efficacy of 0.3 mL intralesional MMR vaccine and 100% topical TCA every two weeks for a total of three sessions noted a more than 75% improvement in 49.43% of patients, with 26.44% showing complete response in the MMR group. Meanwhile, 11.11% had a more than 75% improvement, with only 7.94% showing complete resolution in the TCA group [9].

Pain during injection and flu-like symptoms were the side effects reported by our patients. This was comparable to various other studies [9,12,13]. The limitation of our study was a small sample size.

CONCLUSION

Intralesional MMR vaccine for common warts appears to be a simple, safe, and promising treatment modality with a low recurrence rate. The eradication of distant warts with no scarring and pigmentation are its added benefits. However, further, large, well-designed case–control studies are required to delineate the dosing regimen and duration for its effective use.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Stanley MA. Epithelial cell responses to infection with human papillomavirus. Clin Microbiol Rev. 2012;25:215-22.
2. Groves IJ, Coleman N. Pathogenesis of human papillomavirus-associated mucosal disease. J Pathol. 2015;235:527-38.
3. Salman S, Ahmed MS, Ibrahim AM, Mattar OM, El-Shirbiny H, Sarsik S, Afifi AM, Anis RM, Yakoub Agha NA, Abushouk AI. Intralesional immunotherapy for the treatment of warts: A network meta-analysis. J Am Acad Dermatol. 2019;80:922-30.e4.
4. Bacelieri R, Johnson SM. Cutaneous warts: An evidence-based approach to therapy. Am Fam Physician. 2005;72:647-52.
5. Rivera A, Tyring SK. Therapy of cutaneous human papillomavirus infections. Dermatol Ther. 2004;17:441-8.
6. Vender R, Bourcier M, Bhatia N, Lynde C. Therapeutic options for external genital warts. J Cutan Med Surg. 2013;17 Suppl 2:S61-7.
7. Zamanian A, Mobasher P, Jazi GA. Efficacy of intralesional injection of mumps-measles-rubella vaccine in patients with wart. Adv Biomed Res. 2014;3:107.
8. Thappa DM, Chiramel MJ. Evolving role of immunotherapy in the treatment of refractory warts. Indian Dermatol Online J. 2016;7:364-70.
9. Saini S, Dogra N, Dogra D. A prospective randomized open label comparative study of efficacy and safety of intralesional measles, mumps, rubella vaccine versus 100% trichloroacetic acid application in the treatment of common warts. Int J Res Med Sci. 2016;4:1529-33.
10. Johnson SM, Horn TD. Intralesional immunotherapy for warts using a combination of skin test antigens: A safe and effective therapy. J Drugs Dermatol. 2004;3:263-5.
11. Na CH, Choi H, Song SH, Kim MS, Shin BS. Two-year experience of using the measles, mumps and rubella vaccine as intralesional immunotherapy for warts. Clin Exp Dermatol. 2014;39:583-9.
12. Awal G, Kaur S. Therapeutic outcome of intralesional immunotherapy in cutaneous warts using the mumps, measles, and rubella vaccine: A randomized, placebo-controlled trial. J Clin Aesthet Dermatol. 2018;11:15-20.
13. Chauhan PS, Mahajan VK, Mehta KS, Rawat R, Sharma V. The efficacy and safety of intralesional immunotherapy with measles, mumps, rubella virus vaccine for the treatment of common warts in adults. Indian Dermatol Online J. 2019;10:19-26.
14. Nofal A, Nofal E. Intralesional immunotherapy of common warts: Successful treatment with mumps, measles and rubella vaccine. J Eur Acad Dermatol Venereol. 2010;24:1166-70.
15. Abd El-Magiud EM, Abd El-Samea GM, Gaber HD. Intralesional injection of measles, mumps, and rubella vaccine versus cryotherapy in treatment of warts: A randomized controlled trial. Dermatologic Therapy. 2020;33:e13257.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Severity of acne and quality of life of patients treated at Cameroonian hospitals (sub-Saharan Africa)

Emmanuel Armand Kouotou[1,2], Ulrich Nguena Feungue[3], Dahlia Noelle Tounouga[1,4], Audrey Sandra Ngoune Madjoukeng[2], Grâce Anita Nkoro[2], Berline Odette Sigha[5], Rose Kotto Ekambi[6], Anne Cécile Zoung-Kanyi Bissek[2]

[1]Yaoundé Central Hospital, Cameroon, [2]Faculty of Medicine and Biomedical Sciences, Yaoundé, Cameroon, [3]University Teaching Hospital of Treichville, Abidjan, Ivory Coast, [4]Faculty of Health Sciences, Cotonou, Benin, [5]Faculty of Health Sciences, Bamenda, Cameroon, [6]Faculty of Medicine and Pharmaceutical Sciences, Douala, Cameroon

Corresponding author: Ulrich Nguena Feungue, MD, E-mail: feungueulrich@yahoo.fr

ABSTRACT

Background: The aim of this study was to assess the severity of acne and the impact on the quality of life (QoL) of patients undergoing anti-acne treatment. **Methods:** This was a cross-sectional study conducted from January to April 2017 at three hospitals in Yaoundé. Patients suffering from acne and under treatment were consecutively included. Clinical severity and QoL were assessed with the ECLA and CADI scales, respectively. Data was analyzed with SPSS 23.0. We employed the ANOVA test and linear regression to search for associations between variables. The significance level was at 5%. **Results:** We recruited 113 patients, predominantly female (83%), with a mean age of 26.0 ± 6.4 years. Mild-to-moderate forms were predominant (74%). The mean ECLA score was 10.1 ± 4.6, with a majority of the participants 74.3% (84/113) having mild-to-moderate acne, while 25.7% (29/113) had severe acne. The majority of the patients found the treatment expensive (69%). Therapeutic education had been conducted in 46.9% of the patients, and 60.2% of them reported a relapse during treatment. An impairment in QoL was found in 99% of the patients. The mean global QoL score was 6.3 ± 3.4. The impairment in QoL was positively correlated with clinical severity ($r = 0.40$; $p = 0.003$). **Conclusion:** The study revealed a predominance of mild-to-moderate forms of acne, an alteration in the QoL of almost all patients studied, and a positive correlation between the clinical severity of acne and the impairment in QoL.

Key words: Acne; Clinical severity; Quality of life; Treatment; Cameroon; Sub-Saharan Africa

BACKGROUND

Acne is a chronic inflammatory pathology of the pilosebaceous follicle that progresses in flare-ups [1]. It is a visible dermatological condition [2]. It usually begins at puberty and affects between 40% and 80% of adolescents and may persist beyond adolescence or, to a lesser extent, appear in adulthood [3]. In Cameroon, Kouotou et al. found a prevalence of acne of 74.8% among educated adolescents in 2015 [4].

There are various clinical presentations of acne, among which are retentional lesions (consisting of microcysts and open comedones), superficial and deep inflammatory lesions, and scar lesions. The polymorphic clinical expression may be severe and may bear a negative impact on the quality of life (QoL) of patients and lead to psychiatric consequences, in particular, anxiety, depression, and even suicide, as demonstrated in a metanalysis by Samuels et al. in 2020 [5]. In fact, these lesions appear in adolescence, when self-esteem begins to emerge, which may affect self-confidence and the quality of relationships with others [5-7].

In Cameroon, several years ago, Kouotou et al. found a negative impact of acne on the QoL of patients as well as

How to cite this article: Kouotou EA, Nguena Feungue U, Tounouga DN, Ngoune Madjoukeng AS, Nkoro GA, Sigha BO, Kotto Ekambi R, Zoung-Kanyi Bissek AC. Severity of acne and quality of life of patients treated at Cameroonian hospitals (sub-Saharan Africa). Our Dermatol Online. 2023;14(1):16-22.
Submission: 07.06.2022; **Acceptance:** 30.08.2022
DOI: 10.7241/ourd.20231.4

an association of acne with anxiety and depression [7]. The aim of this study was to evaluate the severity of acne and to assess its impact on the QoL of patients already under treatment in the Cameroonian context, a country in sub-Saharan Africa.

MATERIALS AND METHODS

Type, Place, and Duration of the Study

This was a four-month (from January to April 2017), descriptive and analytical, cross-sectional study conducted at three hospitals in Yaoundé, Cameroon. These hospitals were chosen by convenience based on the availability of a dermatologist: Biyem-Assi District Hospital (HDBA), Elig-Essono District Medical Center (CMA-EE), and Yaoundé Hospital and University Center (CHUY).

Study Population and Selection Criteria

We included patients with acne seen at the aforementioned hospitals: 1) presenting for a follow-up consultation after a medical prescription for an anti-acne medication initiated at least one month earlier; 2) received in dermatology consultation after failure of a current anti-acne treatment or withdrawn less than a month earlier; and 3) having given their informed consent to participate in the study.

Sampling

Sampling was consecutive and exhaustive during the study period. The minimum sample size was calculated with the Cochrane formula for descriptive studies considering a prevalence of 7.7% of acne reported at Cameroonian hospitals by Bissek et al. [8] and a degree of precision of 0.05, hence a minimum number of 109 participants.

Procedures

Data Collection

Data collection was performed with a technical sheet and took place in several stages.

1) Recruitment of participants: During dermatological consultations, the patients fulfilling the selection criteria were selected for the study.
2) Clinical examination: The questionnaire searched for sociodemographic characteristics, acne history and its treatment, and treatment costs. A physical examination allowed the description and classification of the clinical type and the assessment of severity with the acne lesion rating scale (ECLA) grid.
3) Evaluation of the impact of acne on QoL with a Cardiff Acne Disability Index (CADI) questionnaire.

Data Collection Tools

Technical Form

The technical form included sociodemographic characteristics (age, sex, profession, level of education), the history of acne, the clinical type, and the ECLA grid with its three factors (F1, F2, and F3) [9].

CADI Questionnaire (Quality-of-Life Assessment)

Employed was the CADI questionnaire: a QoL grid designed to assess QoL in adolescents and adults with acne containing a total of five items [10].

Interpretation of Scales

Interpretation of the Acne Lesion Rating Scale

The total score was obtained by adding the scores of the factors F1, F2, and F3, ranging from 0 to 36. An ECLA score less than or equal to 12 represented mild-to-moderate acne, while a score greater than 12 represented severe acne.

Interpretation of the CADI Quality-of-Life Score

The score for each response ranged from 0 to 3 points for each question. The CADI score was calculated by adding the score for each question, varying from 0 to 15. The interpretation was as follows: 1) 0: no alteration in QoL; 2) 1–5: mild alteration in QoL; 3) 6–10: moderate alteration in QoL; 4) 11–15: severe alteration QoL.

Statistical Analysis

The data collected was analyzed with SPSS, version 23.0, and Microsoft Excel 2013. The results of our study were presented in the form of tables and figures and expressed, on one hand, in terms of means ± standard deviations for the quantitative variables and, on the other, numbers and percentages for the qualitative variables. Simple linear regression was employed to assess the relationship between the ECLA score and the CADI score. We employed the ANOVA test to search for associations between sociodemographic factors and the CADI score. A p value < 0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

We obtained ethical clearance from the Institutional Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences. Research authorizations were obtained from the competent authorities of the hospitals. We conducted our study in strict accordance with the fundamental principles of the Declaration of Helsinki on research involving human subjects.

Thus, the patients and their parents or guardians for minors were informed about the various aspects of the study, the objective and the benefit, in particular, therapeutic education and the awareness of nursing staff on the psychological impact of acne. Their signed informed consent was obtained. We ensured the anonymity of the participants and the confidentiality of the information collected, which was used only for scientific purposes. Our study presented no risk to the participants.

RESULTS

Sociodemographic Characteristics

During the study period, 1930 patients were seen in dermatology consultation. Among these, we recruited 113 participants, predominantly female (83.2%), with a sex ratio of 0.2. The mean age was 26.0 ± 6.4 years, with extremes of 8 and 48 years.

Students were the most represented (57.5%) in our sample. We also noted a predominance of the higher school education level (70.8%) (Table 1).

Table 1: Sociodemographic characteristics (*n* = 113)

Item	Number (*n*)	Percentage (%)
Age (yrs.)		
≤ 18	10	8.9
19–25	51	45.1
> 25	52	46.0
Sex		
Male	19	16.8
Female	94	83.2
Profession		
Student	65	57.5
Employed	40	35.4
Unemployed	8	7.1
Education		
Primary	7	6.2
Secondary	26	23.0
University	80	70.8

Acne most often began between the ages of fifteen and eighteen (36/113; 31.9%). In addition, in 7.2% of the cases (8/113), acne began after the age of thirty (Fig. 1).

HISTORY OF ACNE IN PATIENTS ON TREATMENT

Duration of Treatment

During the study, 48% of the patients had been treated for one to three months (Fig. 2).

Types of Treatments and Side Effects

In our sample, 44/113 (38.9%), 15/113 (13.3%), and 54/113 (47.8%), respectively, had undergone local treatment, oral treatment, and a combination of oral and local treatments.

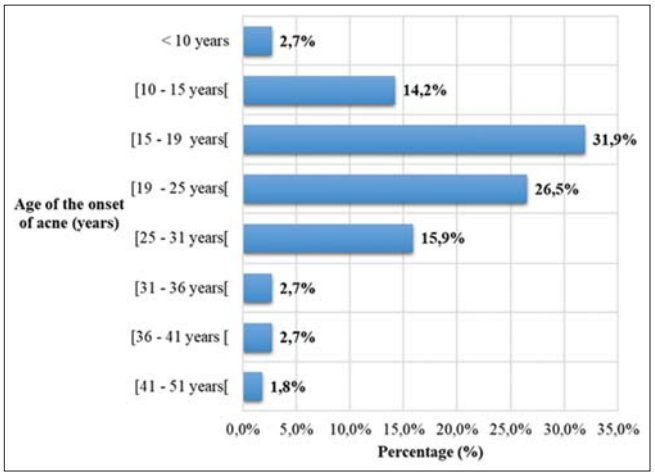


Figure 1: Age of the onset of acne at inclusion (*n* = 113).

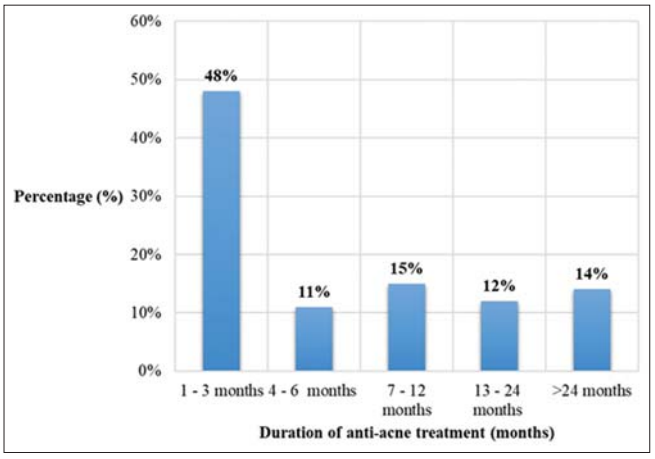


Figure 2: Duration of anti-acne treatment at inclusion (*n*=113)

Local Treatment

The most often prescribed drugs were retinoids (27.9%), followed by antibiotics (23.3%) and glycolic acid + retinaldehyde (12.8%). The most common side effects were exacerbation of acne (51.6%), followed by skin dryness and irritation (45.2%).

Oral Treatment

The most prescribed drugs were oral antibiotics (78.6%), followed by isotretinoin (20.0%). Side effects were reported in fifteen patients (13.3%): the most common were dry lips and mouth in ten out of the fourteen patients receiving isotretinoin (71.4%), as well as the exacerbation of acne (20%).

Previous Treatments

Among the 113 patients, 82 (72.6%), 23 (20.4%), and 8 (7.1%), respectively, had already experienced *1 to 2 cures*, *3 to 4 cures*, and *at least 5 cures* of treatments prior to the inclusion in our study.

Cost Evaluation

The cost of acne treatment was considered highly expensive by the majority of the patients (78/113; 69%) and affordable by 31%.

Assessment of Drug Availability

Systemic drugs remained available for the majority of the patients (79/113; 69.9%) unlike topical drugs (40/113; 35.4%).

Improvement on Treatment

Improvement in the lesions on treatment was noted by 90/113 patients (79.6%). In contrast, 14/113 patients (12.4%) saw no improvement, and 9/113 (8%) noted the worsening of their lesions (Table 2).

Identification of Clinical Forms and Assessment of Acne Severity

Papulopustular acne was the most common clinical form (54/113; 47.8%). The other clinical forms found were retentional acne (34/113; 30.1%), nodular acne (15/113; 13.3%), pigmentogenic acne (5/113; 4.4%), and acne fulminans (1/113; 0.9%). We found post-inflammatory scars in 4/113 (3.5%) patients.

Table 2: History of acne (history, treatment, relapses) (n = 113)

Items	Number (n = 113)	Percentage (%)
Psychologic or psychiatric history		
Yes	4	3.5
No	109	96.5
Therapeutic education		
Yes	56	49.6
No	57	50.4
Relapses under treatment		
Yes	68	60.2
No	45	39.8
Number of relapses		
[1-2]	49	72.1
[3-4]	16	23.5
[5-6]	2	2.9
[7-10]	1	1.5

The clinical assessment of severity with the ECLA score produced an average of 10.1 ± 4.6. In sum, a majority of the participants (84/113; 74.3%) had mild-to-moderate acne, while 25.7% (29/113) had a severe form.

QUALITY OF LIFE OF PATIENT WITH ACNE ON TREATMENT AND ASSOCIATED FACTORS

Quality of Life

The mean overall QoL score was 6.3 ± 3.4, with extremes of 0 and 15. In our sample, we noted a mild, moderate, and severe alteration in QoL, respectively, in 45/113 (39.8%), 54/113 (47.8%), and 13/113 (11.5%). It should be noted that QoL was not altered in one patient (0.9%).

Quality of Life and Sociodemographic Factors

No statistically significant relationship was found between the sociodemographic variables (sex, age, profession, level of education) and the QoL score ($p \geq 0.05$) (Table 3).

Quality of Life and Clinical History

Likewise, no statistically significant relationship was found between a patient's history (relapses, psychological or psychiatric follow-ups) and the QoL score ($p \geq 0.05$) (Table 3).

In addition, the QoL score was positively and weakly correlated with the clinical severity score ($r = 0.04$; $p < 0.05$). Indeed, the more severe was the acne, the more the QoL was altered (Fig. 3).

Table 3: Association between the factors and the CADI score (n = 113)

Variable	Items	CADI Score Mean±SD	p value
Sex	Male	6±3	0.86
	Female	6±3	
Age (yrs.)	< 10	5±6	0.76
	10–24	6±3	
	≥ 25	7±3	
Profession	Unemployed	6±3	0.87
	Employed	6±3	
	Student	6±3	
Relapses	Yes	6±3	0.20
	No	7±3	
Psychologic or psychiatric follow-up			
	Yes	6±1	0.93
	No	6±3	

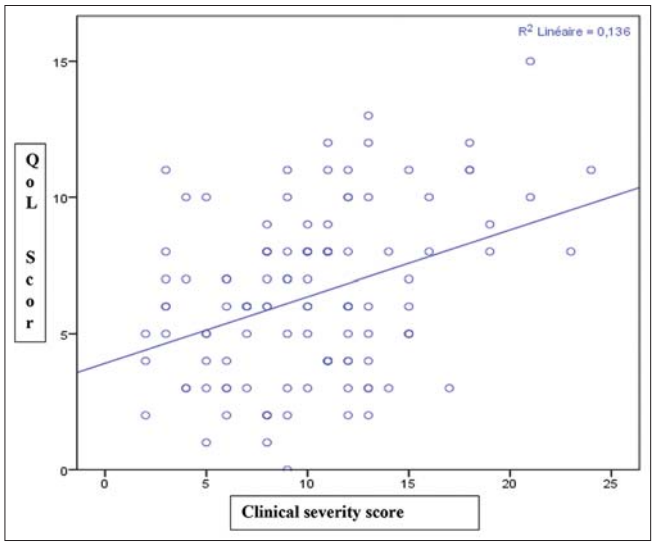


Figure 3: Linear regression of the CADI score with the ECLA score (n = 113).

DISCUSSION

Our study focused on the clinical severity of acne on black skin and assessed the impact of acne on the QoL of patients already on anti-acne treatment in the Cameroonian context, a country in sub-Saharan Africa.

In our series, acne mainly began between the ages of fifteen and eighteen [11,12]. In fact, based on the pathophysiological aspect, acne began at the age of puberty with the androgenic hormonal secretions that it causes. However, in a significant proportion of our participants (7.2%), acne began after the age of thirty. A late onset of acne is not uncommon; it is often the consequence of a genetic predisposition, hyperandrogenism, or the use of depigmenting cosmetics [13]. The mean age was 26.0 ± 6.4 years, with extremes of 8 and 48 years. Similar results were noted two years earlier by Kouotou et al. in Cameroon (25.4 ± 7.1 years) [7]. This observation was also made in other studies such as that by Saka et al. in Togo (23.7 ± 5.7 years) [14] and Dégboé et al. in Benin (24.6 ± 8.5 years) [15]. Acne usually begins in the early teens around the age of twelve, yet the first dermatological consultation is almost always done too late. This delay in consultation observed in our context could be explained by social considerations. Indeed, acne is often overlooked and considered transient in adolescents in our community. Females were more affected (83.2%) by acne in our series. The female predominance was corroborated by numerous series in the literature [7,14,15]. The high proportion of females consulting for acne is linked to the readiness of females to consult more easily than males, especially in the case of skin diseases.

In our patients, the duration of treatment varied from one month to five years. The duration of five years could be explained by inadequate self-medication or poor access to anti-acne drugs [16]. On clinical examination, papulopustular acne was the major clinical form (86.7%) and the clinical severity was classified as mild-to-moderate in 74% of the participants. Other studies also noted the predominance of mild-to-moderate forms on both white and black skin [7,11,14,15]. The anti-acne treatment initiated was most often topical (86.7%), sometimes combined with oral treatment (47.8%), which was in accordance with the acne management algorithm [17]. Due to the chronicity of acne lesions, follow-up is long and lasts several months or even years, requiring frequent reassessments. It usually takes several months to receive a satisfactory result for each treatment initiated [18]. In our case, 48% of the patients had already been on treatment for one to three months and 14% of them had been treated and followed for more than twenty-four months.

The unsightly and chronic nature of acne as well as the long duration of treatment have an impact on the QoL of the patient suffering from acne. QoL was assessed during our work with the Cardiff Acne Disability Index (CADI), an assessment grid for the QoL of patients with acne. QoL was altered in 99% of the participants. The alteration in QoL was mild, moderate, and severe in 40%, 48%, and 11% of the participants, respectively. Around two years earlier, Kouotou et al. found almost identical results in the same city. QoL was altered in all participants; more specifically, it was slightly, moderately, and severely impaired in 49.2%, 41.4%, and 9.4% of patients, respectively [5]. Likewise, in

2016, El-Hamd et al. found trends similar to ours in their study in Egypt, notably, with a mild (54%), moderate (33%), and severe (13%) alteration in the QoL of their patients with acne [19]. Overall, acne patients almost always experience an altered QoL. It would be important to systematically assess the QoL of patients with acne in order to take this into account during management. In addition, some quasi-experimental studies increasingly assess the QoL of the patient before and after treatment, in addition to evaluating the clinical efficacy of the anti-acne treatment [20,21]. The CADI tool could also serve as a routine tool for assessing improvement in QoL during initial and follow-up consultations and help to improve patient care.

Additionally, we noted a significant positive linear correlation between the ECLA score and the CADI score ($r = 0.04$; $p < 0.05$). Numerous African studies showed an association between the severity of clinical lesions and an impaired QoL [7,19,21]. The unsightly or even *frightening* aspect of severe acne lesions, such as nodulocysts, and the profuse nature of moderate-to-severe acne lesions may draw the attention of others to question and pity the patient, thus having a more negative impact on their QoL. In contrast, the team of Gupta et al. did not find a linear correlation between the clinical severity of lesions and the CADI score ($p > 0.05$). In a society seeking beauty and well-being increasingly often, it is possible that QoL is impaired regardless of the severity of clinical lesions [11]. In addition, there was no statistically significant difference in the CADI score depending on sex, profession, relapses, and psychological follow-up in our participants ($p > 0.05$). These sociodemographic factors and the clinical history did not influence the QoL of our patients. This trend was also underlined by Cameroonian [7] and Indian [11] studies. However, environmental factors, in particular, tobacco and alcohol consumption, may have worsened the CADI score of the patients, as evidenced by the work of Gupta et al. [11]. Analytical studies evaluating the effect of environmental factors on the QoL of patients with acne could be performed to document this finding and improve the QoL of these patients.

Limitations of the Study

Certain aspects of this work could constitute limits. The data collection tools, namely the ECLA and CADI grids, which assessed QoL, were validated against a Caucasian population, not Negroid. Nevertheless, our study could constitute a preliminary for further work with rating scales more suitable for dark skin.

CONCLUSION

Our study allowed us to discover that papulopustular acne was the most common clinical form and that acne in our participants was generally mild-to-moderate according to the ECLA scoring grid. Acne almost always induced an altered QoL in the patients. This alteration in QoL was significantly correlated with the clinical severity of lesions. Sociodemographic factors did not influence the QoL of our participants. The assessment of QoL in current practice in front of any patient suffering from acne may help to further understand the patient's suffering with acne and improve its management.

REFERENCES

1. Muguet Guenot L, Vourc'h Jourdain M, Saint Jean M, Corvec S, Lemoigne M, Khammari A, et al. Microscopie confocale et acné de la femme adulte. Ann Dermatol Vénéréol. 2017;144(12, Supplement):S177-8.
2. Troin L, Mallet S, Lagouanelle M-C, Scannapieco F, Lignon C, Gaudy-Marqueste C, et al. [Five years' experience of cosmetic camouflage of disfiguring skin disorders: Patient satisfaction]. Ann Dermatol Vénéréol. 2020;147:4-8.
3. Wolkenstein P, Machovcová A, Szepietowski JC, Tennstedt D, Veraldi S, Delarue A. Acne prevalence and associations with lifestyle: A cross-sectional online survey of adolescents/young adults in 7 European countries. J Eur Acad Dermatol Venereol. 2018;32:298-306.
4. Kouotou EA, Nansseu NJR, Defo D, Bissek ACZ-K. Acné Juvénile : Une Pathologie Fréquente Chez Les Adolescents Scolarisés D'Afrique Sub-saharienne. Health Sci Dis. 2015;16.
5. Samuels DV, Rosenthal R, Lin R, Chaudhari S, Natsuaki MN. Acne vulgaris and risk of depression and anxiety: A meta-analytic review. JAAD. 2020;83:532-41.
6. Saka B, Noude Téclessou J, Akakpo SA, Mahamadou G, Kassang P, Gnossikè P, et al. Acné et comorbidités psychiatriques à Lomé, Togo: étude cas-témoin. Ann Dermatol Vénéréol. 2019;146(12, Supplement):A205.
7. Kouotou EA, Adegbidi H, Bene Belembe R, Sieleunou I, Nansseu JR, Kamga J-P, et al. [Acne in Cameroon: Quality of life and psychiatric comorbidities]. Ann Dermatol Vénéréol. 2016;143:601-6.
8. Bissek AZ-K, Kouotou E, Defo D, Njamnshi KA, Koueke P, Muna W. Epidémiologie des dermatoses à l'Hôpital Général de Yaoundé. Health Sci Dis. 2009;10.
9. Dreno B, Bodoch I, Chivot M, Daniel F, Humbert P, POLI F, et al. La grille ECLA : un système de cotation de l'acné pour la pratique quotidienne du dermatologue. Ann Dermatol Vénéréol. Paris: Masson; 1999;126:136-41.
10. Motley RJ, Finlay AY. Practical use of a disability index in the routine management of acne. CED. 1992;17:1-3.
11. Gupta A, Sharma Y, Dash K, Chaudhari N, Jethani S. Quality of life in acne vulgaris: Relationship to clinical severity and demographic data. Int J Dermatol. 2016;82:292.

12. Ouedraogo AN, Kabre Ouedraogo SSS, Ouedraogo MS, Traore F, Tapsoba PG, Barro-Traore F, et al. Acne: Prevalence, perceptions and beliefs among pupils and students in Ouagadougou, Burkina Faso. Our Dermatol Online. 2017;8:10-6.
13. Poli F, Faye O, Ly F, Le Thuaut A. [Acne in adult female patients: A comparative study in France and sub-Saharan Africa]. Ann Dermatol Vénéréol. 2014;141:336-45.
14. Saka B, Akakpo AS, Téclessou JN, Mouhari-Toure A, Mahamadou G, Gnossike P, et al. Acne in Lomé, Togo: Clinical aspects and quality of life of patients. BMC Dermatol. 2018;18:7.
15. Dégboé B, Koudoukpo C, Agbéssi N, Elégbédé-Adégbitè N, Akpadjan F, Adégbidi H, et al. Acne on pigmented skin: Epidemiological, clinical and therapeutic features in dermatology in Benin. JCDSA. 2019;09:305.
16. Dégboé BE, Koudoukpo C, Agbéssi N, Akpadjan F, Adégbidi H, Atadokpèdé F. Acné sur peau noire: facteurs associés et comorbidités psychiatriques dans les services de dermatologie du Bénin. Ann Dermatol Vénéréol. 2019;146(12, Supplement):A205-6.
17. Le Cleach L, Lebrun-Vignes B, Bachelot A, Beer F, Berger P, Brugère S, et al. Prise en charge de l'acné. Traitement de l'acné par voie locale et générale. Ann Dermatol Vénéréol. 2015;142:692-700.
18. Couic-Marinier F, Pillon F, Chambin O. Renouvellement d'une ordonnance anti-acnéique. Actual Pharm. 2014;53:11-3.
19. El-Hamd MA, Nada EE-DA, Moustafa MA-K, Mahboob-Allah RA. Prevalence of acne vulgaris and its impact of the quality of life among secondary school-aged adolescents in Sohag Province, Upper Egypt. JCD. 2017;16:370-3.
20. Cyrulnik AA, Viola KV, Gewirtzman AJ, Cohen SR. High-dose isotretinoin in acne vulgaris: Improved treatment outcomes and quality of life. Int J Dermatol. 2012;51:1123-30.
21. Zaraa I, Belghith I, Ben Alaya N, Trojjet S, Mokni M, Ben Osman A. Severity of acne and its impact on quality of life. Skinmed. 2013;11:148-53.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Prevalence of anemia among HIV-infected individuals and the associated factors: A single-center, retrospective review of 513 cases

Vikram K Mahajan, Niharika Dhattarwal, Karaninder Singh Mehta, Pushpinder Singh Chauhan, Anuj Sharma, Reena Kumari Sharma, Yog Raj Verma, Monika Chandel

Department of Dermatology, Venereology & Leprosy, Dr. Rajendra Prasad Government Medical College Kangra (Tanda) -176001 (Himachal Pradesh) India.

Corresponding author: Vikram K Mahajan, MD, E-mail: vkm1@rediffmail.com

ABSTRACT

Background: Although a major public health problem around the world, the prevalence of anemia and the associated factors in HIV-infected individuals remains understudied in the Indian context. **Objectives**: The objective was to assess the prevalence of anemia and the associated factors among HIV-infected individuals. **Methods**: The records of 513 HIV-affected individuals (M: F: 244:269) aged 12 to 84 years (mean ± SD: 37.5 ± 12.1) were reviewed retrospectively for the presence of anemia and the associated factors. The anemia was defined and severity was graded per the WHO guidelines. **Results**: Anemia of variable severity was present in 77.7% of the individuals. The female sex(OR: 2.09; Cl: 95%; CI: 1.41–3.10; $p < 0.05$), CD4$^+$ count ≤ 200 cells/microliter (OR: 2.36; Cl: 95%; CI: 1.59–3.52; $p < 0.0001$), WBC count < 4000 cells/mm^3 (OR: 3.29; Cl: 95%; CI: 0.97–11.14; $p < 0.04$), platelet count < 100,000 cells/dL (OR: 0.50; Cl: 95%; CI: 0.31–0.81; $p < 0.05$), before ART (OR: 3.78; Cl: 95%; CI: 2.91–4.91; $p < 0.0001$), and tuberculosis treatment (OR: 5.88; Cl: 95%; CI: 1.38–25.04; $p < 0.05$) were factors significantly associated with anemia. The mean duration of highly active antiretroviral therapy (ART) was 3.15 years, with 395 (77%) individuals being on treatment for ≤ five years. ART significantly improved hemoglobin levels ($p < 0.0001$). **Conclusion**: Anemia of variable severity remains a significant co-morbidity among HIV-infected individuals, especially females, prior to the initiation of ART, and those with a low CD4$^+$ count or thrombocytopenia and on anti-tuberculosis treatment. The fact that this was a single-center study, its small number of subjects, the retrospective design, and no information on red blood cell indices and the viral load were its important limitations.

Key words: AIDS; anemia; ART; CD4$^+$ count; HAART; HIV; India

INTRODUCTION

Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) are some of the major public health problems around the world, in particular, in the developing countries of Africa and southeastern Asia. The number of new cases has declined significantly after highly active antiretroviral therapy (ART) and intensive information, education and communication (IEC) strategies have been implemented. However, India is still estimated to have the third-largest HIV-infected population in the world, after South Africa and Nigeria, with an estimated adult prevalence of 0.22% (0.16–0.30%) in 2017 [1].

Anemia is an important cause of morbidity in HIV-infected individuals around the world, irrespective of highly active ART, which significantly improves quality of life and prevents the progression of HIV disease [2,3]. The acceleration of the disease, a decreased life

How to cite this article: Mahajan VK, Dhattarwal N, Mehta KS, Chauhan PS, Sharma A, Shrma RK, Verma YR, Chandel M. Prevalence of anemia among HIV-infected individuals and the associated factors: A single-center, retrospective review of 513 cases. Our Dermatol Online. 2023;14(1):23-28.

Submission: 18.05.2022; **Acceptance:** 23.07.2022

DOI: 10.7241/ourd.20231.5

expectancy, impaired physical function, the risk of ART-associated hepatotoxicity, psychological distress, and poor quality of life are important consequences of HIV-associated anemia [4-6].

The prevalence of HIV-associated anemia ranges from 10% in asymptomatic HIV disease to 92% among individuals with advanced AIDS and is 24% and 58% in individuals taking ART and up to 35% in those ART-naïve [4,7-10]. However, it may occur at any stage of HIV disease, with a severity that may correlate with the progression of the disease with a higher prevalence among ART-naïve individuals when compared to those taking ART [11,12]. A multitude of factors, such as sex, low nutritional status, anti-tuberculosis treatment (ATT), opportunistic infections, an advanced stage of the HIV disease, a $CD4^+$ count below 200 cells/microliter, a white blood cell (WBC) count below 4000 cells/microliter, and a platelet count below 200,000 cells/microliter, as well as zidovudine-containing ART regimens, have been identified to be associated with anemia among HIV-affected individuals [8,4,13-16]. Pure red cell aplasia, characterized by a normal leukocyte and platelet count, a corrected reticulocyte count below 1%, less than 5% of erythrocyte precursors in the bone marrow, and no hemolysis is an uncommon cause of refractory anemia in HIV/AIDS and occurs consequent to an autoimmune response selectively affecting erythroid cell lines or ART-induced myelosuppression [16-18]. However, the magnitude of these factors varies across regions depending upon socioeconomic and health conditions. Although the prevalence of anemia among the HIV-affected and the associated factors remain understudied in the Indian context, it was 23% to 61.5% in some studies, irrespective of their ART status [6,18-20]. Since the management of anemia in these individuals improves survival and the overall quality of life, we performed this study with the aim to assess the prevalence of anemia and the associated factors in HIVinfected individuals under follow-up in this part of the country having a low prevalence of HIV/AIDS and for an overall paucity of relevant data.

MATERIALS AND METHODS

The medical records of 518 patients on regular ART registered in the institute-affiliated ART Center and under follow-up between January 2015 and December 2019 were analyzed retrospectively for this hospital-based, descriptive, observational study after obtaining approval from the Institutional Ethics Committee. Sociodemographic details, the $CD4^+$ count, previous illnesses and their treatment (if any), hemoglobin (Hb) levels, and the results of complete blood counts recorded before the initiation of ART together with the most recent one were noted from their ART records or booklets maintained in the center. Hemoglobin levels of at least 12 g/dL were considered normal and anemia was defined per the WHO guidelines as hemoglobin values below 13 g/dL in adult males, below 12 g/dL in adult females, below 11 g/dL in children below five years of age, and below 11.5 g/dL in children between five to eleven years of age [21]. The severity of anemia was graded as mild with Hb = 11.0−11.9 g/dL, as moderate with Hb = 8.0−10.9 g/dL, and as severe with Hb < 8.0 g/dL.

Statistical Analysis

Five patients had incomplete records and were excluded from the final analysis. Continuous data was presented as means and standard deviations and categorical variables as frequencies and percentages. Categorical and parametric data was analyzed by χ^2 test and Student's *t*-test. The non-parametric Mann–Whitney test was employed for variables not distributed normally. Odds ratios (ORs) were calculated with a 95% confidence interval. A *p* value below 0.05 (5%) with a 95% confidence interval was considered statistically significant.

RESULTS

Table 1 shows the baseline characteristics of the 513 study subjects, comprising 244 (47.6%) males and 269 (52.4%) females (M: F: 0.9:1) aged between 12 and 84 years (mean ± SD: 37.5 ± 12.1 years). Among the subjects, 380 (74.1%) were aged 16–45 years. The $CD4^+$ cell count varied from 5 to 1824 (mean ± SD = 240.12 ± 187.94) cells/microliter and were ≤ 200 cells/microliter in 252 (49.1%) individuals. All had been on highly active ART with good treatment adherence for two weeks to nine years and four months (mean: 3.15 years), and 395 (77%) individuals had been undergoing treatment for not longer than five years. The major ART regimens were tenofovir + lamivudine + efavirenz (TLE) in 282 (55%), zidovudine + lamivudine + nevirapine (ZLN) in 177 (34.5%), and zidovudine + lamivudine + efavirenz (ZLE) in 22 (4.29%) individuals, respectively. Overall, 199 (38.8%) had been taking zidovudine-containing ART regimens. Six (1.2%) developed nevirapine hypersensitivity syndrome and the initial

Table 1: Baseline characteristics of the patients

Baseline Characteristics		No. of Patients (%) *n*=513
Sex	Male	244 (47.56)
	Female	269 (52.44)
	Females: males	1:1.10
Age range (mean±SD) 12–84 (37.45±12.11) years	< 15 yrs.	34 (6.63)
	16–30 yrs.	80 (15.59)
	31–45 yrs.	300 (58.48)
	46–60 yrs.	86 (16.76)
	> 60 yrs.	13 (2.53)
CD4 cell count (at presentation) range (mean±SD) 5–1824 (240.12±187.94) cells/microliter	> 500 cells/microliter	38 (7.41)
	> 350–500 cells/microliter	52 (10.14)
	> 200–350 cells/microliter	171 (33.33)
	> 100–200 cells/microliter	135 (26.31)
	< 100 cells/microliter	117 (22.81)
Duration of ART range (mean) 2 wk. – 9 yrs. 4 months (3.15 yrs.)	< 1 yrs.	112 (21.83)
	> 1–2 yrs.	92 (17.93)
	> 2–3 yrs.	59 (11.50)
	> 3–4 yrs.	63 (12.28)
	> 4–5 yrs.	69 (13.45)
	> 5–6 yrs.	52 (10.14)
	> 6–7 yrs.	38 (7.41)
	> 7 yrs.	28 (5.46)
ART Drug Regimen	TDF+3TC+EFV (TLE)	282 (54.97)
	ZDV+3TC+NVP (ZLN)	177 (34.50)
	ZDV+3TC+EFV (ZLE)	22 (4.29)
	Abc+NVP	13 (2.53)
	TDF+3TC+NVP (TLN)	11 (2.14)
	Abc+EFV	5 (0.97)
	d4T+3TC+NVP (SLN)	2 (0.39)
	d4T+3TC+EFV (SLE)	1 (0.19)
Hemoglobin Levels Mean±SD (range) (g/dL)	Before ART	10.8±2.02 (4.4–16.5)
	After ART	12.3±1.7 (6–17)
	p value	**< 0.0001**
Anemia	Before ART	368 (77.7)
	After ART	206 (40%)
	P value	**<0.0001**
Grade of Anemia Before ART	Mild anemia (Hb=11–11.9 g/dl)	72 (13.9)
	Moderate anemia (Hb=8–10.9 g/dl)	257 (50.2)
	Severe anemia (Hb<8 g/dl)	39 (7.6)
	No anemia (Hb ≥ 13 g/dL for men, ≥ 12 g/dL for women) adults and adolescents	145 (28.3)

ART: antiretroviral therapy; Abc: abacavir; d4T: stavudine; EFV: efavirenz; 3TC: lamivudine; NVP: nevirapine; TDF: tenofovir disoproxil fumarate; ZDV: zidovudine; Hb: hemoglobin; SD: standard deviation; SLE: stavudine+lamivudine+efavirenz; SLN: stavudine+lamivudine+nevirapine; TLE: tenofovir+lamivudine+efavirenz; TLN: tenofovir+lamivudine+nevirapine; ZLE: zidovudine+lamivudine+efavirenz; ZLN: zidovudine+lamivudine+nevirapine. A *p* value<0.05 at a 95% confidence interval was considered statistically significant and is shown in bold

nevirapine-based ART regimens were changed to a tenofovir + lamivudine + efavirenz (TLE) regimen. Thirty (5.8%) received anti-tuberculosis treatment (ATT) for pulmonary tuberculosis in a recommended dose and schedule before ART was initiated. The only individual with an HBV co-infection had not received any drug(s) other than ART. Laboratory reports for the leukocyte and platelet count were available only for 492 and 451 cases, respectively. Information for body weight/BMI, iron supplements, alcohol abuse, and the presence of concurrent or opportunistic infections or their treatment and prophylaxis, particularly for *Pneumocystis jiroveci* pneumonia, was not available in the records.

Hemoglobin levels varied from 4.4 to 16.5 g/dL (mean ± SD: 10.8 ± 2.02 g/dL). Three hundred and

sixty-eight (77.7%) individuals had anemia before the initiation of ART, which was mild in 72 (13.9%), moderate in 257 (50.2%), and severe in 39 (7.6%) cases, respectively. The female sex (OR: 2.09; Cl: 95%; CI: 1.41–3.10; $p < 0.05$), a CD4$^+$ count ≤ 200 cells/microliter (OR: 2.36; Cl: 95%; CI: 1.59–3.52; $p < 0.0001$), a WBC count < 4000 cells/mm^3 (OR: 3.29; Cl: 95%; CI: 0.97–11.14; $p < 0.04$), a platelet count < 100,000 cells/mm^3 (OR: 0.50; Cl: 95%; CI: 0.31–0.81; $p < 0.05$), before the initiation of ART (OR: 3.78; Cl: 95%; CI: 2.91–4.91; $p < 0.0001$), ATT intake (OR: 5.88; Cl: 95%; CI: 1.38–25.04; $p < 0.05$), and nevirapine hypersensitivity (OR: 0.38; Cl: 95%; CI: 0.07–1.95; $p < 0.04$) were significantly associated with anemia (Table2). However, zidovudine-containing ART regimens were not found to be significantly associated with anemia (OR: 0.71; Cl: 95%; CI: 0.49–1.02; $p = 0.067$). Meanwhile, ART significantly improved hemoglobin levels and corrected anemia, as only 206 (40%) individuals had anemia after ART, as opposed to 368 (77.7%) with anemia before the initiation of ART ($p < 0.0001$).

DISCUSSION

The demographic profile of HIV-affected individuals in this study was similar to what has been described in the past [6,22]. The prevalence of anemia ranged between 10% to 28% in asymptomatic HIV-infected individuals in the pre-AIDS stage and 71–92% in those with AIDS across countries [6,9-11,13]. In general, the prevalence of anemia was higher in those ART-naïve than those on ART, and severity varied from mild to severe [4,9,11-13]. In a recent study, it was mild in 13%, moderate in 14%, and severe in 7.4% of cases, respectively [11]. In our study, the prevalence of anemia was 77.7% before ART was initiated, which was moderate in almost half of the cases, as opposed to mild in 13.9% and severe in 7.6% of the individuals. The prevalence decreased to 28.3% after ART, conforming to the above epidemiological trends. Apart from anemia of a chronic disease, HIV-associated anemia may be due to nutritional deficiencies, blood loss, medication-induced hemolysis, or bone marrow suppression (trimethoprim–sulfamethoxazole, zidovudine, amphotericin) [18]. The female sex, a CD4$^+$ count below 200 cells/microliter, and ATT intake were other significant factors associated with anemia in this study. These observations suggest that HIV infection by itself is an important cause of anemia in the majority of the HIV-affected. HIV infection is believed to affect bone marrow functioning directly or from opportunistic infections especially during the early phase of uncontrolled HIV multiplication, or because of drug toxicity over a period of time [20]. Anemia in individuals before the initiation of ART, a WBC count below 4000 cells/mm^3, and thrombocytopenia (platelet count < 100,000/mm^3) in this study, as well

Table 2: Factors associated with anemia

Factors		Total No. of Patients	Anemia		OR (CI: 95%)	Confidence Interval	*p* value
			No. of Patients				
			Yes	No			
Sex	Female	269	212	57	2.09	1.41–3.10	**0.0002**
	Male	244	156	88	-	-	-
CD4$^+$cell count	≤ 200 cells/microliter	252	201	51	2.36	1.59–3.52	**< 0.0001**
	> 200 cells/microliter	261	163	98	-	-	-
WBC* count	< 4000/mm^3	26	23	3	3.29	0.97–11.14	**0.04**
	> 4000/mm^3	466	326	140	-	-	
Platelet** count	< 100,000/mm^3	306	208	98	0.50	0.31–0.81	**0.005**
	> 100,000/mm^3	145	117	28	-	-	-
ART Status	Before ART	513	368	145	3.78	2.91–4.91	**< 0.0001**
	After ART	513	206	307	-	-	-
ART Regimen	With ZDV	199	70	129	0.71	0.49–1.02	0.067
	Without ZDV	314	136	178	-	-	-
ATT***	Yes	30	28	2	5.88	1.38–25.04	**0.016**
	No	483	340	143	-	-	-
NVR DHS	Yes	6	3	3	0.38	0.07–1.95	**0.04**
	No	507	365	142	-	-	-

ART: anti-retroviral therapy; ATT: anti-tuberculosis treatment; CI: confidence interval DHS: drug hypersensitivity syndrome; g/dL: grams/deciliter; Hb: hemoglobin; NVR: nevirapine; OR: odds ratio; WBC: white blood cells; ZDV: zidovudine. A *P* value<0.05 at a 95% confidence interval was considered statistically significant and is shown in bold.*Reports were available for 492 cases only.
**Reports were available for 451 cases only.
***ART was initiated only after the completion of ATT comprising rifampicin (10 mg/kg), isoniazid (5 mg/kg), ethambutol (15 mg/kg), pyrazinamide (25 mg/kg) for two months in the intensive phase followed by rifampicin and isoniazid for four months in the continuation phase

as the other significant factors ($p < 0.5$) associated with anemia, also reflect some amount of HIV-induced myelosuppression. However, none of our patients were pregnant, had chronic renal failure, or received a blood transfusion for severe anemia or blood loss. Individuals with a low $CD4^+$ cell count have a high viral load and are at an increased risk for opportunistic infections, which in turn may lead to an increased prevalence of anemia. Concurrent opportunistic infections (parvovirus B19, *Pneumocystis jiroveci*, tuberculosis, *Mycobacterium avium complex*) and their therapies, for instance, tuberculosis, due to chronicity, bone marrow suppression, malnutrition, and hemoptysis, and any severe drug toxicity (including from nevirapine) possibly enhance the risk of anemia in these individuals, as was observed in this study [11,15,18]. An improvement in anemia after ART, as in this study, is due to the suppression of the viral replication/load and improved immunity against opportunistic infections and the overall gain in health reinforcing the foregoing [13]. Although zidovudine-containing ART regimens, especially the during the early phase of ART initiation, have been identified to be associated with anemia, especially among individuals with low baseline hemoglobin and pure red cell aplasia in particular, we made no such observations, as individuals with low Hb were not put on zidovudine-containing regimens [13,16,23]. However, only a small number of individuals were on zidovudine-containing ART for a meaningful conclusion and may not reflect the real effect of zidovudine. In our study, details on other risk factors of anemia, such as *Pneumocystis jiroveci* prophylaxis and the nutritional status of the HIV-affected, could not have been ascertained from the records

Limitations

This study was limited by a small number of subjects, its single-center stratification, and its retrospective study design. Data on red blood cell indices, types of anemia, and other potential risk factors, such as alcohol abuse, dietary habits and nutritional statuses, opportunistic infections and their treatment or prophylaxis, which might have influenced the results, at least in some of the cases, was not recorded. The analysis of anemia on a yearly basis was impossible due to retrospective analysis. As ART is regimen-based, the identification of an individual drug responsible for anemia was not possible. Viral-load studies were not part of the study.

CONCLUSION

Anemia may be a significant co-morbidity among HIV-infected individuals, especially in females, before the initiation of ART, and those with a $CD4^+$ count ≤ 200 cells/microliter, a WBC count < 4000 cells/mm^3, thrombocytopenia, a history of nevirapine adverse reactions, or ATT intake. While 50% of affected individuals may have moderate anemia, the spectrum varies from mild to severe anemia, necessitating screening for the overall health of the affected individual. ART significantly improves pre-existing HIV-associated anemia in the majority. The low potential of zidovudine-containing regimens for ART-associated anemia perhaps does not reflect the real effect of zidovudine because of the small number of these cases. Well-designed and prospective studies addressing the limitations of this study are highly desirable to further our understanding of factors associated with anemia and its effect on the overall health of the HIV-affected and the interventions needed.

ACKNOWLEDGMENTS

We would like to thank Mr. Sushant Sharma of community medicine (biostatistics) for helping with statistical analysis and the staff members at the ART Center, Dr. Rajendra Prasad Government College, Kangra (Tanda), H.P., for lending useful input for the study.

Statement of Ethics

The study was approved by the Institutional Ethics Committee (registration number: ECR/490/Inst/HP/2013/RR-16) vide letter no. HFW-H-DRPGMD/Ethics/17/2018-91, dated 19-05-2018. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 as revised in 2013.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. National AIDS Control Organization. India HIV estimations 2017. Technical Report. Department of AIDS Control. Ministry of Health and Family Welfare, New Delhi, India. Available at: http://www.naco.gov.in. [Assessed on Dec 19, 2020]
2. National AIDS Control Organization. India HIV Estimations 2017, Fact Sheets, Himachal Pradesh, 2017. Department of AIDS Control. Ministry of Health and Family Welfare, New Delhi, India. Available at: http://www.naco.gov.in. [Assessed on Dec 19, 2020]
3. Global AIDS Response Progress Reporting (GARPR) estimates. Geneva, Switzerland: UNAIDS; 2016.
4. Wisaksana R, Sumantri R, Indrati AR, Zwitser A, Jusuf H, de Mast Q, et al. Anemia and iron homeostasis in a cohort of HIV-infected patients in Indonesia. BMC Infect Dis. 2011;11:213.
5. De Santis GC, Brunetta DM, Vilar FC, Brandão RA, de Albernaz Muniz RZ, de Lima GM, et al. Hematological abnormalities in HIV-infected patients. Int J Infect Dis 2011;15:e808-11.
6. Mahajan VK, Wadhwa D, Sharma A, Chauhan S, Vashist S, Kumar P, et al. Assessment of liver and renal functions in human immunodeficiency virusinfected persons on highly active antiretroviral therapy: A mixed cohort study. Indian J Dermatol Venereol Leprol.2020;86:499-507.
7. Sah SK, Dahal P, Tamang GB, Mandal DK, Shah R, Pun SB. Prevalence and predictors of anemia in HIV-infected persons in Nepal. HIV/AIDS Res Palliative Care. 2020;12:193-200.
8. Owiredu WK, Quaye L, Amidu N, Addai-Mensah O. Prevalence of anaemia and immunological markers among Ghanaian HAART-naïve HIV-patients and those on HAART. Afr Health Sci. 2011;11:2-15.
9. Denue BA, Kida IM, Hammagabdo A, Dayar A, Sahabi MA. Prevalence of anemia and immunological markers in HIV-infected patients on highly active antiretroviral therapy in Northeastern Nigeria. Infect Dis: Res Treatment. 2013;6:25-33.
10. Gedefaw L, Yemane T, Sahlemariam Z, Yilma D. Anemia and risk factors in HAART naïve and HAART experienced HIV positive persons in south west Ethiopia: A comparative study. PLoS One. 2013;8:e72202.
11. Zenebe WA, Anbese AT, Tesfay TS. Anemia and associated factors among adult people living with HIV/AIDS receiving anti-retroviral therapy at Gedeo Zone, SNNPR, Ethiopia, 2018. HIV/AIDS-Res Palliative Care. 2019;11:351-6.
12. Quiros-Roldan E, Castelli F, Lanza P, Pezzoli C, Vezzoli M. The impact of antiretroviral therapy on iron homeostasis and inflammation markers in HIV-infected patients with mild anemia. J Transl Med. 2017;15:256.
13. Melese H, Wassie MM, Woldie H, Mesfin N. Anemia among adult HIV patients in Ethiopia: A hospital based cross sectional study. HIVAIDS Res Palliative Care. 2017;7:25-30.
14. Wolde HM, Lerebo WT, Melaku YA, Girmay KH. Incidence and risk factors of anemia among HIV/AIDS patients taking anti-retroviral therapy at tertiary hospitals in Addis Ababa, Ethiopia: A retrospective cohort study. J HIV AIDS Infect Dis. 2014;2:1-62.
15. Meidani M, Rezaei F, Maracy MR, Avijgan M, Tayeri K. Prevalence, severity, and related factors of anemia in HIV/AIDS patients. J Res Med Sci. 2012;17:138-42.
16. Mrigh SP, Mishra VA, Shah VD, Sorabjee JS. Refractory anemia in human immunodeficiency virus: Expect the unexpected. J Family Med Prim Care. 2016;5:727-9.
17. Nakamura K, Tateyama M, Tasato D, Haranaga S, Tamayose M, Yara S, et al. Pure red cell aplasia induced by lamivudine without the influence of zidovudine in a patient infected with human immunodeficiency virus. Intern Med. 2014;53:1705-8.
18. Bhattad D, Kulkarni V, Bhave A, Balasubramanian M, Upase DP, Khude S. Refractory anaemia in an immunocompromised patient: What is it? J Assoc Physicians India. 2013;61:673-5.
19. Pandav Amitkumar B, Nilkanth Somesh P, Lanjewar Dhaneshwar N, Bhagwat Rajendra V. Haematological profile of HIV-positive patients in relation to immune status and stage of the disease: A hospital-based cohort from Western India. J Pharm Biomed Sci. 2013;35:1877-86.
20. Pande A, Bhattacharyya M, Pain S, Samanta A. Study of bone marrow changes in antiretroviral naive human immunodeficiency virus-infected anemic patients. Indian J Pathol Microbiol. 2011;54:542-6.
21. WHO. Hemoglobin concentration for the diagnosis of anemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, Switzerland: World Health Organization; 2011 (WHO/NMH/NHD/MNM/11.1). [Assessed on Dec 19, 2020]
22. Mahajan VK, Raina S, Kohli S, Gupta S, Sharma S. Cognitive impairment among persons of rural background living with human immunodeficiency virus infection on antiretroviral therapy: A study from a tertiary care centre of North India. J Neurosci Rural Pract. 2016;7:S1314.
23. Phe T, Thai S, Veng C, Sok S, Lynen L, van Griensven J. Risk factors of treatment-limiting anemia after substitution of zidovudine for stavudine in HIV-infected adult patients on antiretroviral treatment. PLoS One. 2013;8:e60206.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Prevalent dermatoses during the post-electoral crisis in Côte d'Ivoire

Sigha Odette Berline[1,2], Edgar Mandeng Ma Linwa[3], Sangaré Abdoulaye[4]

[1]Faculty of Health Sciences, University of Bamenda, Bambili, Cameroon, [2]Service de dermatologie, Hôpital Laquintinie de Douala, Cameroun, [3]Faculty of Health Sciences, University of Buea, Cameroon, [4]Service de dermatologie, Centre Hospitalier Universitaire (CHU) de Treichville, Abidjan, Côte d'Ivoire

Corresponding author: Sigha Odette Berline, MD, E-mail: osigha@yahoo.fr

ABSTRACT

Background: The 2000–2011 period was for Côte d'Ivoire a period of sociopolitical crisis resulting from an electoral dispute. Skin diseases have long been recognized as an important cause of morbidity among the military, in times of conflict or peace, regardless of their geographic location. In the literature, we found no study on the prevalence of dermatoses in the civilian population during or after the war. In this study, we sought to describe the sociodemographic characteristics of patients and determine the dermatoses observed during this period. **Materials and Methods:** We conducted a retrospective database study of patients who consulted the dermatology department of the CHU of Treichville from April 18 to July 18, 2011. Data collection was performed with a survey form. The data collected was analyzed with EpiData 3.0. **Results:** We analyzed the files of 1755 patients and found that 56.75% were males and 43.25% were females. Teenagers and young adults aged 15 to 49 were the most numerous to consult (71.11%). A total of 1923 dermatoses were diagnosed. The five most frequent dermatoses observed were as follows: immunoallergic dermatoses (35.36%), infectious (bacterial, mycotic, parasitic, and viral) and tropical dermatoses (27.04%), inflammatory dermatoses (7.23%), skin tumors (4.52%), and sexually transmitted infections and dermatoses associated with HIV/AIDS (4.26%). **Conclusion:** The spectrum of dermatoses in the city of Abidjan following the sociopolitical crisis was similar to that prevailing in most large African cities, as industrialization and better living conditions had reduced the prevalence of infectious dermatoses while increased immunoallergic pathologies.

Key words: dermatoses; post-electoral crisis; Côte d'Ivoire

INTRODUCTION

The 2000–2011 period was for Côte d'Ivoire a period of a sociopolitical crisis resulting from an electoral dispute. It caused the massive displacement of the population resulting in household promiscuity, which put individuals at risk of transmissible pathologies, including dermatoses. The immediate consequences of the post-electoral crisis in Côte d'Ivoire were unprecedented in the country's history. It led to the disorganization of the health system, education, and the economy. At the end of the war, the new government decided on the policy of free care in public, parapublic, and community-based health establishments [1]. As a result, people, even if the need was not real, stormed the aisles of hospitals and other health centers. Free care began in the dermatology department of the CHU of Treichville on April 16, 2011. Very quickly, the number of patients increased and the medical staff were overwhelmed. The staff had to deal with the dissatisfaction of patients, the supply of care having momentarily exceeded the strong demand.

Skin diseases have long been recognized as an important cause of morbidity among the military, in times of conflict or peace, regardless of their geographic location [2]. In the eighteenth century, scabies was considered a universal affliction of the military

How to cite this article: Berline SO, Ma Linwa EM, Abdoulaye S. Prevalent dermatoses during the post-electoral crisis in Côte d'Ivoire. Our Dermatol Online. 2023;14(1):29-34.

Submission: 28.05.2022; **Acceptance:** 28.07.2022

DOI: 10.7241/ourd.20231.6

profession. Infectious dermatoses account for the vast majority of wartime skin diseases. Field conditions such as heat, humidity, cold, and lack of hygiene may cause the dramatic exacerbations of these conditions in times of war [3]. Their diagnosis is generally simple and their treatment is of extreme importance, not only for the individual yet also, and especially, for the community, since the rapid cure of an infection is the surest way to prevent its spread [4].

In the literature, we found no study on the prevalence of dermatoses in the civilian population during or after a war. Our study on the prevalence of dermatoses in the general population after the Ivorian crisis, therefore, seems to be an original work. Through this study, we sought to describe the sociodemographic characteristics of patients and determine the dermatoses observed during this period.

METHODOLOGY

Côte d'Ivoire is located in West Africa in the northern hemisphere, between the Tropic of Cancer and the equator, and overlooks the Atlantic in the Gulf of Guinea. It is bordered to the north by Mali and Burkina Faso, to the west by Liberia and Guinea, to the east by Ghana, and to the south by the Atlantic Ocean. Covering an area of 322,462 km^2, its political capital is Yamoussoukro, Abidjan being the economic and administrative capital. The country is part of the ECOWAS (Economic Community of West African States), where it occupies an important place as a strong link in the economic chain [5].

Our study took place in the dermatology department of the CHU of Treichville, which is the only dermatology center in a public hospital in the city of Abidjan. We evaluated the epidemiological aspects and the prevalence of dermatoses in patients who consulted the department during the first three months following the sociopolitical and post-electoral crisis of 2010–2011.

We reviewed the files of patients who consulted the dermatology department of the CHU of Treichville from April 18 to July 18, 2011 (a period of three months). Data collection was conducted with a survey form. The data collected was analyzed with EpiData 3.0. We collected data from consultation registers. Most of the diagnoses were established after questioning and clinical examination.

RESULTS

Sociodemographic Characteristics

We analyzed the files of 1755 patients and found that 56.75% were males and 43.25% were females. Teenagers and young adults aged 15 to 49 were the most numerous to consult (71.11%). In our study, we found that only 17.89% of the patients had a salaried profession, and 33.79% were students or pupils (Table 1). A total of 92.82% of our patients lived in Abidjan. Among the patients residing in Abidjan, a majority (18.06%) came from the Yopougon community, followed by Cocody for 14.99% of the patients; 13.16% of the patients came from Treichville, where the dermatology department is located.

Clinical Features

The shortest consultation period was two days, while the longest was 10,950 days (approx. thirty years). Only 3.30% of our patients had a dermatological history before the consultation. Depigmentation was the most common medical history, with a percentage of 1.03%. A total of 1923 dermatoses were diagnosed in our 1755 patients. Two (240 patients) and three (16 patients) dermatoses could be diagnosed simultaneously.

The five main groups of dermatoses observed were as follows (Table 2):

Table 1: Sociodemographic characteristics of the population

Sociodemographic characteristics	Number	Percentage (%)
Sex	1755	100
Male	996	56.75
Female	759	43.25
Age		
< 5 yrs.	120	6.84
5–14 yrs.	162	9.23
15–49 yrs.	1248	71.11
> 50 yrs.	204	11.62
(unknown)	21	1.20
Profession	1755	100
Salaried	314	17.89
Informal sector	464	26.44
Agro-pastoral	15	0.85
Student /pupil	593	33.79
Unemployed	64	3.65
Housemaid	181	6.15
(unknown)	108	10.31
(N/A)	16	0.91
Residence		
Abidjan	1629	92.82
other city	102	5.81
(unknown)	24	1.37

Table 2: Different dermatoses observed

Dermatoses	Frequency	Percentage (%)
Immunoallergic dermatoses	680	35.36
Infectious (bacterial, mycotic, parasitic, and viral) and tropical dermatoses	520	27.04
Inflammatory dermatoses	139	7.23
Skin tumors	87	4.52
Sexually-transmitted infections and dermatoses associated with HIV/AIDS	82	4.26
Other dermatoses	415	21.59
Total	1923	100

- Immunoallergic dermatoses (35.36%);
- Infectious (bacterial, mycotic, parasitic, and viral) and tropical dermatoses (27.04%);
- Inflammatory dermatoses (7.23%);
- Skin tumors (4.52%);
- Sexually-transmitted infections and dermatoses associated with HIV/AIDS (4.26%).

Eczema (14.61%) was the most common immunoallergic dermatosis in our study. We also found one (0.05%) case of dermatomyositis and one (0.05%) case of scleroderma, which are relatively rare pathologies. Among the infectious dermatoses, mycoses (11.87%) were the most frequent. Buruli ulcer (0.15%) was the most frequently noted tropical dermatosis. Lichen planus (1.92%) was the most common inflammatory dermatosis. Keloid scars (2.60%) were the most common benign skin tumors. Actinic keratoses (0.15%) were the most common malignant skin tumors. Condyloma acuminata was the most common sexually-transmitted infection (1.98%); and Kaposi's disease (0.57%) was the most common pathology associated with HIV/AIDS. Hyperpigmented scars (1.35%) were the most common forms of dyschromia, followed by exogenous ochronosis (1.04%). Leg ulcer (0.42%) came first among vascular pathologies. Nineteen (0.99%) cases of alopecia were found, thus representing the most observed pathology of the skin appendages. We also found two cases of neurofibromatosis and three cases of pyoderma gangrenosum, which are relatively rare pathologies.

DISCUSSION

In the literature, we found no study on the prevalence of dermatoses in the post-conflict civilian population. In our study concerning this segment of the population, our discussion will be on studies performed on black-skinned patients in different countries in times of peace.

The major biases of our study were as follows:

- Free healthcare, as it had led to an increase in the number of patients (over the three-month period, 1,755 patients were studied, which was approx. double the number when compared to the same period the previous year);
- Missing portions of information.

In our study, the proportion of males (56.75%) was higher than females (43.25%). This result is in disagreement with most studies, in particular those by Dlova et al. [6], Ukonu [7], and Yahya [8], in which the proportion of females was significantly higher. Bissek et al. [9] and Mahé et al. [10] found in their studies an almost equal proportion of males and females. The high proportion of females in most studies is due to feminine coquetry. Females are more alarmed to see even small skin abnormalities. We may, therefore, ask ourselves whether the high proportion of males in our study was the result of free healthcare (which led to more males coming for consultation) or the result of growing male coquetry. Adults aged between 15 to 50 years represented 82.73% in our series, while those under 15 years of age represented only 16.07% of the patients. This result is in agreement with all the studies, in particular those by Dlova, Ukonu, and Yahya [6-8], in which adults represented 86.9%, 83.7%, and 79.29% of patients, respectively. The low proportion of children may be explained by the fact that most dermatoses in children are treated by pediatricians and general practitioners and that most cases arriving at the dermatologist are referred by them. All these observations allowed us to conclude that the sociodemographic aspect of dermatoses in post-conflict Côte d'Ivoire differed very little from the period of peace.

In our series, 33.79% of the patients (therefore, a majority) were pupils or students. This result is comparable to that by Bissek et al. [9], who found 37.5% of pupils or students in a study conducted in a rural area of Cameroon. We only found 0.85% working in the agro-pastoral sector versus 47.25% in the study by Bissek et al. [9]. This is explained by the fact that our study took place in Abidjan, which is a highly industrialized urban area.

A total of 92.82% of our patients resided in Abidjan, which is explained by the fact that the dermatology department of Treichville, the only dermatology reference center in Côte d'Ivoire, is located in Abidjan. Among these patients residing in Abidjan, 51.29 % of

our patients came from the north of Abidjan; therefore, the majority of the municipality of Yopougon (18.06%) and 41.54% of our patients came from the south of Abidjan, thus the vast majority of the municipality of Treichville (13.16%). One would normally expect that there would be many more patients coming from the north of Abidjan (the largest and most populated part of the city of Abidjan) than from the south.

This narrow margin (9.75%) between patients coming from the northern and southern part of the city may be explained by the fact that, in the aftermath of the crisis, the municipalities of Yopougon and Abobo located north of the city and the most populous were not yet in the hands of government forces. The patients declaring that they came from the community of Yopougon were in fact in the vast majority of those displaced by war.

In our study, the consulting period ranged from two days to thirty years. This may be explained by the following facts: Not everyone is familiar with dermatology. Skin diseases are most often considered by many as aesthetic problems and, therefore, pushed into the background. More than one has found in free care a way to get to the dermatologist even if the problem has existed for many years.

Only 3.3% of our patients had a dermatological history, voluntary depigmentation was the most found history. A dermatological history is not systematically requested on dermatology consultation. The high rate of voluntary depigmentation indicates the extent of this phenomenon in our society.

Immunoallergic dermatoses were the most frequent in our series; the same has been the case in most African countries since the end of the twenty century [8,11-14]. Industrialization and growing urbanization in major African cities since independence have led to an improvement in living conditions on the one hand, yet on the other these have led to a change in diet and exposed the populations living there to irritants and pollutants, explaining the high prevalence of these dermatoses. It is the same for the city of Abidjan, in which this state of affairs has not changed despite the sociopolitical crisis that shook the country. Infectious and tropical pathologies come second in our study. Fungal diseases were the most common in this group (11.87%); this observation was also made by Bissek et al. (25.4%) [9], Nnoruka (10.2%) [10], Dlova et al. [6], Fekete (13%) [15], Yahya (12%) [8], Shibeshi (15.61%) [14]. This may be explained by the fact that Côte d'Ivoire is located in a tropical zone with a hot and humid climate conducive to the development of this type of pathology. The abusive and uncontrolled use of depigmenting topicals may also be a significant cause. Among the 4.05% of parasitoses that we found, scabies was the most frequent (3.95%). Our result was higher than that observed in most studies. Between 1973 and 2005 [8,15], the prevalence of scabies fell from 11.5% to 1.4% in the Kaduna region of Nigeria. Bissek et al. [9] found in 2010 a prevalence of 2.82% in rural areas, and Nnoruka [12] found a prevalence of 1.91% between 1999 and 2001. This high prevalence of scabies in our series may be explained by the overcrowding and deterioration of living conditions generated by the sociopolitical crisis. In addition, we only found two (0.10%) cases of leprosy, three (0.15%) cases of Buruli ulcer, and one case of mycetoma. As in Côte d'Ivoire, in most African countries today, there is a low prevalence of leprosy [8,14]. This is because the pathology is almost eradicated and the few remaining cases are supported by specialized structures and bodies. It is the same for Buruli ulcer, in which the disease is rampant in rural areas, and in this area, primary care structures exist. The cases seen in the dermatology department of Abidjan often come from the outskirts of the city or are serious cases referred from areas of high endemicity. Côte d'Ivoire is not an endemic area for mycetoma, hence its especially low prevalence.

Among inflammatory dermatoses, the most frequent pathology was lichen planus (1.92%), a result comparable to that by Nnoruka (4.8%) [12], Fekete (5.2%) [15], and Ogunbiyi et al. (3.4%) [16]. We only found 0.41% of cases of psoriasis. This result was similar to most studies done on patients with dark phototypes [6,8,14,15], confirming the low prevalence of this pathology among the black race. The Ivorian crisis, therefore, had no influence on the occurrence of these pathologies, although one might expect the contrary because of the psychosomatic nature of some (lichen planus, psoriasis, pityriasis rosea of Gibert).

The keloid scar (2.60%) was the most common benign tumor in our series. This result was comparable to that by Nnoruka (3.7%) [12]. Moreover, it was higher than that by Yahya (0.7%), Doe et al. (0.22%), Dlova et al. (0.84%), Ogunbiyi et al. (1.5%) [6,8,16,17]. The keloid scar is a particularity of people with dark phototypes, and it is a real problem for these patients because of the pain it may cause and its unsightly character. The low rates in some studies may be explained by the fact

that other medico-surgical disciplines also support this pathology. We found one (0.05%) case of plantar melanoma and three (0.15%) cases of actinic keratosis. In a study by Doe et al. [17], comparing dermatoses in Ghana and the United Kingdom, the incidence of malignant tumors in Ghana was 0.5% (no cases of melanoma) versus 22% in the United Kingdom (dominated by basal cell carcinoma). Dlova et al. (South Africa), and Nnoruka (Nigeria) [6,12] found 0.2% and 0.5% of skin tumors, respectively. Our result was similar to previous ones, confirming the low prevalence of cancers on black skin [18].

Our study was comparable to that conducted by Nnoruka [12] in Nigeria between 1999 and 2001, which found a prevalence of STIs/HIV-related dermatoses to be at 5.4%. In comparison to other studies: Nnoruka (0.31%), Mahé et al. (0.19%), Bissek et al. (0.40%) [9,10,12], we find that the prevalence of Kaposi's disease (0.57 %) is higher in ours. This may be explained, on the one hand, by the high prevalence (4.7%) of HIV/AIDS in Côte d'Ivoire, the most affected country in the West African subregion and, on the other, by the free healthcare with a high number of patients. Condyloma acuminata (1.98 %) was the most found STI in our study. This may be explained by the fact that the treatment is most often by cryotherapy or electrocoagulation. In Abidjan, dermatologists are sometimes the only to master these therapeutic techniques. The other STIs probably benefit from syndromic treatment at the level of peripheral health centers.

In our series, we found eighteen (0.94%) cases of exogenous ochronosis, a consequence of the abusive use of hydroquinone-based topical products with the intention to lighten one's skin. The prevalence of exogenous ochronosis in our series was similar to that found by Nnoruka (1.35%) in Nigeria and Doe et al. (0.88%) in Ghana; it was, nevertheless, lower than in Mali (3.80%) [10,12,17]. This relatively high rate of exogenous ochronosis in the different cities, including Abidjan, may be explained by the free sale of lightening topical products, which is accentuated by the media (abusive advertisements on the issue, erroneous images of beauty and social success). This sector has, therefore, not suffered as a result of the sociopolitical crisis. Skin depigmentation is a real burden in our society. Much effort remains to be exerted in order to decelerate its development by making populations aware of the dangers involved. In South Africa, the government was able to regulate the use and sale of products containing hydroquinone; thus, between 1978 and 2010, the prevalence of exogenous ochronosis fell from 10% to 0.05% [6]. Within three months, we found two (0.10%) cases of dermatitis herpetiformis, one (0.05%) case of dermatomyositis, three (0.15%) cases of neurofibromatosis type 1, and two (0.10%) cases of pyoderma gangrenosum, which are relatively rare pathologies. This may be explained by the free care, which has pushed even the poorest patients to consult, hence the high incidence.

CONCLUSION

The spectrum of dermatoses in the city of Abidjan after the period of the sociopolitical crisis is similar to that prevailing in most large African cities, in which industrialization and the improvement of living conditions have reduced infectious dermatoses while causing an increase in immunoallergic pathologies.

WHAT IS KNOWN?

- Infectious dermatoses account for the vast majority of wartime skin diseases. Field conditions such as heat, humidity, cold, and lack of hygiene may cause dramatic exacerbations of these conditions in times of war.
- In the literature, we found no study on the prevalence of dermatoses in a civilian population during or after a war. Our study on the prevalence of dermatoses in the general population after the Ivorian crisis, therefore, seems to be an original work. Through this study, we sought to describe the sociodemographic characteristics of patients and determine the dermatoses observed during this period and their frequency.

WHAT DOES THIS STUDY ADD?

We analyzed the files of 1755 patients and found that 56.75% were males and 43.25% were females. Teenagers and young adults aged 15 to 49 years were the most numerous to consult (71.11%).

- The profile of dermatoses in the city of Abidjan after the period of the sociopolitical crisis is similar to that prevailing in most large African cities, in which industrialization and the improvement of living conditions have reduced infectious dermatoses while causing an increase in immunoallergic pathologies.

ACKNOWLEDGMENTS

We are grateful to all who had participated in this research.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Cook N. Côte d'Ivoire's post-election crisis. 2011;79.
2. Matz H, Orion E, Matz E, Wolf R. Skin diseases in war. Clin. Dermatol. 2002;20:435-8.
3. Zhou Z, Liu T, Zhang Z. Skin disease in United Nations peacekeepers in Lebanon. BMJ Mil. Health 2017;163:27-30.
4. Cropley TG. Dermatology and skin disease in the American Civil War. Dermatol. Nurs. 2008;20:29-33.
5. Ivory coast [Internet]. Wikipedia 2022 [cited 2022 Mar 16]; Available from: https://en.wikipedia.org/wiki/Ivory_Coast
6. Dlova NC, Mankahla A, Madala N, Grobler A, Tsoka-Gwegweni J, Hift RJ. The spectrum of skin diseases in a black population in Durban, KwaZulu-Natal, South Africa. Int J Dermatol. 2015;54:279-85.
7. Ukonu AB, Eze EU. Pattern of skin diseases at University of Benin Teaching Hospital, Benin City, Edo State, South-South Nigeria: A 12 month prospective study. Glob J Health Sci. 2012;4:p148.
8. Yahya H. Change in pattern of skin disease in Kaduna, north-central Nigeria. Int J Dermatol. 2007;46:936-43.
9. Bissek A-CZ-K, Tabah EN, Kouotou E, Sini V, Yepnjio FN, Nditanchou R, et al. The spectrum of skin diseases in a rural setting in Cameroon (sub-Saharan Africa). BMC Dermatol. 2012;12:7.
10. Mahé A, Cissé IAh., Faye O, N'Diaye HT, Niamba P. Skin diseases in Bamako (Mali): Skin diseases in Bamako Report. Int. J. Dermatol. 1998;37:673-6.
11. Hartshorne ST. Dermatological disorders in Johannesburg, South Africa. Clin Exp Dermatol. 2003;28:661-5.
12. Nnoruka EN. Skin diseases in south-east Nigeria: A current perspective. Int J Dermatol. 2005;44:29-33.
13. Schulz EJ. Skin disorders in Black South Africans: A survey of 5000 patients seen at Ga-Rankuwa Hospital, Pretoria. South Afr Med J Suid-Afr Tydskr Vir Geneeskd. 1982;62:864-7.
14. Shibeshi D. Pattern of skin diseases at the University teaching hospital, Addis Ababa, Ethiopia. Int. J. Dermatol. 2000;39:822-5.
15. Fekete E. The Pattern of diseases of the skin in the Nigerian Guinea Savanna. Int J Dermatol. 1978;17:331-8.
16. Ogunbiyi AO, Daramola OOM, Alese OO. Prevalence of skin diseases in Ibadan, Nigeria. Int J Dermatol. 2004;43:31-6.
17. Doe PT, Asiedu A, Acheampong JW, Rowland Payne CME. Skin diseases in Ghana and the UK. Int J Dermatol. 2001;40:323-6.
18. Agbai ON, Buster K, Sanchez M, Hernandez C, Kundu RV, Chiu M, et al. Skin cancer and photoprotection in people of color: A review and recommendations for physicians and the public. J Am Acad Dermatol. 2014;70:748-62.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Dermatological manifestations during HIV infection in children in Dakar, Senegal

Boubacar Ahy Diatta, Nibirantije Pie, Khadim Diop, Robert Diatta, Mamadou Sarr, Patrice Mendy, Saer Diadie, Maodo Ndiaye, Niar Ndour, Coumba Ndiaye, Assane Diop, Moussa Diallo, Suzanne Oumou Niang

Department of Dermatology, Cheikh Anta Diop University of Dakar, Senegal

Corresponding author: Prof. Boubacar Ahy Diatta, MD, E-mail: ahydiatta@yahoo.com

ABSTRACT

Background: Dermatological manifestations are frequent and often constitute a circumstance of HIV discovery in 70% of cases [1]. They are observed in 83% of patients with AIDS and at an early stage in 75% [2,3,4,5]. The objective of this study was to describe the epidemiological, clinical, therapeutic, and evolutionary aspects of skin manifestations during HIV infection in children. **Materials and Methods:** We conducted a cross-sectional, multicentric, descriptive study over a period of ten years in two dermatology departments and one pediatric department in Dakar, Senegal. We included all HIV-seropositive children aged 0–15 years with mucosal cutaneous manifestations. A dermatologist and a specialist in the medical care of HIV performed the diagnosis of cutaneous manifestations. Data entry and analysis were performed with the SPSS software, version 9.05. **Results:** We collected 206 cases of cutaneous manifestations in 454 children followed for HIV infection. The hospital frequency was 45.3%. The children were male in 115 cases (55.83%) and female in 91 cases (44.17%), giving a sex ratio of 1.26. The mean age of the patients was sixty months, with extremes of one month to fourteen years. A mycotic dermatosis origin was noted in 47.37%, ringworm in 22.37%, dermatophytosis in 8.58%, oral candidiasis in 6.58%, seborrheic dermatitis in 6.58%, and perleche in 3.29%. Bacterial skin diseases were represented by furunculosis in 1.97%, and impetigo in 7.24%. Viral dermatoses included molluscum contagiosum in 10.53%, shingles in 9.21%, warts in 9.87%, and chickenpox in 3.95%. As for parasitic dermatoses, scabies was noted in 8.55, followed by larva migrans in 0.66% and cutaneous leishmaniosis in 0.66%. Immuno-allergic dermatoses accounted for 25% and included prurigo in 94.3%, atopic dermatitis in 1.90%, and fixed pigmented erythema in 1.90%. **Conclusion**: Cutaneous manifestations are a common discovery during HIV infection in children. They are marked by a predominance of infectious dermatoses in sub-Saharan Africa.

Key words: skin diseases; HIV; children; Dakar

INTRODUCTION

Human immunodeficiency virus (HIV) infection in children is a public health issue in several resource-limited countries in sub-Saharan Africa. Indeed, according to the World Health Organization and UNAIDS, in the 2.1 million children who died of AIDS in 2016, 88% lived in sub-Saharan Africa [1]. Dermatological manifestations are frequent and often constitute a circumstance of HIV discovery in 70% of cases. They are observed in 83% of patients with AIDS and in 75% at an early stage [2-5]. They tend to occur early in childhood during HIV infection. The early diagnosis of HIV infection not only improves medical care, yet also helps to improve the prognosis in children. The objective of the following study was to describe the epidemiological, clinical, therapeutic, and evolutionary aspects of skin manifestations during HIV infection in children.

MATERIALS AND METHODS

We conducted a cross-sectional, multicentric, descriptive study over a period of ten years in two dermatology

How to cite this article: Diatta BA, Pie N, Diop K, Diatta R, Sarr M, Mendy P, Diadie S, Ndiaye M, Ndour N, Ndiaye C, Diop A, Diallo M, Niang SO. Dermatological manifestations during HIV infection in children in Dakar, Senegal. Our Dermatol Online. 2023;14(1):35-38.

Submission: 18.05.2022; **Acceptance:** 21.08.2022

DOI: 10.7241/ourd.20231.7

departments and one pediatric department in Dakar, Senegal. We included all HIV-seropositive children aged 0–15 years with mucosal cutaneous manifestations. A dermatologist and a specialist in the medical care of HIV performed the diagnosis of cutaneous manifestations. Serological tests confirming the status of HIV were performed either by ELISA serology confirmed by the western blot or by plasma PCR-RNA in children under fifteen months of age. Data entry and analysis were performed with the SPSS software, version 9.05.

RESULTS

We collected 206 cases of cutaneous manifestations in 454 children followed for HIV infection. The hospital frequency was 45.3%. The children were male in 115 cases (55.83%) and female in 91 cases (44.17%), giving a sex ratio of 1.26. The mean age of the patients was sixty months, with extremes of one month to fourteen years. The age group between 13 and 60 months was the most representative (42.23%) (Fig. 1). Regarding family environment, the children lived with married parents in a couple in ninety cases (43.69%), were fatherless in fifty-one cases (24.76%), were motherless in thirty-four cases (15.04%), and were orphaned by both parents in four cases (1.94%). They had divorced parents in twenty-seven cases (13.10%). The circumstances of the discovery of HIV infection (Table 1) were with the waning of suggestive symptoms in 141 cases (68.45%), during the screening of seropositive parents in 55 cases (24.35%), and during the screening of pregnant women in ten cases (4.85%). Mother-to-child transmission was noted in 163 cases (97.95%) and through breastfeeding in 41 cases (19.9%). Prurigo (23.56%), ringworm of the scalp (15.11%), and molluscum contagiosum (7.11%) were the main circumstances of the skin discovery of HIV infection. Figure 2 shows the main skin manifestations in childhood HIV.

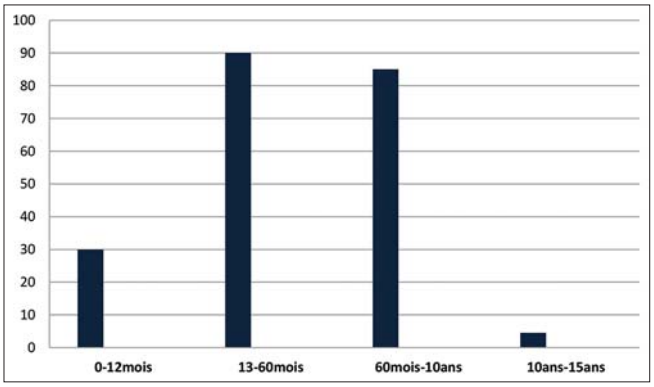


Figure 1: Distribution of the children depending to the age group.

A mycotic dermatosis origin was noted in 47.37%, ringworm in 22.37%, dermatophytosis in 8.58%, oral candidiasis in 6.58%, seborrheic dermatitis in 6.58%, and perleche in 3.29%. Bacterial skin diseases were represented by furunculosis in 1.97%, and impetigo in 7.24%. Viral dermatoses included molluscum contagiosum in 10.53%, shingles (Fig. 3a) in 9.21%, warts in 9.87%, and chickenpox in 3.95%. As for parasitic dermatoses, scabies was noted in 8.55% followed by larva migrans in 0.66% and cutaneous leishmaniasis (Fig. 3b) in 0.66%. Immuno-allergic dermatoses accounted for 25% and included prurigo in 94.3%, atopic dermatitis in 1.90%, and fixed pigmented erythema in 1.90%. Virologically, the children were positive for HIV-1 in 200 cases (97.09%) and HIV-2 in 6 cases (2.91%). A CD4 count assay was performed in 108 cases (52.4%). Table 2 illustrates the distribution of patients according to the CD4 count. From a therapeutic standpoint, all children had received antiretroviral treatment and specific

Table 1: Circumstance of the discovery of the child's HIV

	CLINICAL SIGNS	NUMBER (%)
General signs	Fever	10 (2.02)
	Chronic adenopathy	70 (14.1)
	Weight loss	14 (2.8)
	Failure to thrive	6 (1.21)
	Malnutrition	108 (21.8)
Digestive	chronic diarrhea	10 (2.02)
	Splenomegaly	5 (1.01)
	Hepatomegaly	5 (1.01)
Pulmonary	Interstitial lung disease	5 (1.01)
	Pulmonary tuberculosis	6 (1.2)
	Pneumonia	13 (2.6)
	Bronchial dilatation	3 (0.6)
	Pneumocystosis	2 (0.4)
Skin diseases	Cutaneous infections	226 (45.6)
Orthonaso-pharyngological	Recurrent otitis	8 (1.6)
	Parotidomegaly	3 (0.6)

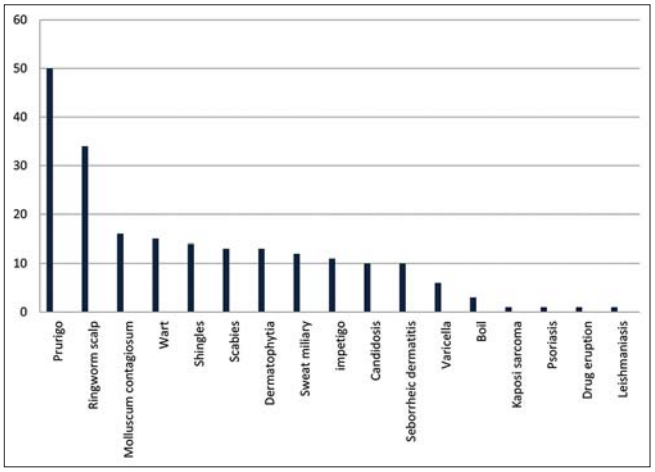


Figure 2: Distribution of the dermatoses during HIV infection in children.

medical care for the associated dermatosis. The course of the dermatosis was favorable in 70% of the cases. However, a recurrence of the dermatosis was noted in 8.89%, 11% were lost to follow-up, and the mortality rate was 11%.

DISCUSSION

Our study was particular by the high frequency of cutaneous manifestations in children infected with HIV at 40.5%. The high prevalence of skin diseases during HIV was also reported by several series in sub-Saharan Africa, Ethiopia, and Tanzania (Table 3) [6-11]. The average age of the children was sixty months, with their age ranging from 13 months to 120 months in 74.27%. The 0–5 year age group was more represented in our study as well as in the one reported in Africa [12-15]. This was related to a high prevalence of mother-to-child transmission of HIV infection [4,5]. A lack of regular HIV monitoring among pregnant women as well as denial and stigma were the contributing factors.

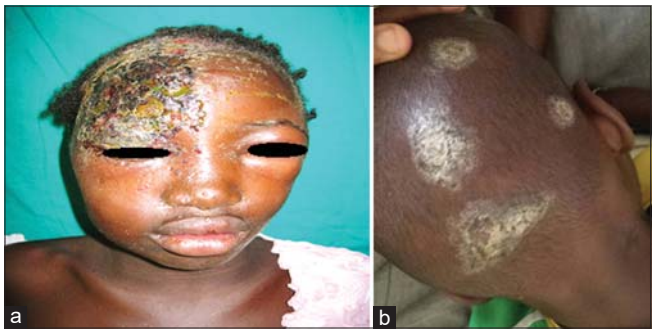


Figure 3: (a) Ophthalmic shingles in childhood HIV. (b) Cutaneous leishmaniasis in childhood HIV.

Table 2: Distribution of patients according to the CD4 count

Etiology of Dermatosis	CD4<200	200 < CD4 < 400	400 < CD4 < 499	CD4>500
Immunoallergic	15	10	10	10
Fungal	19	10	8	8
Viral	10	-	8	7
Bacterial	-	6	10	8
Parasitic	1	-	1	2
Other	2	5	11	10

Clinically, the predominant mucosal cutaneous manifestations were the circumstance of discovery in 46% and were in the following decreasing order: prurigo, profuse dermatophytosis, profuse molluscum contagiosum, flat facial warts, multi-metameric shingles, profuse chickenpox, profuse generalized scabies, recurrent pyoderma, ulcerative crusty cutaneous leishmaniosis, and Kaposi's disease.

Infectious dermatoses were the most observed in 67.5%. These results were consistent with previous works reported from tropical Africa [7-9]. Among infectious dermatoses, superficial mycosis represented the majority (47.37%). They were specific in the diffuse nature of the lesions as well as the severe mucosal cutaneous involvement indicative of immunosuppression in children. Viral dermatoses were represented by molluscum contagiosum in 7.11%. This prevalence was also similar to that observed in Guinea (7.69%) [9]. In fact, molluscum contagiosum is observed in 5% to 18% of children infected with HIV, more particularly in patients whose CD4 count is below 200 cells/mm^3 [16]. Molluscum contagiosum is frequent in children; however, in seropositive patients, the localization may be diffuse, atypical on the neck and on the face in particular [16,17].

Shingles was noted in 6.22%. It is a common occurrence in HIV. In Africa, its prevalence in HIV is estimated at 7.69% in Guinea [9], 0.7% in Tanzania [11], and 2.3% in Mali [10].

Bacterial dermatosis consisted mainly of pyoderma, with a predominance of impetigo and folliculitis. They were characterized by a diffuse and necrotic appearance.

Table 3: Our study compared to other African studies

	Our study	Mali [10]	Guinée[9]	Tanzanie[11]
Hospital frequency %	40.5	30.5	50	80.5
Sex-ratio	1.26	1.51	0.91	1.07
Circumstance of discovery	Prurigo 23.56%	Prurigo 25.1%	Candidiasis 38.46%	Prurigo 45.5%
	Ringworm scalp 15.11%	Ringworm scalp 14%	Prurigo 29.23%	Wart 20%
	Molluscum contagiosum 7.11%	Sweat miliary 12.8%	Molluscum contagiosum 7.69%	Ringworm scalp 16%
Antiretroviral therapy	43.69%	50%	100%	91.2%
Favorable outcome	70%	92.3%	75.38%	-
Mortality	11.11%	0	16.92%	-

Parasitic dermatoses were mainly represented by scabies (5.78%). In children with HIV infection, the lesions appeared diffuse, with the involvement of the face-characterized scabies and scalp. We noted two cases of Kaposi's disease, which is rarely reported in childhood HIV. It was Kaposi with the diffuse involvement of the tegument.

CONCLUSION

Cutaneous manifestations are a common discovery of HIV infection in children. They are marked by a predominance of infectious dermatoses in sub-Saharan Africa. Diagnosis, early treatment, and strengthening the prevention of mother-to-child transmission of HIV infection improve the prognosis of HIV-infected children.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Mohammed B, Lyamuya E, Mugusi F, Aris E, Shalé S, Magao P, et al. The prevalence and pattern of skin diseases in relation to CD4 count among HIV-infected Police officers in Dar es Salam. Trop Doc. 2003;33:44-8.
2. Mankahla A, Mosam A. Common skin conditions in children with HIV/AIDS. Am J Clin Dermatol. 2012;13:153-66.
3. Britto G, Augustine M. Mucocutaneous manifestations of human immunodeficiency virus (HIV) infection in children in relation to the degree of immunosuppression. Int J Dermatol. 2019;58:1165-71.
4. Monsel G, Ly F, Canestri A, Diousse P, Ndiaye B, Caumes E. [Prevalence of skin disorders in HIV patients in Senegal and relationship to degree of immunosuppression]. Ann Dermatol Venereol. 2008;135:187-93.
5. Atadokpede F, Yedomon H, Adegbidi H, Sehonou J, Ango-Padonou F. [Mucocutaneous manifestations of human immunodeficiency virus infection in Cotonou, Benin]. Med Trop. 2008;68:273-6.
6. Kobangué L, Dibéré K, Mossoro K, Fossi N, Niamba P. Manifestations cutanees et/ou muqueuses de l'infection a vih au service de dermatologie et de venereologie de Bangui. Rev Cames Sante. 2013;1:29-32.
7. Mbaye AD, Signaté SH, Diagne NR, Ba A, Sylla A, Diouf S, et al. [Epidemiological and clinical aspects of paediatric HIV infections in Albert-Royer Paediatric Hospital (Dakar, Senegal)]. Arch Pediatr. 2005;12:404-9.
8. Fofana Y, Traoré B, Dicko A, Faye O, Berthe S, Cissé L, et al. [Epidemio-clinical profile of dermatoses in children receiving dermatological consultation in the Department of Dermatology at the National Center for Disease Control in Bamako (Mali)]. Pan African Med J. 2016;25:238.
9. Soumah MM, Bangoura MA, Keïta M, Tounkara TM, Diané BF, Sylla D, et al. Skin manifestations of HIV infection in children in pediatric services of Conakry University Hospital (Guinea). J Cosmet Dermatol Sci Appl. 2018;8:39-46.
10. Konaré HD, Cissé I, Oumar AA, Diagne D, Traoré HC, Keitun MM, et al. Prévalence des dermatoses chez les enfants infectés par le VIH en milieu tropical au Mali. Rev Tunis Infectiol. 2013;7:111-5.
11. Panya M, Mgonda YM, Massawe AW. The pattern of muco-cutaneous disorders in HIV-Infected children attending care and treatment centres in Dar es Salaam, Tanzania. BMC Public Health. 2009;9:234.
12. Traoré A, Niamba P, Ouedraogo T, Sanon H, Sanou I, Kam KL, et al. Manifestations dermatologiques au cours du SIDA pédiatrique en milieu hospitalier de Ouagadougou (Burkina Faso). Nouv Dermatol. 2000;19:39-43.
13. Duko MG, Deribe B, Bedaso A, Ayalew M. Patterns of common skin infections among children living with HIV/AIDS in Hawassa City, Ethiopia: A cross sectional study. BMC Res Notes. 2018;11:881.
14. Doni S, Mitchell S, Bogale Y, Walker SL. Skin disorders affecting human immunodeficiency virus-infected children living in an orphanage in Ethiopia. Clin Exp Dermatol. 2011;37:15-9.
15. Ogunbiyi OA, Owoaje E, Ndahi U. Prevalence of skin disorders in school children in Ibadan, Nigeria. Ped Dermatol. 2005;22:6-10.
16 Mendiratta V, Mittal S, Jain A, Chander R. Mucocutaneous manifestations in children with human immunodeficiency virus infection. Indian J Dermatol Venereol Leprol. 2010;76:458-66.
17. Madhivanan P, Mothi SN, Kumarasamy N, Yepthomi T, Venkatesan C, Lambert JS, et al. Clinical manifestations of HIV infected children. Indian J Pediatr. 2003;70:615-20.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Pregnancy and cutaneous changes

Priya Selvakumar[1], Prabhalya Senthil Kumar[2], Shwetha Selvakumar[3]

[1]Department Of Dermatology, Karpaga Vinayaga Institute of Medical Sciences, Chengalpattu, India, [2]Vani Nursing Home, Chennai, India, [3]Department of Obstetrics and Gynaecology, PSP Medical College Hospital And Research Institute, Oragadam, India

Corresponding author: Priya Selvakumar, MD, E-mail: priyaselvakumar26@gmail.com

ABSTRACT

Background: Pregnancy is associated with a number of changes in the skin. Some are directly related to pregnancy (dermatoses of pregnancy), some are modified by pregnancy, and yet others are referred to as physiological. We undertook a clinical study to determine the frequency and pattern of skin changes in pregnant females. **Materials and Methods:** A six-month, multi-centric, cross-sectional study was conducted. A total of 250 pregnant females participated in the study. Detailed history taking and complete dermatological examination were performed. Results were tabulated and analyzed. **Results:** Physiological skin changes were the most common finding, with pigmentary changes in 98% of the cases. Specific dermatoses of pregnancy were observed in 6.8% of the cases, with atopic eruption of pregnancy being the most common (4.8%). The prevalence of fungal infections was 9.6%. One case of psoriasis was exacerbated by pregnancy. **Conclusion:** Pregnant females are more likely to experience cutaneous manifestations. In order to establish the diagnosis, thorough history taking and knowledge of the clinical presentation are necessary.

Key words: Pregnancy-specific dermatoses; Pregnancy; Physiological changes; Skin

INTRODUCTION

Pregnancy causes physical changes to the body, including cutaneous. Immunological, vascular, metabolic, and endocrine alterations are thought to be responsible for the physiological and pathological skin changes that occur during pregnancy. To categorize pregnancy dermatoses, a classification has been developed [1]. They are, in general, the physiological skin changes that occur during pregnancy, dermatoses impacted by pregnancy, and dermatoses developing exclusively during pregnancy. Our study sought to determine the prevalence and distribution of these skin alterations in expectant mothers and to document any coincidental dermatoses that appeared simultaneously with pregnancy.

MATERIALS AND METHODS

A total of 250 pregnant females who visited the hospital for their scheduled antenatal checkup participated in this multi-centric, cross-sectional study based in the city of Chennai. Before collecting a history and conducting an examination, the patient's informed consent was obtained. Demographic information, the duration of the pregnancy, the obstetric score, any current dermatological complaints and their onset in relation to the pregnancy, and any dermatological disorder that happened during the previous pregnancies were included in the proforma. This was followed by a complete dermatological examination. The diagnosis was based mainly on clinical grounds. Wherever appropriate, bedside tests such as KOH and skin scrapings were performed. Results were tabulated and analyzed with IBM SPSS, version 20.0.

Ethics Statement

Participants enrolled for the study gave their informed consent after a verbal explanation.

RESULTS

A total of 250 pregnant females participated in our study for a period of six months. Among them,

How to cite this article: Priya S, Prabhalya S, Shwetha S. Pregnancy and cutaneous changes. Our Dermatol Online. 2023;14(1):39-42.
Submission: 14.07.2022; **Acceptance:** 01.09.2022
DOI: 10.7241/ourd.20231.8

62% (n = 155) were primigravida. The average age was twenty-four years, ranging from 20 to 36 years. The third trimester was the time when a majority of the cases (n = 197; 78.8%) first appeared (Table 1).

Pregnancy-related physiological skin alterations were the most frequent presentations, observed in all cases (Table 2). The majority of the physiological changes (n = 245; 98%) were pigmentary changes. Linea nigra was the most prevalent pigmentary alteration (n = 228; 91.2%). Vascular alterations were found in 43 (17.2%) cases, bilateral pitting edema of the feet was the most frequent manifestation of vascular alterations, occurring in 37 cases (14.8%). In 127 cases (50.8%), connective tissue abnormalities manifesting as striae distensae were observed. Four cases (1.6%) of hair alteration were observed, three (1.2%) of which were telogen effluvium and one (0.4%) involved the onset of hirsutism during pregnancy.

There were seventeen cases of specific pregnancy-related dermatoses (6.8%). Atopic eruption of pregnancy was the most frequent presentation (n = 12; 4.8%). Five cases of polymorphic eruptions were noted (2%) (Table 3).

The course and symptoms of other dermatoses seen during the course of pregnancy were unmodified by pregnancy, with the exception of one patient, whose psoriasis was aggravated by pregnancy (Table 4).

Table 1: Distribution of the cases according to the trimester

Trimester of pregnancy	Number of cases	Percentage (n = 250)
First trimester	8	3.2%
Second trimester	45	18%
Third trimester	197	78.8%

Table 2: Distribution of physiological skin changes during pregnancy (LSCS: lower segment C-section)

Physiological skin changes seen	Number of cases	Percentage (n = 250)
Pigmentary changes		
Linea nigra	228	91.2%
Secondary areola	100	40%
Melasma	52	20.8%
Localized pigmentation (abdomen, gluteal)	45	18%
LSCS scar pigmentation	6	2.4%
Vascular changes		
Bilateral pitting pedal edema	37	14.8%
Varicose vein	6	2.4%
Connective tissue changes		
Striae distensae	127	50.8%
Hair changes		
Telogen effluvium	3	1.2%
Hirsutism	1	0.4%

DISCUSSION

We found that all pregnant females in our study (n = 250; 100%) revealed some signs of physiologic skin alterations. Pregnancy is known to cause hyperpigmentation in 90% of females according to one study [2]. Pigmentary changes were observed in 98% (n = 245) of our cases. Muzaffar et al. found pigmentary changes in 90.7 % of their cases [3], Fernandes et al. found pigmentary changes in 87.95% [4], Panicker et al. found hyperpigmentation in 87.67% [5], and Kannambal et al. found pigmentary changes in 90.8% [6]. Pregnancy pigmentary changes are thought to be caused by elevated serum levels of melanocyte-stimulating hormone, estrogen, and possibly progesterone [1]. Linea nigra was the most frequently observed pigmentary change in our study (n = 228; 91.2%). Linea alba, or the abdominal midline, darkens to become the linea nigra [7]. This usually runs from the pubic symphysis to the umbilicus yet may extend up to the xiphoid process [8]. Linea nigra was also identified as the most common pigmentary change in studies conducted by Panicker et al. (87.67%) and Hassan et al. (80%) [5,9].

Vascular alterations during pregnancy are believed to be caused by persistently high amounts of circulating estrogen, resulting in vessel dilation and proliferation [10]. In our study, bilateral pitting pedal edema was seen in 37 (14.8%) of the cases. Muzaffar et al. reported vascular abnormalities in 34.2% of their patients, with non-pitting pedal edema in 48.5% [3]. Kannambal et al. reported vascular alterations in 23.6% (n = 118) of their patients, with 16.4% exhibiting non-pitting pedal edema [6].

Table 3: Distribution of specific pregnancy dermatoses (AEP: atopic eruption of pregnancy; PUPP: pruritic urticarial papules and plaques of pregnancy)

Types of pregnancy specific dermatoses	Number of cases	Percentage (n = 250)
AEP	12	4.8%
PUPP	5	2%

Table 4: Distribution of miscellaneous dermatoses observed during pregnancy

Types of dermatoses	Number of cases	Percentage (n = 250)
Dermatophytosis	24	9.6%
Scabies	4	1.6%
Acne vulgaris	8	3.2%
Psoriasis	1	0.4%
Acute urticaria	10	4%
Pityriasis versicolor	7	2.8%

The prevalence of striae gravidarum was found to be 50.8% (n = 127) among our participants. The onset was more frequent during the third trimester (67.8%). Adrenocortical hormones, estrogen, relaxin, and physical factors such as straining caused by an increase in abdominal circumference may contribute to the higher occurrence of striae during the third trimester [6].

Telogen effluvium (n = 3; 1.2%) and hirsutism (n = 1; 0.4%) were the two types of hair alterations observed in our study. Muzaffar et al. found hair alterations in eighteen (12.8%) patients. Seven (38.9%) of the eighteen cases had diffuse scalp hair thinning and 50% experienced hair lengthening and improvement [3]

According to our results, atopic eruption of pregnancy was the most common type of specific pregnancy dermatosis (n = 12; 4.8%) for which atopic eczema developed for the first time during pregnancy. This began around the second trimester in all cases, which were all primigravidae. The neck and upper back were the most commonly affected areas. The four disorders listed in Holmes and Black's [11] initial classification of pregnancy-specific dermatoses were herpes gestationis (also known as pemphigoid gestationis), polymorphic eruption of pregnancy, prurigo, and pruritic folliculitis of pregnancy. Atopic eruption of pregnancy was also the most common specific pregnancy dermatosis observed by Fernandes et al. (70.88%) and Hassan et al. (50%) [4,9]. PUPPP (pruritic urticarial papules and plaques of pregnancy) was observed in five cases (2%) during our study. They were all primigravidae and the onset occurred during the third trimester. According to a hypothesis, rapid abdominal wall distension in primigravidae damages the connective tissue in the striae by converting non-antigenic molecules into antigenic, inducing an inflammatory reaction [1,12,13].

The most common concurrent dermatological disorder observed during pregnancy was dermatophytic infection (n = 24; 9.6%), which was confirmed by skin scarping and a KOH mount. Pregnancy had no effect on the course or characteristics of the dermatoses reported (Table 4), except for one patient, whose psoriasis was exacerbated during the pregnancy period. According to a study by Murase et al., 55% of their patients reported an improvement during pregnancy, 21% showed no change, and 23% reported the worsening of their psoriasis [14]. In another study, 63.3% of participants reported an improvement in their psoriasis and 87.7% experienced a postpartum flare, most commonly in four months of childbirth [15].

Pregnancy may necessitate a change in psoriasis treatment. During pregnancy, careful consideration should be given to the toxicity of the drugs and their safety for the mother and fetus. Topically applied drugs are the first-line treatment during pregnancy [16,17]. Emollients and moisturizers should be employed first for limited disease, as they are well-tolerated and produce few side effects [18]. As a second-line treatment, potent or super-potent topical corticosteroids may be administered. Current research suggests that they are associated with an increased risk of low birth weight [18,19]. During pregnancy, the first-line treatment for patients with moderate to severe psoriasis is phototherapy with NB-UVB. Methotrexate is categorized as category X by the FDA. It is contraindicated during pregnancy [20,21]. TNF inhibitors are probably the best option for the systemic therapy of psoriasis during pregnancy based on increasing evidence that these medications have no teratogenic, embryotoxic, or fetotoxic effects [22].

CONCLUSION

Clinical decision-making between active intervention and reassurance is aided by a strong clinical ability to distinguish between physiological skin changes and specific dermatoses of pregnancy. Intervention during pregnancy may be challenging because it necessitates thorough care for both the mother and the fetus.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Kroumpouzos G, Cohen LM. Dermatoses of pregnancy. J Am Acad Dermatol. 2001;45:1-22.
2. Winton GB, Lewis CW. Dermatoses of pregnancy. J Am Acad Dermatol. 1982;6:977-98.
3. Muzaffar F, Hussain I, Haroon TS. Physiologic skin changes during pregnancy: A study of 140 cases. Int J Dermatol. 1998;37:429-31.
4. Fernandes LB, Amaral WN. Clinical study of skin changes in low

and high risk pregnant women. An Bras Dermatol. 2015;90:822-6.
5. Panicker VV, Riyaz N, Balachandran PK. A clinical study of cutaneous changes in pregnancy. J Epidemiol Glob Health. 2017;7:63-70.
6. Kannambal K, Tharini GK. A screening study on dermatoses in pregnancy. J Clin Diagn Res. 2017;11:WC01-WC05.
7. George AO, Shittu OB, Enwerem E, Wachtel M, Kuti O. The incidence of lower mid-trunk hyperpigmentation (linea nigra) is affected by sex hormone levels. J Natl Med Assoc. 2005;97:685-8.
8. Wong RC, Ellis CN. Physiologic skin changes in pregnancy. J Am Acad Dermatol. 1984;10(6):929-940.
9. Hassan I, Bashir S, Taing S. A clinical study of the skin changes in pregnancy in Kashmir valley of north India: A hospital-based study. Indian J Dermatol. 2015;60:28-32.
10. Millintgton GWM, Brown GRAC. Skin and skin disease throughout life. In: Burns T, Breathnach S, Cox N, Griffiths C. Rook's Textbook of Dermatology, 8thedn. Wiley – Blackwell publications, 2010;8.9-13.
11. Holmes RC, Black MM. The specific dermatoses of pregnancy. J Am Acad Dermatol. 1983;8:405-12.
12. Ambros-Rudolph CM, Müllegger RR, Vaughan-Jones SA, Kerl H, Black MM. The specific dermatoses of pregnancy revisited and reclassified: Results of a retrospective two-center study on 505 pregnant patients. J Am Acad Dermatol. 2006;54:395-404.
13. Beckett MA, Goldberg NS. Pruritic urticarial plaques and papules of pregnancy and skin distention. Arch Dermatol. 1991;127:125-6.
14. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and postpartum. Arch Dermatol. 2005;141:601-6.
15. Boyd AS, Morris LF, Phillips CM, Menter MA. Psoriasis and pregnancy: Hormone and immune system interaction. Int J Dermatol. 1996;35:169-72.
16. Babalola O, Strober BE. Management of psoriasis in pregnancy. Dermatol Ther. 2013;26:285-92.
17. Bae YS, Van Voorhees AS, Hsu S, Korman NJ, Lebwohl MG, Young M, et al; National Psoriasis Foundation. Review of treatment options for psoriasis in pregnant or lactating women: From the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol. 2012;67:459-77.
18. Das A, Panda S. Use of topical corticosteroids in dermatology: An evidence-based approach. Indian J Dermatol. 2017;62:237-50.
19. Chi CC, Wang SH, Wojnarowska F, Kirtschig G, Davies E, Bennett C. Safety of topical corticosteroids in pregnancy. Cochrane Database Syst Rev. 2015;2015:CD007346.
20. Rademaker M, Agnew K, Andrews M, Armour K, Baker C, Foley P, et al. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration. Australas J Dermatol. 2018;59:86-100.
21. Bangsgaard N, Rørbye C, Skov L. Treating psoriasis during pregnancy: Safety and efficacy of treatments. Am J Clin Dermatol. 2015;16:389-98.
22. Balakirski G, Gerdes S, Beissert S, Ochsendorf F, von Kiedrowski R, Wilsmann-Theis D. Therapy of psoriasis during pregnancy and breast-feeding. J Dtsch Dermatol Ges. 2022;20:653-83.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Original Article

Factors determining the occurrence of hyperglycemia in women practicing voluntary depigmentation in four hospitals in Yaoundé, Cameroon

Karl Anthony Mouangue[1], Grace Anita Nkoro[2], Odette Berline Sigha[3], Claude Martine Etoa[2], Dahlia Noëlle Tounouga[4], Rose Kotto[5], Defo Defo[6], Martine Nida[4], Emmanuel Armand Kouotou[2]

[1]Higher Institute of Sciences and Health, Université des Montagnes, Cameroon, [2]Faculty of Medicine and Biomedical Sciences, Université of Yaoundé 1, Cameroon, [3]Faculty of Health Sciences, University of Bamenda, Cameroon, [4]National University Teaching Hospital of Cotonou, Benin, [5]Faculty of Medicine and Pharmaceutic Sciences, Université of Douala, Cameroon, [6] Yaoundé Central Hospital, Cameroon

Corresponding author: Dahlia Noëlle Tounouga, MD, E-mail: ntounouga@gmail.com

ABSTRACT

Background: Voluntary depigmentation (VD) is a cosmetic practice with potentially local and systemic complications such as hyperglycemia. The aim of this study was to find determinants of hyperglycemia in women who practices VD. **Methodology:** we carried out a retrospective cohort study with from February to August 2020 in four hospitals in Yaoundé, Cameroon. This study included two groups of women: one made up of women who practices VD (exposed group) and the other of women who does not practices VD (group of "unexposed"). Data were collected on CSPro 7.4 software and analyzed on SPSS 25 software. The association between hyperglycemia and VD was measured using Chi-square test. **Results:** We recruited 181 women: 60 exposed and 121 unexposed. Prevalence of hyperglycemia in the exposed group was 43.3% versus 27.3% in the unexposed group. After logistic regression, the relative risk was significantly higher (RR=5.7; 95% CI: 2.04-15.60) in women practicing DV (p=0.001). The second determinant significantly associated with hyperglycemia was the presence of metabolic syndrome (RR=16.5; 95% CI: 4.82-56.04; p<0.001). **Conclusion:** VD is a risk factor for the occurrence of hyperglycemia in our context.

Key words: Voluntary depigmentation; Hyperglycemia; Diabetes; Cameroon

INTRODUCTION

Voluntary depigmentation (VD) is a process aimed at obtaining a lightening of the skin for cosmetic purposes [1]. It is an old and widespread practice in black African countries, which is also observed in genetically pigmented populations, living in Europe, especially in France, and in United States [2-5]. this phenomenon is called differently depending on the country; it is called "xeesal" in Senegal, "tcha tcho" in Mali, "kwanza" in Gabon or "ndjansang" in Cameroon. It is a practice with real dangers [6-8]. In some countries, light skin is the ideal of beauty; VD offers a relatively quick and inexpensive solution, with, however, underestimated complications [9-11].

Although unknown, systemic complications can appear, depending on the nature and duration of usage of products [7]. Among systemic complications we have hypertension, obesity, diabetes, adrenal insufficiency, hypercorticism, neurological disorders and nephropathy etc. [6,7,12-15]. In sub-Saharan Africa, researchers have been interested on the systemic complications of VD. Thus, in 2005, Raynaud et al. demonstrated in a population of 147 women living in Dakar that VD significantly increased the risk of onset of diabetes

How to cite this article: Mouangue KA, Nkoro GA, Sigha OB, Etoa CM, Tounouga DN, Kotto R, Defo D, Nida M, Kouotou EA. Factors determining the occurrence of hyperglycemia in women practicing voluntary depigmentation in four hospitals in Yaoundé, Cameroon. Our Dermatol Online. 2023;14(1):43-48.

Submission: 07.08.2022; **Acceptance:** 28.10.2022

DOI: 10.7241/ourd.20231.9

[16]. In Togo in 2015, in a case-control survey involving 450 participants, Akakpo et al. demonstrated that high blood pressure, obesity and hyperglycemia were the classical complications found [15].

In Cameroon, few studies have been done on this topic. However, data exist on various epidemiological and clinical aspects of VD. In a study conducted in 2003, Sobngwi et al. highlighted the dangers of VD on adrenal function, and it has been clearly established that prolonged use of topical steroids can lead to adrenal insufficiency and diabetes mellitus [17].

In the light of previous studies and observations, with regard to the Cameroonian context two major problems can be individualized: the first is to know if there is a correlation between VD and hyperglycemia, and the second is to know what are determinants of hyperglycemia in depigmented women. Thus, this study aimed to explore the relation between VD and hyperglycemia, and highlight the contributing factors.

MATERIALS AND METHODS

Design and location of the study

We conducted a retrospective cohort study. Data collection was carried out between February and August 2020 in four hospitals in Yaoundé; Cameroon: General Hospital of Yaoundé, University Teaching Hospital of Yaoundé, Gynecological and Obstetrics Hospital of Yaoundé and Elig-Essono District Medical Center. These hospitals were chosen by convenience based on the availability of an experienced dermatologist.

Study population and criteria of selection

We included adult women aged at least 18 years received in the above-mentioned hospitals, who voluntarily agreeing to take part to the study and whose capillary blood glucose level was below 100 mg/dL before.

We excluded: (i)- any woman presenting with any affection or condition that could lead to hyperglycemia, prior to exposure (Cushing›s syndrome, medical corticosteroid therapy, antiretroviral treatment), (ii)- any pregnant women.

We formed two groups of women: one made up of women practicing VD (exposed group) and the other of women not practicing VD (unexposed group).

Sampling

Our sampling was non-probabilistic.

The minimum sample size was 81 women divided into 27 exposed and 54 unexposed, obtained from Schlesselman's formula [18]:

We used data collected by Bigna et al. [19], to determine p1, which represented the combined prevalence of diabetes and prediabetes in the general adult population.

Digital Application:
- Confidence interval: 95%
- Power: 90%
- Ratio of unexposed to exposed: 2
- Percentage of non-exposed with results: 12.9%

Procedure

Data were collected from patients present at the study sites using a pre-established and pre-tested questionnaire. We collected their socio-demographic characteristics (age, religion, profession, marital status), their clinical characteristics (antecedents, weight, height, blood pressure, fasting capillary glycemia). Among the exposed group, we collected data on exposure (type of product, nature of active ingredient, frequency and duration of use). The glycemia considered was the fasting glycemia; fasting referred to the absence of caloric intake dating back more than 8 hours [20]. Blood glucose was taken after careful disinfection of the patient's hands. A lancing device was used to take a drop of blood from the patient's finger. The drop of blood was put on the reading head of the glucometer strip and the result appeared after a few seconds. Blood glucose was given in milligrams per deciliter. We considered hyperglycemia for any value greater than or equal to 100 mg/dL [20].

Statistical analysis

Sociodemographic data, history, clinical data and capillary fasting blood glucose were collected on CS Pro 7.4 software and analyzed on SPSS 25 software. Association between hyperglycemia and VD was measured using the Chi test -square. Relative risk and its 95% confidence interval (95% CI) were used to investigate, if any, the strength of association between VD and hyperglycemia, as well as risk factors for hyperglycemia in women practicing VD. We used a

logistic regression model. The statistical significance threshold was set at $p < 0.05$.

Ethics Statement

We have obtained ethical clearance from the Institutional Ethics and Research Committee of Université des Montagnes (2020/075/UdM/PR/CIE); and research authorizations were obtained from the competent authorities of the hospitals. We conducted our study in strict accordance with the fundamental principles of the Helsinki Declaration on Research Involving Persons. Aspects and procedures were fully presented to each potential participant and we included only those who voluntarily gave their consent. Patients who refused to participate did not suffer of any prejudice with regard to their medical follow-up. Fingers have been thoroughly cleaned (with soap and water) before taking the blood sugar, so as to minimize any risk of infection of the injection site. The data was kept confidential and participants received their blood glucose results immediately. Those with abnormal values were referred to the dedicated services for following up. All participants were advertised about adverse effects of VD.

RESULTS

We recruited 181 women, of whom 60 constituted our exposed group and 121 constituted our unexposed group. The age varied between 18 and 64 years, the modal class was [18-30] years (54.2%) (Table 1). The values of age, Body Mass Index (BMI) and systolic blood pressure in exposed group were lower than those of the unexposed group with, respectively, 30 ± 8.6 years; 26.2±2.7kg/m²; 120.1±14.5mmHg. Mean capillary glycaemia in the exposed group (94.9 ± 24.4 mg/dL) was higher than in the unexposed group (91.11 ± 27.2 mg/dL) (Table 2). Active ingredients used for VD were hydroquinone derivatives (48.3%), corticosteroids (28.3%), fruit acids (15%), glutathione (3.3%), caustics (3.3%) and mercury and its derivatives (1.7%) (Fig. 1). Prevalence of hyperglycemia among users of whitening products was 43.3%. The use of whitening products (RR = 5.7, 95% CI: 2.05-15.60; p = 0.001) and metabolic syndrome (RR = 16.5; 95% CI: 4.82-56.04; p < 0.001) were significantly associated with occurrence of hyperglycemia compared to the reference group (Table 3). The use of whitening products whose active ingredient was corticosteroid (p = 0.001) and a longer duration of usage (more than one year) increased the risk of occurrence of hyperglycemia (p = 0.009) (Figs. 2 and 3).

Table 1 : sociodemographic characteristics of the population

variables	Number (N)	Frequency (%)
Age (years)		
[18-30]	98	54.2
[30-45]	55	30.3
[45-64]	28	15.5
Total	181	100
Marital status		
Maried	46	25.4
Single	49	27.8
Cohabiting	76	42
widow	10	4.8
Total	181	100
Occupation		
Trader	43	23.8
Student	45	24.9
Self-employed	43	23.8
Employed	50	27.5
Total	181	100
Religion		
Christian	165	91.2
Muslim	16	8.8
Total	181	100

Table 2 : Clinical characteristic

Variables	Mean	
	Cases (N=60)	Controls (N=121)
Age (years)	30±8.6	33.8±11.5
BMI (kg/m²)	26.2±2.7	26.3±1.19
Systolic Blood Pressure (mmHg)	120.1±14.5	120.4±17.2
Diastolic Blood Pressure (mmHg)	77.2±8.6	76.7±6.1
Abdominal Circumference (cm)	83.4±11.4	83.0±10.7
Glycemia (mg/dL)	94.9±24.4	91.1±27.2

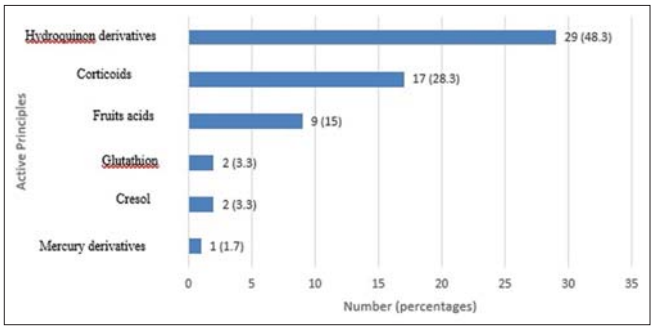


Figure 1: Active Principles used for VD.

DISCUSSION

Prevalence of hyperglycemia in our exposed group was 43.3%, which is similar to 46.3% found by Raynaud et al. among 147 Senegalese women practicing VD [16]. This high prevalence of hyperglycemia among users of lightening products could be explained by the

Table 3 : Associated factors of hyperglycemia after logistic regression

Variables	Relatif Risk RR	CI (95%)		*p* Value
Usage of whitening products	5.65	2.05	15.60	0.001
Metabolic Syndrome	16.45	4.83	56.04	<0.001
Family history of diabetis	2.08	0.80	5.35	0.130
<45 years	3.18	0.73	13.83	0.122
HBP	2.40	0.46	12.60	0.302
Underweight/Obesity	1.33	0.58	3.61	0.579
Tabagism	1.76	0.24	12.93	0.576

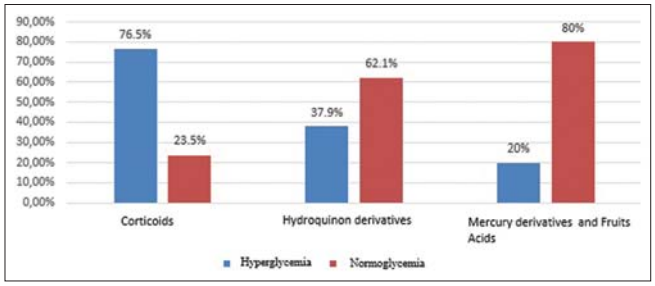


Figure 2: Repartition of hyperglycemia among exposed patient according to active principle.

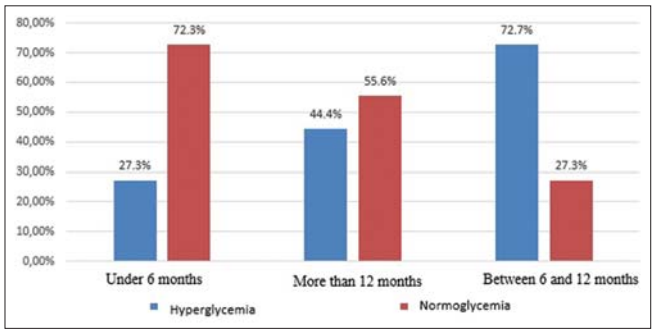


Figure 3: Repartition of hyperglycemia among exposed patient according to the duration of exposition.

high proportion of women using products containing corticosteroids (28.3%), an active ingredient which was strongly associated with hyperglycemia (76.5%). Corticosteroids are well known for their hyperglycemic effect [21,22]. Causality and power of the association between VD and occurrence of hyperglycemia were measured and evaluated. This enabled us to establish a relative risk of hyperglycemia associated to VD of 5.7 (95% CI: 2.05-15.60; p = 0.001). This result can be compared to that found in 2015 by Akakpo et al. who found a correlation between VD and hyperglycemia (OR= 1.5; 95% CI: 1.2-9.65) in a sample of 450 women whose clinical characteristics were similar to those of our sample, but whose definition of hyperglycemia (glycemia greater than or equal to 1.5 g/L) was different from ours [15]. Two hypotheses explain the association between VD and the onset of hyperglycemia. Firstly, the usage of topical corticosteroids for VD; the systemic effects of topical corticosteroids have been well described, particularly the occurrence of chronic hyperglycemia [23,24]. Corticosteroids increases hepatic gluconeogenesis and increases resistance of muscle cells to insulin [25]. Secondly, the non-mention of harmful active ingredients, in particular hydroquinone and corticosteroids on most whitening products, could induce underestimation of the number of products containing corticosteroids.

The class of corticosteroid (p = 0.001) and usage longer than one year (p = 0.009) were significantly associated with the occurrence of hyperglycemia. Whitening products made with corticosteroids were those most often associated with hyperglycemia. We found that 76.5% users of these products had hyperglycemia compared with 37.9% users of lightening products based on hydroquinone and 20% users of products containing the other active ingredients (AHA, glutathione, cresol). This is due to the fact that after prolonged application of topical corticosteroids, they are absorbed by the skin and reach the general circulation [23,24].

Various studies mentioned the harmful effect of corticosteroids, culminating in their alteration of mechanisms regulating carbohydrate metabolism, which leads irremediably to hyperglycemia [23-25]. As far as the other active ingredients are concerned, no study has clearly highlight relation between them and hyperglycemia, with regard to hydroquinone [26], AHAs [27] and glutathione [28]. In these cases, hyperglycemia can be due to factors other than the nature of the lightening product such as metabolic syndrome or the existence of an unmentioned active ingredient [29-31].

The longer a woman uses a lightening product, the more she is exposed to hyperglycemia. Proportion of women with hyperglycemia among users of lightening products increased from 27.3% for those who used products for less than 6 months, to 44.4% for those who used them between 6 and 12 months, then 72.7% for those over one year old. These results are in line with those of Phan et al., who demonstrated the association between the risk of having type 2 diabetes and usage of topical corticosteroids [23]. The potency of this combination depends on cumulative dose and cumulative duration of use [23]. The same result was found by Andersen et al. whose study showed the existence of a dose-dependent relationship between topical corticosteroids and occurrence of type 2 diabetes [24]. In this study, an increased risk of having

type 2 diabetes was found in patients whose duration of use exceeded one year, compared to those whose duration did not exceed one year.

Metabolic syndrome was significantly associated with hyperglycemia (relative risk 16.5; 95% CI: 4.82-56.04; $p < 0.001$). This could be explained by the fact that metabolic syndrome is a clinical entity whose elements, taken individually, are able to cause hyperglycemia such as abdominal obesity and high blood pressure [32,33].

Limits

Various constraints have plagued our work. Covid-19 pandemic slowed the progress of our study, which was suspended during April and May. Once recruitment resumed, we had to face the low attendance of hospitals by the targeted patients. Despite the fact that this is the first study in Cameroon interested in the relationship between VD and hyperglycemia, usage of non-probability sampling limits its representativeness. On the other hand, it was difficult to demonstrate the absence of hyperglycemia before exposure.

CONCLUSION

VD is a risky cosmetic practice. The prolonged use of topical corticosteroids accentuates the occurrence of hyperglycemia in users of lightening products in our context. Preventive measures should be undertaken to screen for glycemic disorders in people practicing VD.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Petit A. Skin lightening and its motives: A historical overview. Ann Dermatol Venereol. 2019; 146: 399-409.
2. Del Giudice P. Prevalence and correlates of skin bleaching. Int J Dermatol. 2019; 58: e185.
3. Mahé A. The practice of skin bleaching for a cosmetic purpose in immigrant communities. J Travel Med. 2014; 21: 282-287.
4. Michalek IM, Liu B, Benn EK, Dos Santos FL. Skin lightening products's violations in Europe: an analysis of the rapid alert system for dangerous non-food products 2005-2008. Reg Toxicol Pharm. 2019; 106: 50-54.
5. Benn EK, Alexis A, Mohamed N, Wang YH, Khan IA, Liu B. Skin bleaching and dermatologic health of African and Afro-Caribbean populations in the US: new directions for methodologically rigorous, multidisciplinary, and culturally sensitive research. Dermatol Ther (Heidelb). 2016; 6: 453-459.
6. Sommerlad M. Skin lightening: causes and complications. Clin Exp Dermatol. 2022; 47: 264-270.
7. Olumide YM, Akinkugbe AO, Altraide D, Mohammed T, Ahamefule N, Ayanlowo S, Onyekonwu C, Essen N. Complications of chronic use of skin lightening cosmetics. Int J Dermatol. 2008; 47: 344-353.
8. Masub N, Khachemoune A. Cosmetic skin lightening use and side effects. J Dermatolog Treat. 2020; 10: 1-6.
9. Kourouma S, Gbery IP, Kaloga M, Ecra EJ, Sangaré A, Kouassi IY, et al. Dépigmentation cutanée cosmétique des femmes noires: résultats d'une enquête CAP à Abidjan (Côte d'Ivoire). Pan Afr Med J. 2016; 24: 159.
10. Kouotou EA, Nansseu JRN, Adegbidi H, Zoa Mebara TCJ, Ndjitoyap Ndam EC. Skin whitening among Cameroonian female university students: knowledge, attitudes, practices and motivations. BMC Womens Health. 2017; 17: 33.
11. Yusuf MA, Mahmoud ND, Rirash FR, Stoff BK, Liu Y, McMichael JR. Skin lightening practices, beliefs, and self-reported adverse effects among female health science students in Borama, Somaliland: A cross-sectional survey. Int J Womens Dermatol. 2019; 5: 349-355.
12. Chan TYK, Chan APL, Tang HL. Nephrotic syndrome caused by exposures to skin-lightening cosmetic products containing inorganic mercury. Clin Toxicol (Phila). 2020; 58: 9-15.
13. Ho YB, Abdullah NH, Hamsan H, Tan ESS. Mercury contamination in facial skin lightening creams and its health risks to user. Regul Toxicol Pharmacol. 2017; 88: 72-76.
14. Hodé AK, Dédjan H. Adrenocortical corticotropic insufficiency secondary to the use of cosmetic dermocorticoids. Arch Clin Cases. 2021; 6: 81-84.
15. Akakpo S, Mouhari-Toure A, Saka B, Téclessou J, Elegbede Y, Boukari T. Complications systémiques de la dépigmentation cosmétique volontaire chez les femmes au Togo : étude cas-témoins. Ann Dermatol Venerol. 2015; 143: 197-201.
16. Raynaud E, Cellier C, Perret J-L. Dépigmentation cutanée à visée cosmétique: enquête de prévalence et effets indésirables dans une population féminine sénégalaise. Ann Dermatol Venerol. 2001; 128: 720-724.
17. Sobngwi E, Lubin V, Ury P, Timsit F-J, Gautier J-F, Vexiau P. Adrenal insufficiency and diabetes mellitus secondary to the use of topical corticosteroids for cosmetic purpose. Ann Endocrinol. 2003; 64: 202-204.
18. Schlesselman JJ. Sample size requirements in cohort and case-control studies of disease. Am J Epidemiol. 1974; 99: 381384.
19. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: A systematic review and meta-analysis. Diabetes Res Clin Pract. 2018; 137: 109118.
20. Monnier L. Définitions et classifications des états diabétiques. Diabétologie 3ème édition. Elsevier Masson; 2019. p. 38.
21. Morton A, Menon A, O'Moore-Sullivan T. A young African woman with hyperglycaemia. Aust Fam Physician. 2016; 45: 206-207.
22. Sue LY, Milanesi A. Acute Hyperglycemia due to topical corticosteroid administration. Case Rep Endocrinol. 2019; 1-3.
23. Phan K, Smith SD. Topical corticosteroids and risk of diabetes mellitus: systematic review and meta-analysis. J Dermatol Treat. 2019; 2019; 345-349.
24. Andersen YMF, Egeberg A, Ban L, Gran S, Williams HC, Francis NA, et al. Association between topical corticosteroid use and type 2 diabetes in two european population-based adult cohorts. Diabetes Care. 2019; 42: 1095-1103.

25. Tamez-Pérez HE, Quintanilla-Flores DL, Rodríguez-Gutiérrez R, González-González JG, Tamez-Peña AL. Steroid hyperglycemia: prevalence, early, detection and therapeutic recommendations: a narrative review. World J Diabetes. 2015; 6: 1073-1081.
26. Owolabi JO, Fabiyi OS, Adelakin LA, Ekwerike MC. Effects of Skin Lightening Cream Agents – Hydroquinone and Kojic Acid, on the Skin of Adult Female Experimental Rats. Clin Cosmet Investig Dermatol. 2020;13: 283-289.
27. Sharma DK, Pandey J, Akhilesh K, Mukherjee D. Synthesis of heteroaryl/aryl kojic acid conjugates as stimulators of glucose uptake by GLUT4 translocation. Eur J of Med Chem. 2014; 85: 727-736.
28. Sitohang IBS, Ninditya S. Systemic Glutathione as a Skin-Whitening Agent in Adult. Dermatol Res Pract. 2020; 2020: 1-6.
29. Maneli MH, Wiesner L, Tinguely C, Davids LM, Spengane Z, Smith P, van Wyk JC, Jardine A, Khumalo NP. Combinations of potent topical steroids, mercury and hydroquinone are common in internationally manufactured skin-lightening products: a spectroscopic study. Clin Exp Dermatol. 2016; 41: 196-201.
30. Gbetoh MH, Amyot M. Mercury, hydroquinone and clobetasol propionate in skin lightening products in West Africa and Canada. Environ Res. 2016; 150: 403-410.
31. Desmedt B, Courselle P, De Beer JO, Rogiers V, Grosber M, Deconinck E, De Paepe K. Overview of skin whitening agents with an insight into the illegal cosmetic market in Europe. J Eur Acad Dermatol Venereol. 2016; 30: 943-950.
32. Grundy SM. Metabolic syndrome update. Trends Cardiovasc Med. 2016; 26: 364-373.
33. Engin A. The definition and prevalence of obesity and metabolic syndrome. Adv Exp Med Biol. 2017; 960: 1-1.

Source of Support: This article has no funding source,

Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Brief Report

Topical steroid menace: A case series of severe debilitating infections during the COVID-19 pandemic

Deena Patil, Kanakapura Nanjundaswamy Shivaswamy, Namitha Subramani Reddy, Tharayil Kunneth Sumathy

Department of Dermatology, M S Ramaiah Medical College and Hospital, Bengaluru, India

Corresponding author: Deena Patil, MD, E-mail: deenajc22@yahoo.com

ABSTRACT

Background: Topical corticosteroids is a boon and also a bane in treating chronic skin conditions. The risk of cutaneous infections due to topical steroids increases with their potency, dose, and duration of treatment. Herein, we present a case series of severe debilitating infections secondary to topical steroid abuse. **Materials and Methods:** We came across five cases of severe skin infection following the prolonged application of topical steroids. These cases gave a history of the use of steroid creams for persistent skin conditions and the inability to visit the hospital due to the prevailing COVID-19 pandemic. **Observations**: We came across two cases of crusted scabies, two cases of Fournier's gangrene, and a case of erosio interdigitalis blastomycetica. These cases had been using topical steroids for a prolonged period for other dermatological conditions. **Conclusion**: We propose that, as crusted scabies and erosio interdigitalis blastomycetica mimic various other papulosquamous disorders, a KOH examination is a diagnostic tool. Topical steroid abuse is one of the predisposing factors for Fournier's gangrene.

Key words: Topical Steroids; Crusted Scabies; Fournier's Gangrene; COVID-19.

INTRODUCTION

The skin, as a protective organ, provides both a mechanical and immunological barrier to environmental pathogens. The mechanical barrier is due to the arrangement of epidermal keratinocytes, tight junctions, and the lipid bilayer. The immunological barrier is by SALT (skin-associated lymphoid tissue), which constitutes keratinocytes, Langerhans cells, mast cells, and B- and T-lymphocytes [1]. Glucocorticoids produce qualitative and quantitative immunosuppressive effects on the immune system. Both the anti-inflammatory and immunosuppressive effect is exerted through the inhibition of NF-kB and other transcription factors. The risk of cutaneous infection to topical steroids increases with the potency, dose, and duration of treatment [2,3]. Herein, we present a case series of severe debilitating infections that caused a secondary to topical steroid menace.

MATERIALS AND METHODS

During the period from January 2020 to December 2021, we came across five cases of severe skin infection following the prolonged application of topical steroids. All these cases gave a history of using steroid creams in view of persistent skin conditions and itching. The cases also expressed their inability and difficulty to visit the hospital due to the prevailing COVID-19 pandemic. These cases were seen as outpatient cases and inpatient referrals from other departments.

Ethics Statement

A written informed consent was obtained from all the cases. The examination of the patients was conducted according to the principles of the Declaration of Helsinki.

How to cite this article: Patil D, Shivaswamy KN, Reddy NS, Sumathy TK. Topical steroid menace: A case series of severe debilitating infections during the COVID-19 pandemic. Our Dermatol Online. 2023;14(1):49-55.

Submission: 02.09.2022; **Acceptance:** 05.11.2022

DOI: 10.7241/ourd.20231.10

Case 1

The first case was a 66-year-old male presenting with itchy, scaly lesions on the lower abdomen, lower back, and buttocks persistent for three months, of insidious onset, gradually progressive, associated with minimal nocturnal itching and no relieving factors. There were similar complaints in three other family members. He had a history of being treated for chronic plaque psoriasis with 0.05% clobetasol propionate cream, which he continued to apply to the skin lesions for one year. A dermatological examination revealed multiple, thick, scaly plaques in the gluteal area (Fig. 1a), flank (Fig. 1b), and lower abdomen, sparing the web spaces. Some plaques showed fissuring (Fig. 1c). Umbilical hernia was noted (Fig. 1d). Relevant routine blood investigations were normal. Serology for HIV 1 and 2 were non-reactive. KOH mount scraping from the lesion on the abdomen revealed *Sarcoptes scabiei* mites and eggs (Figs. 1e and 1f). A diagnosis of crusted scabies was reached.

Case 2

The second case was a 68-year-old male presenting with itching all over the body with scaly, crusted lesions on the back and web spaces present for eight months. The lesions were insidious in onset, gradually progressive, and aggravated in the last two months. The patient was previously diagnosed as a case of exfoliative dermatitis and had been applying topical 0.05% clobetasol propionate cream and continued the application for the present symptoms as well. An examination revealed large areas of scaly, hyperpigmented plaques on the back on a background of mild erythema. Some ecchymotic patches and erythematous, discrete papules were also observed (Fig. 2a). Multiple, scaly hyperkeratotic plaques were present on the first web spaces of both hands and axillae with fissuring and crusts (Fig. 2b and 2c). Relevant routine blood investigations were normal. Serology for HIV 1 and 2 were non-reactive. KOH mount from the hyperkeratotic lesion revealed the *Sarcoptes scabiei* mite (Fig. 2d). A diagnosis of crusted scabies was reached.

Case 3

The third case was a 62-year-old female presenting with itchy lesions on the hands present for four years, aggravated on and off on exposure to water and detergents, temporarily relieved by taking treatment. The patient was clinically diagnosed as allergic contact dermatitis and had been applying topical 0.05% halobetasol propionate cream. In view of persistent lesions, the patient continued to apply the cream to the lesions for more than six months. An examination

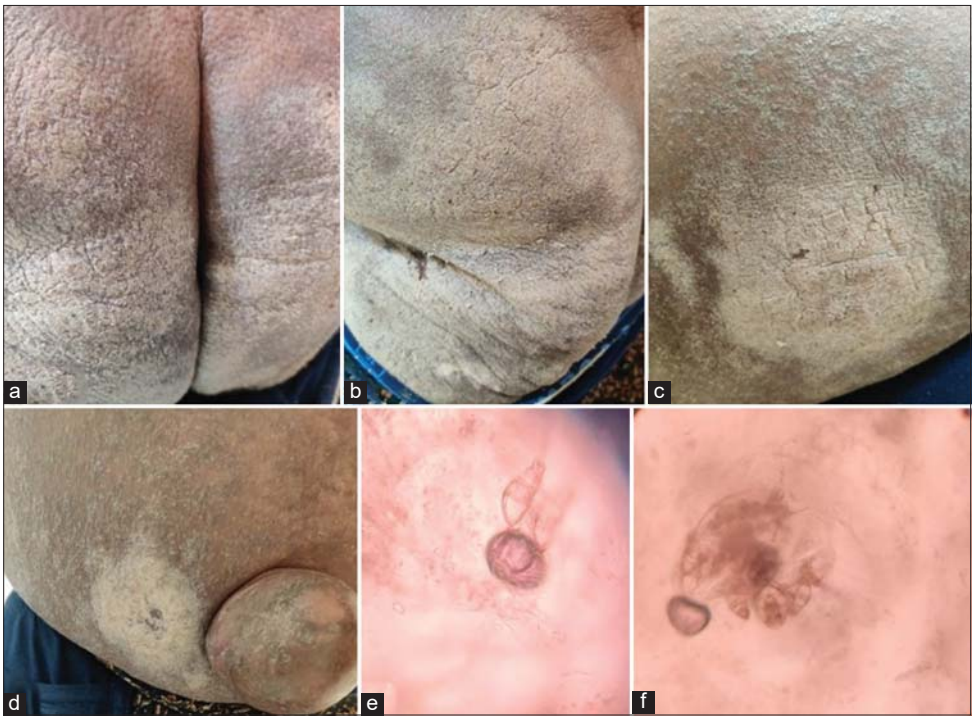


Figure 1: Thick, scaly plaques present on (a) the gluteal area, (b) flanks, (c-d) lower abdomen showing fissuring and umbilical hernia. (e-f) Sarcoptes scabiei mites and eggs (10% KOH mount, 400×).

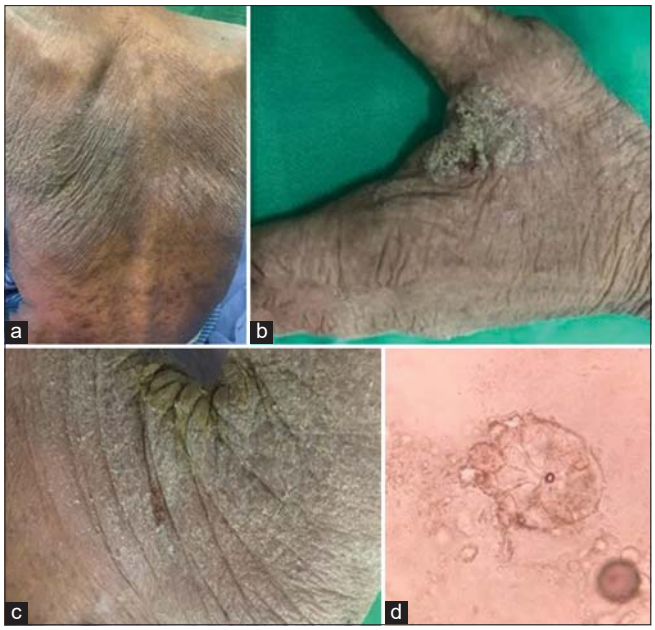


Figure 2: (a) Scaly, hyperpigmented plaques present over the back on a background of mild erythema with discrete papules. (b-c) Scaly, hyperkeratotic plaques present over the first web spaces of both hands with fissuring and crusts. (d) Sarcoptes scabiei mite (10% KOH mount, 400×)

revealed hyperpigmented, hyperkeratotic plaques with thick, adherent, yellowish crusts and scales on the palms, extending to the web spaces and the dorsa of the hands (Figs. 3a and 3b). Discoloration and onycholysis of the fingernails on the right hand and the nails of the left thumb and index finger were present (Figs. 3c and 3d). Routine investigation revealed microcytic hypochromic anemia. Serology for viral screening was non-reactive. 10% KOH mount of the scrapings from the hyperkeratotic plaque showed pseudo hyphae with yeast-like cells (Fig. 3e). Thus, the final diagnosis was erosio interdigitalis blastomycetica of the palms.

Case 4

The fourth case was a 65-year-old male presenting with swelling and wound on the scrotal area persistent for five days, sudden in onset, progressive in nature, associated with foul-smelling pus discharge and pain. The patient had been applying a topical cream consisting of 0.05% clobetasol propionate, neomycin, and miconazole for eight months. An examination revealed hyperpigmented, scaly patches on the groin folds extending to the mons pubis, lower abdomen, medial aspect of both the thighs, with several areas of erythema and atrophic skin (Fig. 4a). A large ulcer was present on the scrotum, extending to the penile shaft and glans penis with yellowish purulent slough over the penile shaft (Fig. 4b). Routine blood tests were normal, and HIV 1 and 2, HCV, and HBsAg were non-reactive. Tissue culture showed *Citrobacter koseri* and *enterococcus* species, which was pan-resistant to antibiotics. A KOH examination from the scaly plaque on the groin showed long, refractile branching hyphae. A diagnosis of Fournier's gangrene of the scrotum with tinea incognito was established.

Case 5

The fifth case was a 47-year-old male presenting with a burning sensation and itching on the scrotum persistent for six months. The patient had been using a combination cream of 0.05% clobetasol propionate, neomycin, miconazole, and chlorhexidine cream for the same. The patient also gave a history of a wound on the scrotal area with pain, associated with purulent discharge for which he had undergone debridement of the ulcers on the scrotal area one month previously. An examination revealed scaly, hyperpigmented patches on the groin folds, extending to the scrotum, mons pubis, and medial aspect of both thighs (Fig. 5a). Irregular, healing ulcers of 3 × 2 cm and 4 × 3 cm with yellowish slough over the floor were seen on the scrotum (Fig. 5b). Routine blood tests were normal and viral screening was non-reactive. Tissue culture done at the time of surgical debridement showed pan-resistant *Escherichia coli*. A KOH examination of the scaly plaques revealed long, branching, refractile hyphae. A diagnosis of Fournier's gangrene with tinea incognito was established.

Table 1 summarizes a detailed history of topical steroid use in all of the above-mentioned cases and their management.

RESULTS

Among the five cases presented here, four were males and one was a female. The age distribution observed showed that there were four elderly patients (older than sixty years) one case in the fourth decade of life. The duration of the application of steroids in all cases ranged from three to eight months. The associated co-morbidities were type 2 diabetes mellitus, hypertension, and chronic obstructive pulmonary disease. The topical steroids used by the patients belonged to class 1 (superpotent). The approximate amount of total steroid application in all cases varied from 15 to

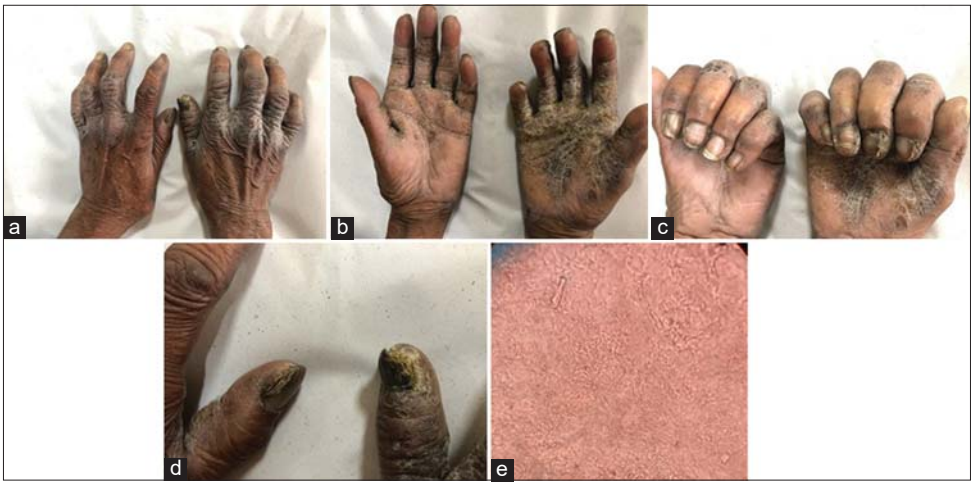


Figure 3: (a-b) Hyperkeratotic plaques with thick, adherent, yellowish crusts and scales on the palms extending to the web spaces and on the dorsa of the hands with several fissures. (c-d) Yellowish-white discoloration with onycholysis on the fingernails over the right hand and nail of the left thumb. (e) Pseudo-hyphae with yeast-like cells (10% KOH mount, 400×).

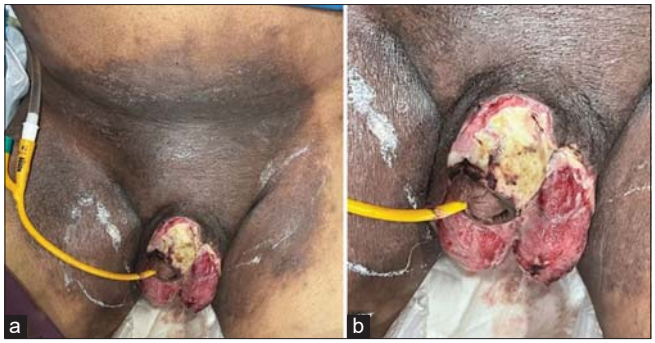


Figure 4: (a) Hyperpigmented, scaly patches present over the groin folds extending to the mons pubis, lower abdomen, medial aspect of both thighs, with some areas of erythema and atrophic skin. (b) Large ulcer on the scrotum, extending onto the onto the penile shaft and glans penis with yellowish, purulent slough on the penile shaft.

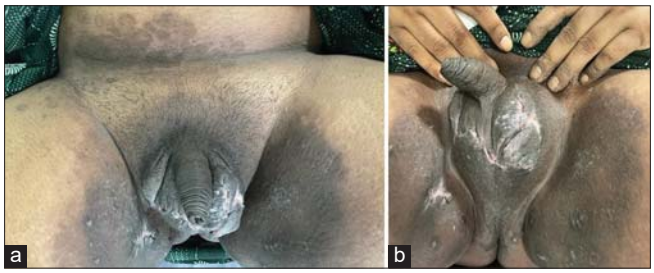


Figure 5: (a) Scaly, hyperpigmented patches present on the groin folds, extending to the scrotum, mons pubis, and medial aspect of both thighs with some areas of atrophic scars. (b) Irregular ulcers with minimal yellowish slough on the scrotum.

120 gm/week. The severe infections were two cases of crusted scabies, two cases of Fournier's gangrene, and one case of erosio interdigitalis blastomycetica of the palms. It was also noted that the patients with underlying diabetes mellitus had good control of their glycemic index.

DISCUSSION

The first side effect of topical corticosteroids was reported in 1955, in which twenty cases experienced weight gain and sodium retention due to systemic absorption of topical fludrocortisone [4]. The anti-inflammatory property of topical corticosteroids is both a boon and bane in treating chronic skin conditions. The most common side effects of topical corticosteroids are seen on the site of application [3,5]. The potency of the steroid, vehicle employed, and site and duration of application determine the local adverse effects [5]. Apart from the immunosuppressive effect of topical steroids, epidermal thinning along with decreased formation of lipid lamellar bodies leads to delayed barrier recovery and, thus, makes the patient prone to cutaneous infections [3,5]. The most common infections seen as adverse effects of prolonged topical steroid application are tinea imbricata, demodex folliculitis, furunculosis, herpes simplex infection, granuloma gluteale infantum, and rarely crusted scabies [3,5,6]. Many times, the patient presents to the dermatologist with a bag of empty, twisted steroid tubes (tortured tube sign), which indicates a topical steroid menace [6]. It is also observed that, as the skin ages, there is epidermal thinning with reduced Langerhans cells and decreased antigen-specific immunity, which explains the increased susceptibility to skin infections [7].

Crusted scabies is a severe form of highly contagious infestation caused by *Sarcoptes scabiei*. In crusted scabies, there are around 4000 mites per gram of skin [8]. It is usually seen because of worsened host

Table 1: Case details of steroid use and their management.

Case (age/sex)	Symptom duration	Pre-existing condition for which the steroid was employed	Associated comorbidities	Topical steroid applied	Approx. amount of steroid applied per week	Present diagnosis	Treatment given
Case 1, 66 yrs./male	3 months	Chronic plaque psoriasis	*CVD, +T2DM, ‡HTN, §COPD	0.05% clobetasol propionate cream	60–90 g/week	Crusted scabies	Permethrin 5% cream, twice a week for 3 weeks T. ivermectin 12 mg, once a week for 3 weeks T. hydroxyzine 25 mg at night
Case 2, 68 yrs./male	8 months	Exfoliative dermatitis	§COPD	0.05% clobetasol propionate cream	100–120 g/week	Crusted scabies	Permethrin 5% cream, twice a week for 3 weeks T. ivermectin 12 mg, once a week for 3 weeks T. hydroxyzine 25 mg at night
Case 3, 62 yrs./female	6 months	Chronic hand dermatitis	‡HTN	0.05% halobetasol propionate cream	30–40 g/week	Superficial hyperkeratotic candidiasis	Topical luliconazole lotion, twice a day Topical salicylic acid 6% ointment, at night
Case 4, 65 yrs./male	8 months	Tinea cruris	+T2DM	Topical 0.05% clobetasol propionate, neomycin, and miconazole	15–20 g/week	Fournier's gangrene	Injection linezolid 600mg ‖BID Injection clindamycin 300mg ‖BID (for Fournier's gangrene) Oral Itraconazole 200mg ¶ OD for 3 weeks Topical Luliconazole cream ‖BID for 3 weeks Surgical debridement done
Case 5, 47 yrs./male	6 months	Tinea cruris	+T2DM ‡HTN	Topical 0.05% clobetasol propionate, neomycin, miconazole, and chlorhexidine cream	40–50 g/week	Fournier's gangrene	Inj. Linezolid 600mg ‖BID (for Fournier's gangrene) Oral Itraconazole 200 mg ¶ OD for 3 weeks. Sertaconazole cream ‖BID (for Tinea incognito)

*CVD, Cardiovascular disease; +T2DM, Type 2 Diabetes Mellitus; ‡HTN, Hypertension; §COPD, Chronic obstructive pulmonary disease; ‖BID, bis in die; ¶ OD, omne in die

immunity to the mite. Some of the predisposing factors for crusted scabies are HIV infection, mental debilitation conditions, and immunosuppressive therapies [9]. There are very few reported cases of crusted scabies secondary to topical steroid abuse (Table 2) [10-12]. The characteristic feature of crusted scabies is the presence of hyperkeratotic plaques with millions of mites and a lack of intense itching as compared to classical scabies. Crusted scabies is a severe disease with higher mortality than classical scabies. The most dreadful complication is septicemia [8,9]. In a retrospective study conducted by Davis et al. in Australia on crusted scabies, a novel grading of the severity of scabies was suggested. The two cases of crusted scabies described there were graded as moderate severity [8]. The two important predisposing factors for crusted scabies in our cases were prolonged use of class 1 topical steroids and decreased skin immunity in aged skin [7,8]. Along with the clinical findings, the demonstration of mites, eggs, and mite feces (scybala) is a diagnostic of scabies [9]. Along with topical scabicidal drugs, oral ivermectin in three doses (0,1,7) is found to be effective in crusted scabies [8].

Cutaneous candidiasis presents in varied forms, such as intertrigo, paronychia, onychomycosis, erosio interdigitalis blastomycetica, and granuloma gluteale infantum. Various predisposing conditions for erosio interdigitalis blastomycetica are diabetes mellitus, prolonged exposure to moisture and detergents, and immunosuppressive conditions [13]. It presents as an erosion or ulcer with a white collarette of macerated epidermis in the interdigital web spaces (Table 2). It may extend to the fingers and palms with satellite lesions [13,14]. The patient usually complains of pain and pruritus in the affected area. In our case, there was maceration in the interdigital webspace with a hyperkeratotic plaque extending to the palms and fingers, which is a rare presentation in erosio

Table 2: Case reports of similar infections secondary to prolonged topical steroid use by other authors.

Current case	Other similar case report	Primary reason for steroid use	Duration of steroid use	Findings after prolonged use of topical steroids
Crusted scabies (case 1 and 2)	Ivana binic et el. (2010)	Skin changes secondary to hypothyroidism	5 months	• Hyperkeratotic scaly plaques on the trunk and limbs. • Crusted lesions on the scalp and external ears.
	Vincent Marliere et al. (1999)	Generalised eczema	1.5 months	• Hyperkeratotic crusted plaques on the dorsa of the feet, toes, and soles. • Pruriginous, crusted papules on the hands and genitals.
	Jaramillo et al. (1998)	Seborrheic dermatitis/ psoriasis	36 months	• Hyperkeratotic and fissured plaques on the extremities and sacral areas. • Dystrophic nails with hyperkeratosis.
Erosio interdigitalis blastomycetica (case 3)	Luo DQ et al. (2011) Report of 4 cases	Non-healing interdigital ulcer	Case 1: 1 month Case 2: 3 months Case 3: 2 months Case 4: 2 months	• Non-healing ulcer with maceration on surrounding skin in the interdigital webspace of the foot.
Fournier's gangrene (case 4 and 5)	Osime et al. (2002)	Skin bleaching	60 months	• Ulceration on the scrotal area.
	Shyam verma (2020) Report of 4 cases	Tinea corporis	Case 1: 4 months Case 2: 1.5 months Case 3: 5 months Case 4: not mentioned	• Several painful, oval ulcers showing overhanging borders with some large ulcers adopting the pattern of striae.

interdigitalis blastomycetica. Prolonged use of topical corticosteroids reduces the local inflammatory response and cell-mediated immunity, allowing candida to thrive and cause infection [13,14]. Sitheeque et al. suggested that a candida invasion in the epithelium initiates a hyperplastic response, which is responsible for chronic hyperplastic changes in oral mucosal candidiasis [15]. The probable factors responsible for atypical presentation of erosio interdigitalis blastomycetica in our case were prolonged use of corticosteroids, elderly age, and repeated contact with water.

Fournier's gangrene is a necrotizing fasciitis of perineum and genitalia with high mortality. It is more commonly seen in the fourth-to-sixth decade of life. In a study conducted in South India by Sockkalingam et al., the male-to-female ratio was 33:1 [16]. The major predisposing factors were diabetes mellitus, trauma, post-urogenital surgeries, and HIV infection [16,17]. To the best of our knowledge, there has only been a single case report of Fournier's gangrene secondary to prolonged topical steroid application wherein topical steroid was employed as a bleaching agent (Table 2) [18]. There are some case reports of skin ulceration secondary to steroid application as a result of epidermal atrophy and impaired wound healing, yet tissue cultures were negative [19]. Thus, prolonged use of steroid creams leads to ulceration and increases the susceptibility to infections. In our cases of Fournier's gangrene, both topical steroid application and trauma secondary to scratching were major predisposing factors.

CONCLUSION

In all cases presented here, topical steroid misuse was the initiating factor for the manifestation of such severe debilitating conditions. In the presence of well-controlled diabetes mellitus and other comorbidities, elderly individuals should use topical steroids cautiously to prevent life-threatening infections. Herein, we propose that, as crusted scabies and hyperkeratotic erosio interdigitalis blastomycetica mimic various other papulosquamous disorders, a simple KOH examination aids in diagnosis. Prolonged topical steroid use is one of the predisposing factors for Fournier's gangrene, a life-threatening disease.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Quaresma JAS. Organization of the skin immune system and compartmentalized immune responses in infectious diseases. Clin Microbiol Rev. 2019;32:e00034-18.
2. Cutolo M, Seriolo B, Pizzorni C, Secchi ME, Soldano S, Paolino S, et al. Use of glucocorticoids and risk of infections. Autoimmun

Rev. 2008;8:153-5.
3. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: A long overdue revisit. Indian Dermatol Online J. 2014;5:416-25.
4. Fitzpatrick TB, Griswold HC, Hicks JH. Sodium retention and edema from percutaneous absorption of fludrocortisone acetate. J Am Med Assoc. 1955;158:1149-52.
5. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006;54:1-15.
6. Abraham A, Roga G. Topical steroid-damaged skin. Indian J Dermatol. 2014;59:456-9.
7. Chambers ES, Vukmanovic-Stejic M. Skin barrier immunity and ageing. Immunology. 2020;160:116-25.
8. Davis JS, McGloughlin S, Tong SY, Walton SF, Currie BJ. A novel clinical grading scale to guide the management of crusted scabies. PLoS Negl Trop Dis. 2013;7:e2387.
9. Karthikeyan K. Crusted scabies. Indian J Dermatol Venereol Leprol. 2009;75:340-7.
10. Binić I, Janković A, Jovanović D, Ljubenović M. Crusted (Norwegian) scabies following systemic and topical corticosteroid therapy. J Korean Med Sci. 2010;25:188-91.
11. Marlière V, Roul S, Labrèze C, Taïeb A. Crusted (Norwegian) scabies induced by use of topical corticosteroids and treated successfully with ivermectin. J Pediatr. 1999;135:122-4.
12. Jaramillo-Ayerbe F, Berrío-Muñoz J. Ivermectin for crusted Norwegian scabies induced by use of topical steroids. Arch Dermatol. 1998;134:143-5.
13. Schlager E, Ashack K, Khachemoune A. Erosio interdigitalis blastomycetica: A review of interdigital candidiasis. Dermatol Online J. 2018;24:13030/qt8tm443f6.
14. Luo DQ, Yang W, Wu LC, Liu JH, Chen WN. Interdigital ulcer: An unusual presentation of Candida infection. Mycoses. 2011;54:e780-4.
15. Sitheeque MA, Samaranayake LP. Chronic hyperplastic candidosis/candidiasis (candidal leukoplakia). Crit Rev Oral Biol Med. 2003;14:253-67.
16. Sockkalingam VS, Subburayan E, Velu E, Rajashekar ST, Swamy AM. Fournier's gangrene: Prospective study of 34 patients in South Indian population and treatment strategies. The Pan African Med J. 2018;31:110.
17. Eskitaşcıoğlu T, Özyazgan I, Coruh A, Günay GK, Altıparmak M, Yontar Y, et al. Experience of 80 cases with Fournier's gangrene and "trauma" as a trigger factor in the etiopathogenesis. Ulus Travma Acil Cerrahi Derg. 2014;20:265-74.
18. Osime OC, Iribhogbe PI. Fournier's gangrene secondary to prolonged use of steroid-containing cream: A case report. Ann Biomed Scien. 2002;1:152-5.
19. Verma SB, Madke B. Topical corticosteroid-induced ulcerated striae. An Bras Dermatol. 2021;96:94-6.

Source of Support: This article has no funding source.
Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Brief Report

Xeroderma pigmentosum: Twelve cases at the National Hospital of Niamey, Niger

Salissou Laouali[1], Nouhou Diori Adam[2], Hamani Issaka[3], Oueodraogo Mamadou Maïmouna[1], Laouali Idi Mamane Sani[1], Moussa Doulla[1], Nouhou Hassan[4]

[1]Department of Dermatology Venereology, National Hospital of Niamey, Niger, [2]Department of Ophthalmology, National Hospital of Amirou Boubacar Diallo of Niamey, Niger, [3]Laboratory of Cytology and Genetic, Faculty of Health Sciences, ABDOU Moumouni University of Niamey, Niger, [4]Laboratories of Pathological Anatomy, Faculty of Health Sciences, ABDOU Moumouni University of Niamey, Niger

Corresponding author: Salissou Laouali, MD, E-mail: danmata@yahoo.com

ABSTRACT

Background: Xeroderma pigmentosum (XP) is a usually autosomal recessive disorder linked to a deficiency of the enzyme systems of DNA repair. The pathological sensitivity to the sun exposes the patient to develop multiple cancers. **Materials and Methods:** We conducted a retrospective study over a period from January 2006 to December 2014. A total of twelve patients were enrolled. **Results:** These were nine male cases and three female, with a sex ratio of 3/1. The average age was 7.9 years, ranging from 1 to 40 years. Consanguinity between the parents was found in ten cases (83.3%). The first non-tumor cutaneous manifestations appeared in eight patients before the age of six months. During follow-up, seven patients, including three (43%) at the age of eight years, died from metastasis. **Conclusion:** XP is complicated in the development of cancers, even in children, and is linked to the intensity of solar radiation in Niger.

Keywords: xeroderma pigmentosum; skin cancers; tongue amputation; Niamey, Niger

INTRODUCTION

Xeroderma pigmentosum (XP) is a usually autosomal recessive disorder, linked to a deficiency of the enzyme systems of DNA repair. It is characterized by a pathological sensitivity to the sun, exposing the patient early to develop cancer. It was first described in 1970 by Hébra and Kaposi. It is a relatively rare disease whose frequency varies from 1/10,000 (Tunisia) to 4/1,000,000 in Europe and the U.S. [1-3]. No currently available treatment seems completely effective; the evolution is constantly toward aggravation and death by cachexia due to the outbreak of multiple cancers, in particular mucocutaneous, ocular, and/or neurological [4-6]. The objective of this study was to describe the epidemiological, clinical, and evolutionary profile of XP in Niger (West Africa), a tropical and especially sunny country.

MATERIALS AND METHODS

This was a retrospective study conducted over a period of eight years from January 2006 to December 2014 at the National Hospital of Niamey, Niger. The diagnosis of XP was essentially clinical and based on the characteristic skin and/or mucous lesions: photophobia, xeroderma, conjunctivitis hemorrhagic, corneal pillowcases, and ulcerations. The epidemiological data studied were: age, sex, the duration of evolution on the first consultation. For each family of the patient, the following were researched: a notion of consanguinity among the parents, the existence of one or more similar cases in the family, and the economic situation of the parents. The diagnosis of a tumor lesion was confirmed by pathological examination.

How to cite this article: Laouali S, Adam ND, Issaka H, Maïmouna OM, Mamane Sani LI, Doulla M, Hassan N. Xeroderma pigmentosum: Twelve cases at the National Hospital of Niamey, Niger. Our Dermatol Online. 2023;14(1):56-59.

Submission: 26.05.2022; **Acceptance:** 17.08.2022

DOI: 10.7241/ourd.20231.11

RESULTS

We collected twelve cases of XP, which were the subjects of this study, including nine male cases and three female, giving a sex ratio of 3/1. The average age was 7.9 years, ranging from 1 to 40 years. Consanguinity between the parents was found in ten cases (83.3%) out of the twelve, and the existence of similar conditions in the family was noted in nine cases (75%). All patients came from a poor socioeconomic background. The first non-tumor cutaneous manifestations appeared in eight patients before the age of six months. The average consultation time was 45 months, ranging from 2 to 360 months. Xeroderma was the most frequent reason for consultation on the cutaneous level (six cases) (Fig. 1a) and photophobia on the ophthalmological level (four cases) (Fig. 1b). The first cutaneous tumor appeared between the age of four and six years in seven cases (Table 1). On clinical examination, photophobia and xeroderma were found in all patients, who, moreover, all presented with a malignant tumor—six squamous cell carcinomas (SCC) and six basal cell carcinomas (BCC)—and the SCCs and BCCs were associated in three cases (Table 2). On average, there were three tumors in one patient, ranging from two to six, eight times out of the twelve patients (Figs. 2a and 2b). The locations were: ocular (five cases), labial (one case), nasal (three cases), and the tip of the tongue (four cases, including two amputations of the tongue). (Figs. 3a and 3b). The other mucocutaneous manifestations observed were, among others lentigines, dyschromic macules, corneal sheaths, corneal ulcerations, and hemorrhagic conjunctivitis (Table 3). Classic XP was observed in eleven cases; only one (aged forty) had a variant form (Fig. 4). On the therapeutic level, the patients received advice on photoprotection and the excision of tumor lesions was performed (twelve cases). During follow-up, seven patients, including three (43%) at the age of eight years, died from metastasis (Figs. 5a and 5b B).

DISCUSSION

XP is a rare autosomal recessive disease whose sexual predominance varies depending on the study. The male predominance observed in our sample was already reported by some authors [2,6-8]. On the other hand, Chidzonga et al. [9] in Zimbabwe found eight females and four males, giving a sex ratio of 2/1. Khatri et al. [10] and Fazaa et al. [11] also found a female predominance, with rates of 23/19 and 7/5, respectively. The annual average concerning our series was 1.5 cases and was more important in consanguineous marriages [2,11,12]. In our study, as in most of the series reported, patients with XP were generally from consanguineous marriages. Gul et al. reported these in 83.3% of cases [8], Boujard et al. in 95% [11], and Dieng et al. in five out of six cases [13]. This could also explain the high frequency of similar cases in the family. Similar cases noted in the families of patients (83.3%) were reported in certain series [8,13-15]. The predominant achievement of the age group in our study was that of one to five years. For Witold [6], the most affected age group was that of ten months and twenty-one years and, for El Fékih et al., that of 17.6 ± 11.04 years [2]. As in the

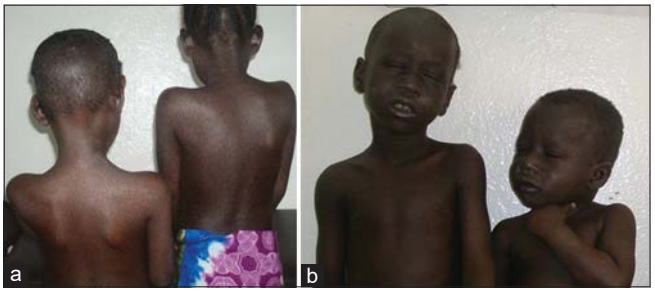


Figure 1: (a) Xeroderma, poïkiloderma (brother and sister); (b) photophobia (two brothers).

Figure 2: Ulcerative budding tumors of the cheeks in two patients with left corneal pillowcase in one patient: (a) Left cheek injury (SCC), (b) Right cheek injury (BCC).

Table 1: Distribution of the patients according to the age at the appearance of the first tumor

Age of Onset of First Tumor (Year)	Number of Cases	Percentage
≤ 3	2	16.7
4–6	7	58.3
> 6	3	25.0
Total	12	100.0

Table 2: Types and numbers of carcinomas observed

Type	Number of Cases	Percentage
Squamous cell carcinoma (SCC)	6	60.0
Basal cell carcinoma (BCC)	6	60.0
SCC and BCC	3	30.0

In ten cases, the types and numbers of cancers were determined, that is, 60% of squamous cell carcinomas (SCCs), 60% of basal cell carcinomas (BCCs), and 30% of the two forms associated.

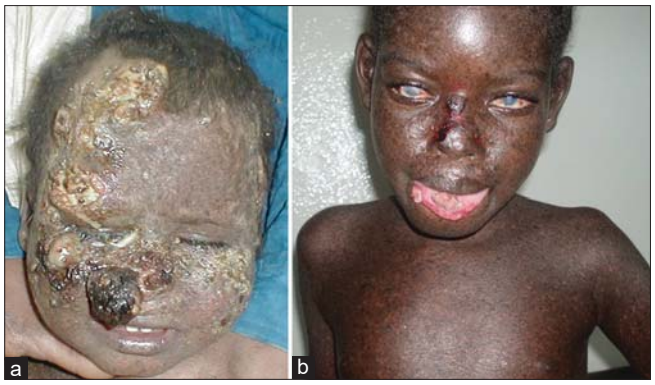
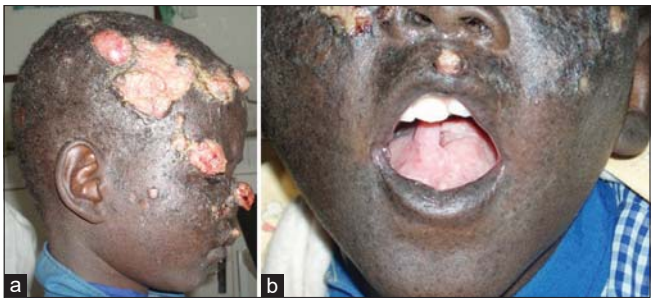


Figure 3: (a) Squamous cell carcinoma of the temple, check, nasal mucosa on the right and eyelid; (b) squamous cell carcinoma of the lip, tongue tip, and bilateral corneal pillowcase.

Figure 4: XP variant form in the forty-year-old adult (onset of signs at the age of thirty): xeroderma, skin tumors on the face, and a bilateral corneal sheath.

report by Witold [6], our patients also all came from families of low socioeconomic level, which explained the often long average consultation time (45 months). The early appearance of signs of the disease in countries south of the Sahara may be explained by the significant and aggressive sun exposure in this pediatric environment [16,17]. The clinical presentations of XP are in its classic form with seven complementation groups (from XPA to XPG) and in the so-called variant form (XPV) [1]. Without the possibility of conducting biological studies for the distinction of these forms, we



Figures 5: Multiple end-stage tumors in the same patient: (a) cutaneous involvement of the right scalp, (b) lingual involvement with its mutilation.

Table 3: Characteristics of the mucocutaneous and ophthalmological lesions

Areas Affected and Type of Lesions	Number of Cases	Percentage
Damage to photo-exposed parts	12	100.0
Damage to hidden parts	12	100.0
Dyschromic macules	12	100.0
Xeroderma	12	100.0
Lentigine	12	100.0
Ulcerovetting tumors	9	75.0
Kerato-acanthomas	5	41.6
Botriomycomas	6	50.0
Tongue tumor	4	33.3
Tongue amputation	2	16.6
Actinic keratosis	1	8.3
Involvement of the eyelids	12	100.0
Hemorrhagic conjunctivitis	12	100.0
Corneal pillowcase	12	100.0
Photophobia	12	100.0
Corneal ulceration	10	83.3
Eye tumors	5	41.7

resorted to clinical classification [18,19]. Based on the absence of neurological signs [1-2,17] in our patients, we classified eleven cases with the classic form of the XPC group and the twelfth case with the variant form. In classic XP, photophobia and xeroderma, the usual and early signs, were constant in our patients and in those reported by some authors [9,10]; meanwhile, they are late in the variant form [12]. The lingual involvement with amputation that we noted was also reported in some series [8,9]. The ocular and palpebral manifestations, such as hemorrhagic conjunctivitis, ulcerations, and corneal cavities or tumors observed in the classic form of XP as well as in the variant form, were regular in our study and were also reported by some authors [1,8,12]. We noted no cases of leukemia, contrary to the literature [2,10,14]. Basal cell carcinoma and squamous cell carcinoma were observed equally in six cases each. The latter were the most frequently reported [1,6,17] and highly often as in our series without melanoma [9,10]. Almost all of our patients

received photoprotection and an excisional biopsy as treatment because the extent and number of the tumor lesions were contraindications to surgical removal. Chidzonga et al. [9], as well as Bouadjar et al. [12], opted for surgical excision in the event of a tumor in patients seen early. Patients with XP usually die especially young. Seven cases of death before the age of eight were noted following infectious complications, hemorrhage, malnutrition, and the multiplication of carcinomatous tumors. Chidzonga et al., in their study [9], noted that the patient who survived the longest died at the age of eighteen. At the time of this study, we have two patients lost to follow-up and three alive, including the forty-year-old presenting the XP variant. Would photoprotection prescribed early in these patients have had a positive impact on the prevention of skin tumors in a country in which sunshine is present all year round? It is difficult to say, given that patients are received at the stage of tumor lesions. However, in those living at the time of this study, we see the beneficial effect of photoprotection by slowing down the birth of new tumor lesions. Thus, monitoring live cases will allow us to better appreciate the beneficial effect of long-term photoprotection despite its significant cost.

CONCLUSION

Xeroderma pigmentosum is a rare yet serious genetic disorder in Niger. While photoprotection is currently the mainstay of treatment, genetic therapy is raising hope for affected families. We must concentrate our efforts on genetic counseling and antenatal diagnosis in families at risk and dermatological follow-up of cases, given the early onset of skin cancers in Niger.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patient her consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Kraemer KH, Lee MM, Scotto J. Xeroderma Pigmentosum: Cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol. 1987;123:241-50.
2. El Fékih N, Fredji M, Aounallah-Skhiri H, Fazaa B, Zghal M, Ridha Kamoun M. Neurological damage in xeroderma pigmentosum. Rev Neurological. 2009;165:967-70.
3. Zghal M, Fazaa B, Abdelhak S, Mokni M. Xeroderma pigmentosum. Ann Dermatol Venereol. 2018;145:706-22.
4. Moussala M, Behar-Cohen F, D'hermies F, Bisseck A-C, Renard G. Xeroderma pigmentosum and its ocular manifestations. J Fr Ophthalmol. 2000;23:369-74.
5. Christen-Zazech S, Imoto K, Khan S G, Tamura D, DiGiovanna J J, Boyle J, et al. Unexpected occurrence of xeroderma pigmentosum in an uncle and nephew. Arch Dermatol. 2009;145:1285-91.
6. Witold K J. Xeroderma Pigmentosum in black South Africans. Intern Jr Dermatol. 1999;38:511-4.
7. Hebert J.C, Lefait vJ-F, Hebert O. Xeroderma Pigmentosum in black-skinned children: Five observations in Mahorais children. Ann Dermatol Venereol. 1994;121:382-6.
8. Gul U, Kihç A, Gonul M, 9akmak SK, Soylu S. Xeroderma pigmentosum: A Turkish case series. Intern J Dermatol. 2007;46:1125-8.
9. Chidzonga MM, Mahomva L, Makunike-Mutasa R, Masanganise R. Xeroderma pigmentosum: A retrospective case series in Zimbabwe. J Oral Maxillo Fac Surg. 2009;67:22-31.
10. Khatri M L, Bemghazil M, Shafi M, Machina A. Xeroderma pigmentosum in Libya. Intern J Dermatol. 1999;38:520-4.
11. Fazaa B, Zghal M, Zeglaoui F, Goucha S, Mokhtar I, Kharfi M, et al. Melanoma and xeroderma pigmentosum: 12 cases. Ann Dermatol. Venereol. 2001;128:503-6
12. Bouadjar B, Belkacem FA, Daya-Grosjean L, Larbaoui LS, Ferhat R, Cherid MC et al. Xeroderma pigmentosum: Study of 40 Algerian patients. Ann Dermatol Venereol. 1996;123:305-6.
13. Dieng MT, Niang SO, Dangou JM, Ndiaye B, Xeroderma pigmentosum: Report of 6cases in Dakar, Senegal. Bull Cancer. 2001;88:199-202.
14. Zghal M, Fazaa B, Zghal A, Mokhtar I, Sarasin A, Kamoun MR, et al. Xeroderma pigmentosum: Clinical and genetic particularities of a family in which all members are affected. Ann Dermatol. Venereol. 2003;130:31-6.
15. Rubaie SMA, El Darouti MA. Clinical and genetic study of xeroderma pigmentosum. Intern J Dermatol. 1990;29:126-8.
16. Salissou L, Moumouni H, Sani R, Nouhou H. Xeroderma pigmentosum: First observation in Niger. Ann Univsers A M Niamey. 2013;XV-A:1-8.
17. Salissou L, Doulla M, Harouna MZ, Salha I, Timmi N, Dan Sono AA, et al. Xeroderma pigmentosum: Squamous cell carcinoma infiltrating and disfiguring facial, in a girl of 3 years and a half. Our Dermatol Online. 2017; 8(Suppl. 1):28-31.
18. Ahmed H, Hassan R Y, Pindiga U. Xeroderma in three consecutive siblings of a Nigerian family: Observations of oculocutaneous manifestations in black African children. Br J Ophthalmo. 2001;85:110-1.
19. Zghal M, Fazaa B, Kamoun MR. Xeroderma pigmentosum. EMC (Elsevier SAS, Paris), Dermatology. 206;98-660-A-10.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Brief Report

Paradoxical cutaneous manifestations induced by TNF inhibitors in patients with inflammatory bowel disease

Rhita Alaoui[1], Sofia Alami[2], Nawal Lagdali[1], Maryeme Kadiri[1], Camélia Berhili[1], Fatima-Zahra Chabib[1], Mohamed Borahma[1], Imane Benelbarhdadi[1], Fatima-Zahra Ajana[1]

[1]Department of Hepato-Gastroenterology "Medicine C", Ibn Sina University Hospital Center, Mohammed V University Rabat, Morocco, [2]Department of Dermatology, Ibn Sina University Hospital Center, Mohammed V University Rabat, Morocco

Corresponding author: Rhita Alaoui, MD, E-mail: rhita.alaoui.m@gmail.com

ABSTRACT

Background: Anti-TNF drugs have revolutionized the management of numerous inflammatory diseases, yet they may produce paradoxical effects. **Materials and Methods:** A descriptive study was conducted on patients with chronic inflammatory bowel disease (IBD) on anti-TNF therapy who had developed paradoxical psoriasis. **Results:** Out of a total of 218 patients followed for IBD on TNF inhibitors, five presented with paradoxical psoriasis. In four patients, a specific treatment for psoriasis was associated with anti-TNF treatment. In one patient, a swap to ustekinumab was decided. Good progress was noted in four patients. In one, there was no improvement of the psoriasis on methotrexate, which was switched to another anti-TNF agent. **Conclusion:** In our experience, TNF inhibitor-induced psoriasis is relatively rare (prevalence of 2.3%). The choice of treatment is reached by assessing the benefit-risk balance.

Key words: Paradoxical cutaneous manifestations; TNF inhibitors; Cutaneous manifestations; Inflammatory bowel disease

INTRODUCTION

Anti-TNF drugs are among the therapeutic tools that have revolutionized the management of numerous inflammatory diseases, including chronic inflammatory bowel disease (IBD) and psoriasis. However, these treatments may produce paradoxical effects and induce the very disease they were designed to treat, as in the case of psoriasis. Thus, when faced with TNF inhibitor-induced psoriasis in a patient with IBD, there is a dilemma. The question is whether the treatment should be continued or stopped or whether the therapeutic class should be changed. Herein, we report five cases of TNF inhibitor-induced psoriasis in patients followed for IBD.

MATERIALS AND METHODS

A prospective descriptive study was conducted on 218 patients with chronic IBD on anti-TNF therapy who developed paradoxical psoriasis when on treatment. The assessment of the severity of skin involvement took into account the extent of the psoriatic rash, its location, and its impact on the patient's quality of life.

Ethics Statement

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

How to cite this article: Alaoui R, Alami S, Lagdali N, Kadiri M, Berhili K, Chabib FZ, Bourahma M, Benlbarhdadi I, Ajana FZ. Paradoxical cutaneous manifestations induced by TNF inhibitors in patients with inflammatory bowel disease. Our Dermatol Online. 2023;14(1):60-64.

Submission: 18.08.2022; **Acceptance:** 02.10.2022

DOI: 10.7241/ourd.20231.12

RESULTS

Out of a total of 218 patients followed for IBD on TNF inhibitors, five presented with paradoxical psoriasis, giving a prevalence of 2.3%. Among them were three females and two males, with an average age of 43 years. Our patients had no personal or family history of psoriasis. All five patients had Crohn's disease, among whom two had ano-perineal manifestations. Three patients were on adalimumab and two on infliximab. The mean time to the onset of paradoxical psoriasis was nine months from the beginning of the treatment. In four cases, the psoriasis lesions appeared during the clinical and endoscopic remission of IBD and, in only one case, the patient was in a clinical relapse. These were two cases of inverse psoriasis (Figs. 1a – 1c), one of genital psoriasis (Figs. 2a and 2b), one of plaque psoriasis, and one of scalp psoriasis. Skin involvement was moderate in three cases and mild in two (Table 1). Histological confirmation was required in one patient.

Table 1: A summary of the location and severity of psoriasis

	Site of Lesions	PASI Score	DLQI Score
Patient 1 [Figure 1]	Cutaneous fold •Infra-mammary •Retro-auricular •Intergluteal •Umbilical	Moderate	Moderate
Patient 2 [Figure 2]	Genital • Pubis • Penis • Scrotum	Mild	Mild
Patient 3	Cutaneous fold • Intergluteal • Perineal	Moderate	Severe
Patient 4	Arm Trunk	Mild	Mild
Patient 5	Scalp	Moderate	Moderate

In four patients, TNF-inhibitor therapy was maintained and combined with psoriasis-specific treatment (dermocorticoids in two cases, methotrexate in one, and keratolytic cream in one). In the only patient with moderate psoriasis who was in a Crohn's disease relapse, TNF-inhibitor therapy was suspended and a swap to ustekinumab was decided by a bi-disciplinary concertation. Good progress was noted in four patients. In one, there was no improvement of the psoriasis on methotrexate, hence the need for a switch to another anti-TNF agent, with good progression thereafter.

DISCUSSION

Anti-TNF-α drugs have been clearly shown to be effective in the treatment of numerous inflammatory diseases, including chronic inflammatory bowel disease (IBD) and psoriasis. Paradoxically, these treatments may induce and/or worsen psoriatic skin lesions. The prevalence of TNF inhibitor-induced psoriasis in IBD is estimated to be between 1.6% and 2.7% [1,2], which is consistent with our experience (2.3%).

In the current literature, infliximab is the most frequently reported TNF-α inhibitor to induce psoriatic eruptions, followed by etanercept, adalimumab, certolizumab pegol, and golimumab [3]. Despite this, the incidence rate of TNF inhibitor-induced psoriasis remains the same for all anti-TNF agents [2]. In our experience, adalimumab was responsible for psoriasis in three cases and infliximab in two.

The different risk factors identified as predisposing to TNF inhibitor-induced psoriasis are smoking, the

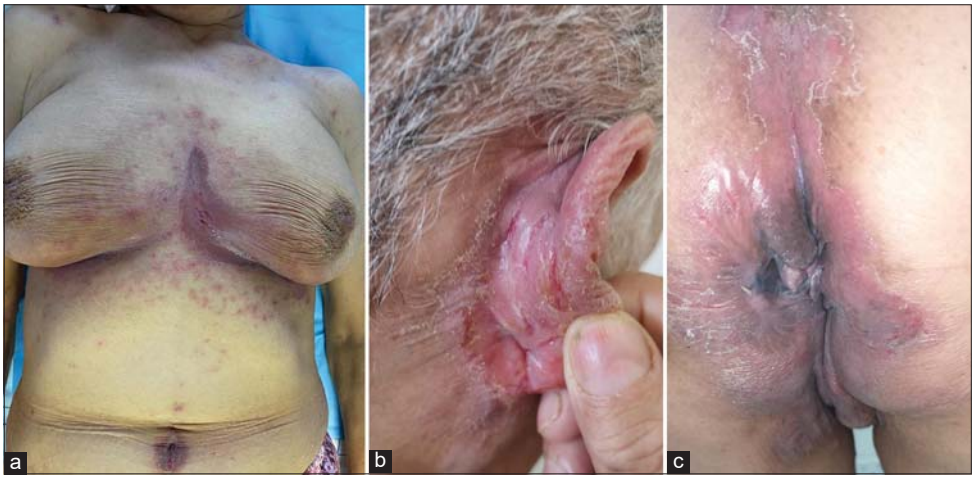


Figure 1: Inverse psoriatic lesions in a (a) umbilical and submammary, (b) retroauricular, (c) and intergluteal location.

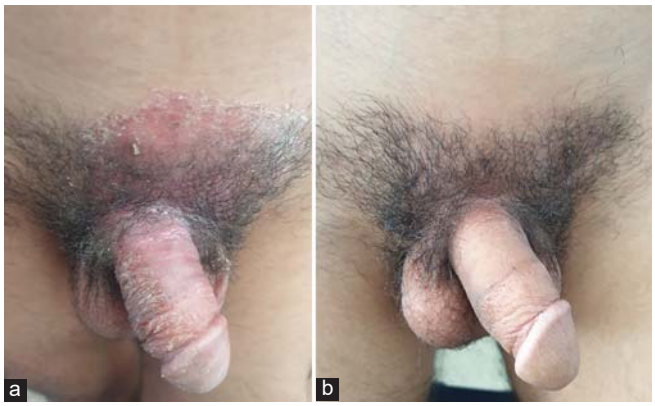


Figure 2: (a) Genital psoriasis lesions; (b) evolution after treatment with dermocorticoids.

female sex, and a genetic predisposition to psoriasis [2]. In two studies, patients with IBD and TNF inhibitor-induced psoriasis had no personal or family history of psoriasis [1,2], which was also the case in our experience.

Clinically, patients may present with different forms of psoriasis, including plaque psoriasis, palmoplantar pustular psoriasis, guttate psoriasis, and inverse psoriasis [4]. The most common phenotype of psoriasis was palmoplantar pustulosis [1]. In our experience, there were two cases of inverse psoriasis, one case of genital psoriasis, one of plaque psoriasis, and one of scalp psoriasis.

The median time from the beginning of treatment to the appearance of skin lesions was twelve months (maintenance period). In our experience, the time from the initiation of treatment to the appearance of skin lesions was nine months on average.

Induced psoriasis lesions most often appeared during the remission of IBD, as shown in a study on fourteen pediatric patients [5]. In our experience, psoriatic lesions appeared during the remission of IBD in four cases.

Regarding treatment, there is no standard approach to the management of TNF-induced psoriasis, making the treatment of TNF inhibitor-induced psoriasis a challenge. A review of the literature was presented on TNF inhibitor-induced psoriasis with a proposed treatment algorithm [6], which takes into account both the severity of the rash and the characteristics of the underlying disease. The decision to continue, suspend, or replace anti-TNF therapy should be carefully discussed with the patient, taking into account the severity of the rash, the needs of the underlying disease, and the availability of other treatment options. It should be noted that the severity of the rash should be defined taking into account the extent of the psoriatic rash as well as its impact on the patient's quality of life (e.g., the involvement of the palms, soles, face, and genitals, and the psychological impact), as recommended by the National Psoriasis Foundation [7].

For patients with mild psoriatic disease and stable underlying disease, a "continuous treatment" strategy is employed, in which anti-TNF therapy is continued in combination with conventional psoriasis-specific therapy (topical steroids, UV therapy, methotrexate (MTX), cyclosporine and acitretin) [6]. Cyclosporine should be used in the short term and with great caution, especially in patients with severe IBD, as it may be lethal in combination with anti-TNF drugs [8,9]. A 2016 study revealed that 45% of patients on MTX achieved a 75% reduction in the psoriasis severity index score after 12–16 weeks [10]. Furthermore, the largest study to assess the efficacy of MTX in patients with IBD showed 59.9% and 40% efficacy for CD and UC, respectively, with rates comparable to smaller studies on this issue [11]. In our experience, the only patient who received MTX in combination with an anti-TNF agent had no improvement of their psoriatic lesions.

This "continuous treatment" strategy resulted in a complete resolution in 26% to 41% of cases and a partial response in 25% to 57.4% [3,12,13], making it a highly attractive treatment option, especially since the discontinuation of TNF inhibitors may worsen gastrointestinal symptomatology.

However, for patients with mild psoriatic disease and underlying IBD poorly controlled by TNF inhibitors or in patients with moderate to severe psoriasis and IBD stabilized on TNF inhibitors, it has been proposed to switch to another anti-TNF agent while maintaining psoriasis-specific treatment. However, the success rate of this approach is limited as complete resolution has only been observed in 5% to 36.7% of cases, with a partial response in 18.4% of cases [3,12-14]. More than half of patients may experience a recurrence of skin lesions after the reintroduction of another TNF inhibitor or the same TNF inhibitor [2,15]. In our experience, the only patient who had a switch of their anti-TNF agent had an improvement of their psoriatic lesions without recurrence.

In the refractory cases of TNF inhibitor-induced psoriasis and patients with moderate to severe rash whose underlying a disease is not well controlled, it is suggested that a change of the drug class in combination with a topical or systemic psoriasis therapy should be undertaken. This may increase the chance of the resolution of paradoxical psoriasis and the underlying IBD. Indeed, it has been reported that, in approx. 64.3% of cases, patients who discontinue TNF inhibitors and switch to non-anti-TNF treatments see the resolution of their psoriatic lesions [14]. In our experience, the only patient who was swapped to ustekinumab was in the process of improving their psoriatic lesions.

The change in the therapeutic class would be toward ustekinumab (anti-IL12/23 agent), which is indicated both for the treatment of active and anti-TNF refractory IBD and for moderate to severe psoriasis. Dermatologically, ustekinumab is an effective and safe treatment for psoriasis [16]. Some studies have shown that ustekinumab resolved skin lesions in more than 75% of cases [17], and one study reported that resolution was complete in 75% of cases. Yet, even with this seemingly revolutionary molecule, some cases of paradoxical psoriasis have been described [18-20].

It is also recommended that immunosuppressive agents, such as 6-mercaptopurine and azathioprine, should be reconsidered in some cases, when compared to novel biological therapies [6].

CONCLUSION

TNF inhibitor-induced psoriasis is a real dilemma for the gastroenterologist and dermatologist because of a lack of a standard approach to its management. The benefit/risk balance must be assessed in order to avoid deleterious effects on either the gastrointestinal tract or the skin. The choice of treatment depends on the severity of the underlying pathology and the dermatological lesions and should be made on a case-by-case basis and by a bi-disciplinary consultation. The difficulty lies in the fact that all drug classes may cause paradoxical psoriasis.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Afzali A, Wheat CL, Hu JK, Olerud JE, Lee SD. The association of psoriasiform rash with anti-tumor necrosis factor (anti-TNF) therapy in inflammatory bowel disease: A single academic center case series. J Crohns Colitis. 2014;8:480-8.
2. Guerra I, Pérez-Jeldres T, Iborra M, Algaba A, Monfort D, Calvet X, et al. Incidence, clinical characteristics, and management of psoriasis induced by anti-TNF therapy in patients with inflammatory bowel disease: A nationwide cohort study. Inflamm Bowel Dis. 2016;22:894-901.
3. Brown G, Wang E, Leon A, Huynh M, Wehner M, Matro R, et al. Tumor necrosis factor-α inhibitor-induced psoriasis: Systematic review of clinical features, histopathological findings, and management experience. J Am Acad Dermatol. 2017;76:334-41.
4. Joyau C, Veyrac G, Dixneuf V, Jolliet P. Anti-tumour necrosis factor alpha therapy and increased risk of de novo psoriasis: Is it really a paradoxical side effect? Clin Exp Rheumatol. 2012;30:700-6.
5. Eickstaedt JB, Killpack L, Tung J, Davis D, Hand JL, Tollefson MM. Psoriasis and psoriasiform eruptions in pediatric patients with inflammatory bowel disease treated with anti-tumor necrosis factor alpha agents. Pediatr Dermatol. 2017;34:253-60.
6. Li SJ, Perez-Chada LM, Merola JF. TNF Inhibitor-induced psoriasis: Proposed algorithm for treatment and management. J Psoriasis Psoriatic Arthritis. 2019;4:70-80.
7. Pariser DM, Bagel J, Gelfand JM, Korman NJ, Ritchlin CT, Strober BE, et al. National Psoriasis Foundation clinical consensus on disease severity. Arch Dermatol. 2007;143:239-42.
8. Maser EA, Deconda D, Lichtiger S, Ullman T, Present DH, Kornbluth A. Cyclosporine and infliximab as rescue therapy for each other in patients with steroid-refractory ulcerative colitis. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2008;6:1112-6.
9. Leblanc S, Allez M, Seksik P, Flourié B, Peeters H, Dupas JL, et al. Successive treatment with cyclosporine and infliximab in steroid-refractory ulcerative colitis. Am J Gastroenterol. 2011;106:771-7.
10. Gladman DD. Should methotrexate remain the first-line drug for psoriasis? The Lancet. 2017;389:482-3.
11. Rouiller-Braunschweig C, Fournier N, Pittet V, Dudler J, Michetti P. Efficacy, safety and mucosal healing of methotrexate in a large longitudinal cohort of inflammatory bowel disease patients. Digestion. 2017;96:220-7.
12. Collamer AN, Battafarano DF. Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: Clinical features and possible immunopathogenesis. Semin Arthritis Rheum. 2010;40:233-40.
13. Collamer AN, Guerrero KT, Henning JS, Battafarano DF. Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: A literature review and potential mechanisms of action. Arthritis Rheum. 2008;59:996-1001.
14. Ko JM, Gottlieb AB, Kerbleski JF. Induction and exacerbation of psoriasis with TNF-blockade therapy: A review and analysis of 127 cases. J Dermatol Treat. 2009;20:100-8.
15. Iborra M, Beltrán B, Bastida G, Aguas M, Nos P. Infliximab and adalimumab-induced psoriasis in Crohn's disease: A paradoxical side effect. J Crohns Colitis. 2011;5:157-61.
16. Kimball AB, Papp KA, Wasfi Y, Chan D, Bissonnette R, Sofen H, et al. Long-term efficacy of ustekinumab in patients with moderate-to-severe psoriasis treated for up to 5 years in the PHOENIX 1 study. J Eur Acad Dermatol Venereol JEADV. 2013;27:1535-45.
17. Tillack C, Ehmann LM, Friedrich M, Laubender RP, Papay P,

Vogelsang H, et al. Anti-TNF antibody-induced psoriasiform skin lesions in patients with inflammatory bowel disease are characterised by interferon-γ-expressing Th1 cells and IL-17A/IL-22-expressing Th17 cells and respond to anti-IL-12/IL-23 antibody treatment. Gut. 2014;63:567-77.

18. Lee HY, Woo CH, Haw S. Paradoxical flare of psoriasis after ustekinumab therapy. Ann Dermatol. 2017;29:794-5.
19. Deheb Z, Schmutz JL, Bursztejn AC, Poreaux C, Barbaud A. À propos d'un cas : réaction paradoxale sous ustékinumab. Ann Dermatol Vénéréologie. 2014;141:S434.
20. Benzaquen M, Flachaire B, Rouby F, Berbis P, Guis S. Paradoxical pustular psoriasis induced by ustekinumab in a patient with Crohn's disease-associated spondyloarthropathy. Rheumatol Int. 2018;38:1297-9.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Report

Carbamazepine-induced pellagra: Dermoscopic findings and response to oral nicotinamide

Shagufta Rather, Saika Reyaz, Aaqib Aslam Shah, Malik Nazim

Department of Dermatology, Venereology and Leprosy, Government Medical College, Srinagar, University of Kashmir, Jammu and Kashmir, India

Correspondingauthor: Shagufta Rather, MD, E-mail: shagufta.giri@gmail.com

ABSTRACT

Pellagra is a nutritional disorder characterized clinically by the four Ds: dermatitis, diarrhea, dementia, and severe systemic photosensitivity manifesting as death. The disorder results from a deficiency of niacin or its precursor tryptophan and is mainly associated with compromised dietary intake of niacin and tryptophan or excessive intake of leucine (a natural antagonist). Other causes include chronic alcohol intake, malabsorption, metabolic disorders, and the administration of certain medications. Herein, we report the clinical and dermoscopic findings in a twenty-year-old male with seizure disorder presenting with carbamazepine-induced pellagrous dermatitis that resolved after the administration of niacin.

Key words: Pellagra; Photosensitivity; Carbamazepine; Dermoscopy; Niacin

INTRODUCTION

Pellagra is a systemic nutritional disorder caused by a deficiency of vitamin B_3 (niacin), which is an essential component of several coenzymes. Pellagra is characterized by the four Ds: photosensitive dermatitis, diarrhea, dementia, and death. Death is included as a cardinal clinical feature in this photosensitivity syndrome [1]. Herein, we present the case of a twenty-year-old male with seizure disorder who had developed carbamazepine-induced dermatitis, which resolved with niacin therapy.

CASE REPORT

A twenty-year-old male presented to the skin outpatient department with complaints of itchy, red, raised lesions on the face, neck, and dorsum of the hands persistent for the last one month as well as oral lesions in the form of inflammation and fissuring at the angles of the mouth with difficulty in opening the mouth and ingesting spicy meals. The itching and burning sensation aggravated on sun exposure. He had a medical history of seizure disorder, for which he had been receiving levetiracetam for the last ten years and carbamazepine for the last three years. There was no history of fever, loose motions, pain in the abdomen, gastrointestinal surgery, or afflicted mental faculties. He denied exposure to chemical agents, contact allergens, and home remedies.

General and systemic examinations were normal. A dermatological examination revealed well-demarcated, symmetric, erythematous to hyperpigmented, dry, and scaly plaques of a yellowish-brown hue on the face, nape, sides of the neck, and dorsa of the hands (Figs. 1a – 1d) with a sharp demarcation at the wrist joint (glove sign or gauntlet sign). A mucous examination revealed commissural cheilitis and glossitis. Routine hematological and biochemical investigations were within the normal ranges. Serology for anti-nuclear antibodies was negative. Dermoscopy of the skin lesions with DermLite DL4 in the non-polarized and polarized mode revealed peripheral double-edged, white scale detached from outward inward, perifollicular scaling, reddish-brown polygonal areas and structures, white, follicular dots, follicular plugs, and red and brown dots and globules on a pinkish background. Short, linear,

How to cite this article: Rather S, Reyaz S, Shah AA, Nazim M. Carbamazepine-induced pellagra: Dermoscopic findings and response to oral nicotinamide. Our Dermatol Online. 2023;14(1):65-68.

Submission: 09.07.2022; **Acceptance:** 28.09.2022

DOI: 10.7241/ourd.20231.13

arborizing vessels and dotted vessels were also observed in the polarized mode (Figs. 2a – 2f).

The histopathological findings observed were hyperkeratosis, parakeratosis, acanthosis, marked vacuolar changes in the upper half of the stratum Malpighian layer, and increased pigment throughout the layers of the epidermis (Figs. 3a and 3b).

The estimation of serum niacin could not be performed due to financial constraints. Based on the history and physical examination, a diagnosis of drug-induced

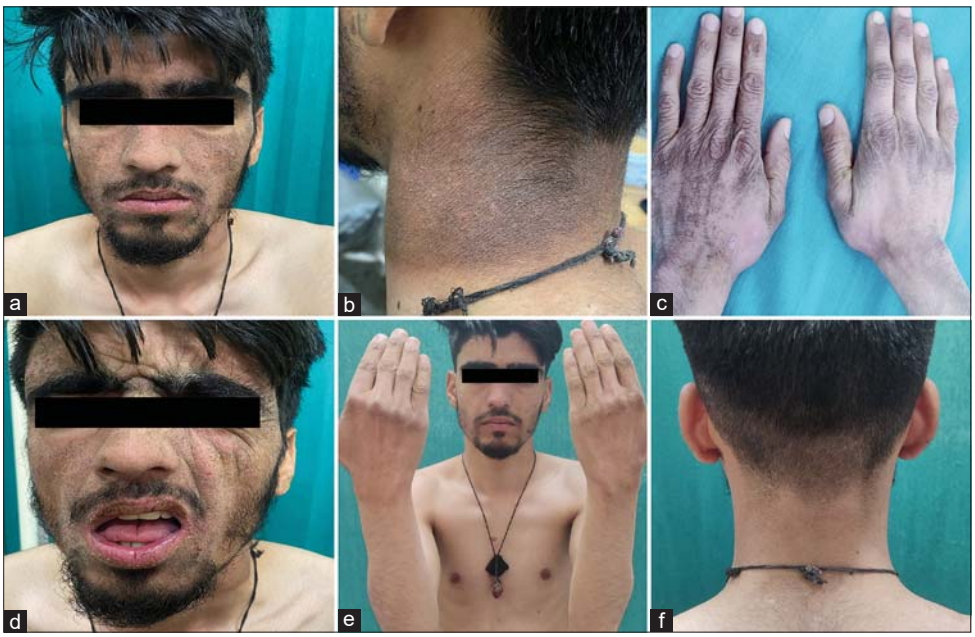


Figure 1: (a) Hyperpigmented scaly plaques on the face. (b) Scaly, hyperpigmented plaques on the sides and the nape of the neck. (c) Hyperpigmented, dry, and scaly plaques on the dorsum of the hands. (d) Difficulty in opening the mouth with commissural cheilitis. (e-f) Complete regression of the lesions on the face, dorsum of the hands, and nape of the neck after two weeks of treatment.

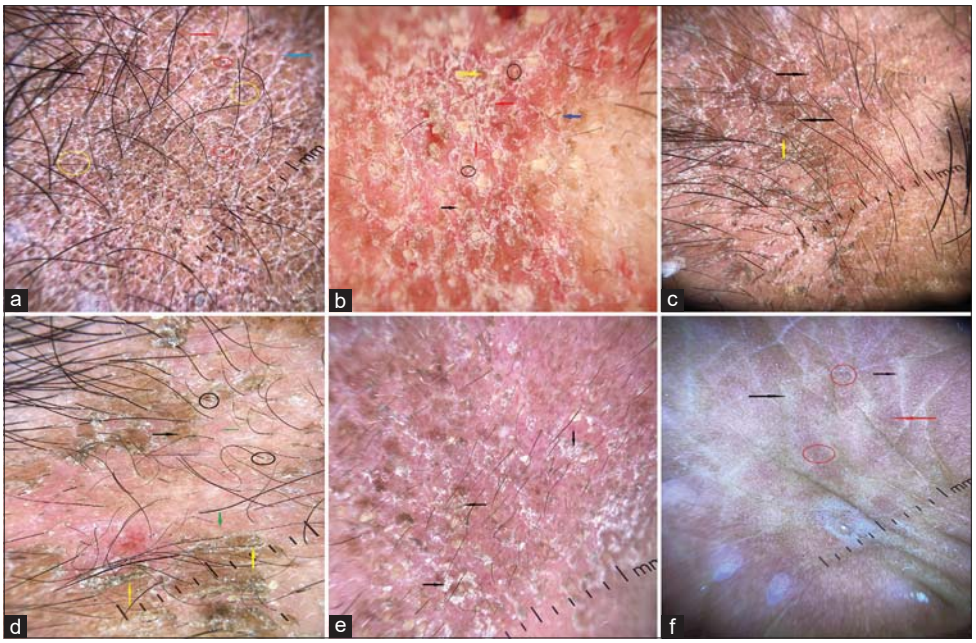


Figure 2: Dermoscopy of pellagra: (a) numerous brown and black dots (yellow and red circles), whitish scales (blue arrow), and brown areas (red arrow), on a reddish-brown background; (b) perifollicular scales (blue arrows), follicular, keratotic plugs (black arrows), brownish areas (yellow arrow), and white dots (black circles); (c) white, double-edged scales (black arrow) and brownish areas (yellow arrow); (d) brownish-white, double-edged, scales (yellow arrows), brownish areas (black arrow), and unfocussed linear vessels (green arrow); (e) white, double-edged scales; (f) post-treatment dermoscopy showing whitish, structureless areas (black arrow), pink, structureless areas (red arrow), and gray dots (red circles). (polarized DermLite DL4; original magnification: 10×).

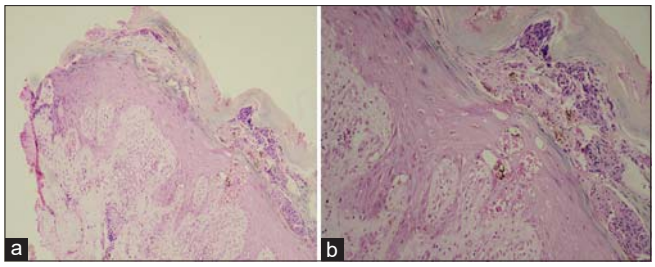


Figure 3: (a-b) Hyperkeratosis, mild spongiosis, acanthosis, increased basal layer pigmentation; the dermis showing edema with perivascular chronic inflammatory infiltrate (H&E, 4×).

pellagra-like dermatitis was established. The patient was started on tablets of nicotinamide 300 mg daily in three divided doses with a multivitamin B complex. Carbamazepine was discontinued. The lesions healed completely within two weeks of nicotinamide therapy (Figs. 1e and 1f). Proper nutrition with a high-protein diet and physical sunscreen cream were also added to the treatment protocol.

DISCUSSION

Gaspar Casal first described pellagra among the poor peasants of the Asturias province of Spain in 1735. In vernacular Italian, *pellagra* means *rough or sour skin* and refers to the thickened skin observed in patients suffering from the condition.

Niacin (vitamin B_3) is essential for adequate cellular function because of its role in two similar yet distinct coenzymes (that is, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP)). Both are cofactors that may be recycled by serving as both oxidizing (NAD, NADP) and reducing (NADH, NADPH) agents. A deficiency of NAD and NADP may lead to pellagra, resulting in a classical triad of dermatitis, diarrhea, and dementia. Pellagra is often an evolving process, which, if untreated, may lead to progressive deterioration and death (the fourth and last "D") over a period of years [2].

Pellagra is associated with compromised dietary intake of niacin and tryptophan or excessive intake of leucine (natural antagonist).

Other leading causes of pellagra-like dermatitis include chronic alcohol intake, individuals with significant malabsorption, certain metabolic disorders, and the administration of specific medications [2]. Drug-induced pellagra may be caused by drugs such as antitubercular drugs, 5-fluorouracil, 6-mercaptopurine, phenytoin, chloramphenicol, azathioprine, and phenobarbital. Isoniazid, pyrazinamide, and ethionamide are structurally similar to NAD and competitively replace NAD from metabolic pathways. Hence, tissues with high-energy requirements, such as the brain, or with a high turnover rate, such as the skin and gut, are affected in pellagra [3]. The inhibited conversion of tryptophan to niacin by 5-fluorouracil leads to pellagra, and 6-mercaptopurine causes pellagra-like dermatitis by inhibiting Korenberg's enzyme (NAD phosphorylase). The exquisite photosensitivity seen in pellagra may result from a cutaneous deficiency of urocanic acid, the accumulation of kynurenic acid, a deficiency of NAD and NADP, and altered porphyrin metabolism, which may induce a phototoxic reaction [4].

The exact mechanism by which anticonvulsants cause pellagra is unknown. The alteration of the absorption of either niacin or other related essential vitamins has been proposed as one. A direct effect of the medication or its metabolites on the synthetic pathway of niacin is also possible [5].

The cutaneous rash of pellagra is bilateral, well-defined, symmetrical, and limited to sun-exposed sites, most prominently on the dorsum of the hands, the "V" of the neck, the face, the radial aspects of the forearms, and the exposed skin on the legs and feet. Persistent erythema and scaling are sequelae of the acute eruption. Chronic lesions reveal marked hyperpigmentation, skin thickening, dryness, and roughness. Various signs described in association with pellagra are the glove or gauntlet sign, the boots sign, and the Casal's necklace [6].

The WHO recommends 300 mg of nicotinamide given in a divided daily dose for 3–4 weeks. Parenteral nicotinamide administration of 1 g 3–4 times daily is recommended for severe cases. Nicotinamide is preferred over niacin in the treatment of pellagra as it does not cause vasomotor disturbances, such as flushing, itching, or burning [7]. Our report describes a patient with carbamazepine-induced pellagra that resolved by the replacement of niacin and other essential vitamins. Although the condition is rare, we as dermatologists should be familiar with this entity, because the skin findings are its most diagnostic feature and the condition is easily treatable.

The dermoscopy of pellagra dermatitis observed was similar to that described in an earlier report [8].

Dermoscopy as a non-invasive modality in conjunction with clinical and histopathological features and a therapeutic response may help in correcting the diagnosis.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Karthikeyan K, Thappa DM. Pellagra and skin. Int J Dermatol. 2002;41:476-81.
2. Prabhu D, Dawe RS, Mponda K. Pellagra a review exploring causes and mechanisms, including isoniazid-induced pellagra. Photodermatol Photoimmunol Photomed. 2021;37:99-104.
3. Nabity SA, Mponda K, Gutreuter S, Surie D, Zimba SB, Chisuwo L, Moffitt A, Williams AM, et al. Isoniazid-associated pellagra during mass scale-up of tuberculosis preventive therapy: A case-control study. Lancet Glob Health. 2022 May;10:e705-e714. Li R.
4. Wan P, Moat S, Anstey A. Pellagra: A review with emphasis on photosensitivity. Br J Dermatol. 2011;162:1188-200.
5. Boileau M, Azib S, Staumont-Sallé D, Dezoteux F. Increased risk of pellagra in an alcoholic patient treated with antiepileptic drugs. Ann Dermatol Venereol. 2022; 24:S0151-9638(22)00037-0.
6. Barro/Traoré F, Diallo B, Tapsoba P, Andonaba J-B, Kéré M, Niamba P, et al [Pellagra: Epidemiological and clinical features in the western region of Burkina Faso]. Our Dermatol Online. 2013;4:479-83.
7. Rani R, Sharma RK, Gupta M. Zinc-responsive acral hyperkeratotic dermatosis. Our Dermatol Online. 2022;13:308-10.
8. Murthy SC, Shankar M. Pellagra dermatitis: Five cases with dermoscopic findings. Int J Dermatol. 2022;61:e56-8.

Source of Support: This article has no funding source, **Conflict of Interest:** The authors have no conflict of interest to declare.

Our Dermatology Online

Case Report

Multiple autoimmune syndrome (vitiligo with Crohn's disease and thyroid disease) in a single patient: A variant type

Mohammad Shahatha Nayaf[1,2]

[1]*Department of Dermatology, Tikrit University, College of Medicine, Iraq,* [2]*Internal Medicine Department, Tikrit University, College of Medicine, Iraq*

Corresponding author: Mohammad Shahatha Nayaf, PhD, E-mail: nayaf_mohammad@yahoo.com

ABSTRACT

The co-existence of different autoimmune disorders in the same individual is known as multiple autoimmune syndrome (MAS), which was described by Humbert and Dupond in 1988. Pathogenesis in the immune system occurs with more recurrence in patients with a background marked by another immune disorder. Around 25% of patients with immune system sicknesses tend to foster more immune disorders. In MAS, patients frequently have, at any rate, one dermatological condition, usually vitiligo or alopecia areata. Herein, we report a case of MAS in a sixteen-year-old male suffering from vitiligo with Crohn's disease and thyroid disease.

Key words: Multiple Autoimmune Syndrome (Mas); Inflammatory Bowel Disease (Ibd); Gastrointestinal Tract (Git); Crohn's Disease (Cd)

INTRODUCTION

Vitiligo is an acquired pigmentary anomaly of the skin manifested by white, depigmented patches surrounded by a normal or hyperpigmented border [1]. There is a complete loss of melanocytes in the affected areas [2]. Most patients with vitiligo have no other associated findings; however, vitiligo has been reported to be associated with alopecia areata, hypothyroidism, Graves' disease, Addison's disease, pernicious anemia, insulin-dependent diabetes mellitus, uveitis, chronic mucocutaneous candidiasis, polyglandular autoimmune syndromes, and melanoma [3].

Inflammatory bowel disease (IBD) is a chronic, immune-mediated disorder comprised of Crohn's disease and ulcerative colitis [4]. The etiology of IBD remains unclear; however, recent research indicates that the pathophysiology of IBD involves abnormalities in disease susceptibility genes, environmental factors, and intestinal bacteria [5]. Crohn's disease (CD) is a compulsive idiopathic IBD that chiefly arises in the small intestine and at the beginning of the large intestine. CD results from T-cell initiated characteristic inflammation caused usually by innocuous commensal bacteria or bacterial products. In CD, the covering of the gastrointestinal tract becomes inflamed. Any portion of the tract may be altered, although generally the ileum and colon are affected [6].

Thyroid sickness happens with either unusually raised or lowered thyroid hormones. Hyperthyroidism is, for the most part, described by an overabundance of thyroid hormones with diminished serum thyroid-stimulating hormone and raised triiodothyronine and thyroxine concentrations. Conversely, hypothyroidism is, by and large, portrayed by diminished thyroid chemical blend and raised thyroid-stimulating hormone, as well as low triiodothyronine and thyroxine concentrations [7]. The most common cause of thyroid dysfunction is an iodine deficiency, and two billion individuals are estimated to have insufficient iodine intake. In countries with

How to cite this article: Nayaf MS. Multiple autoimmune syndrome (vitiligo with Crohn's disease and thyroid disease) co-existing in a single patient: A variant type. Our Dermatol Online. 2023;14(1):69-72.

Submission: 07.08.2022; **Acceptance:** 02.10.2022

DOI: 10.7241/ourd.20231.14

routine iodine supplementation, however, autoimmune thyroid disorders are the most common causes of thyroid disorders [8].

MAS is defined as the occurrence of at least three autoimmune diseases in the same patient [9]. The most frequent autoimmune diseases in such patients include dermatological conditions such as alopecia areata and vitiligo [10].

The pathogenesis of MAS is unknown. However, the autoimmune tautology theory proposes that autoimmune diseases share common immunogenic, physiopathological, and genetic mechanisms. This may lead to the presentation of similar signs and symptoms, demonstrating their common origin [11].

MAS may be divided into three gatherings, as indicated by the commonness of their relationship. Class one comprises myasthenia gravis, thymoma, polymyositis, and giant cell myocarditis. Class two comprises Sjögren's syndrome, rheumatoid arthritis, primary biliary cirrhosis, scleroderma, and autoimmune thyroid disease. Class three comprises autoimmune thyroid disease, myasthenia and/or thymoma, Sjögren's syndrome, pernicious anemia, idiopathic thrombocytopenic purpura, Addison's disease, insulin-dependent diabetes, vitiligo, autoimmune hemolytic anemia, systemic lupus erythematosus, and dermatitis herpetiformis. For this group, HLA-B8 and/or -DR3 or -DR5 seem to be an important factor [12].

CASE REPORT

The sixteen-year-old Iraqi male who presented to the clinic was first diagnosed with vitiligo when he was nine years old. His family history included vitiligo in her mother. A dermatological examination revealed multiple, well-demarcated, depigmented macules and patches mostly on the legs and arms (Figs. 1 and 2) and scattered lesions on the trunk and face; the hair, anogenital area, nails, and oral cavity were normal. Wood's lamp examination was employed to diagnose the hypopigmented patches on the trunk as vitiligo. Non-segmental vitiligo of the generalized type was diagnosed, for which he was treated by others doctors with a topical steroid preparation and topical methoxsalen. There was a moderate response to the treatment with some repigmentation.

His past medical history revealed that he had had gastrointestinal symptoms such as abdominal pain, diarrhea, and weight loss since 2012. He underwent colonoscopy and histopathology in July 2020. Colonoscopy revealed a small, painful, low-rectal ulcer, and a biopsy was taken from the ileal, colonic, and rectal sites. A diagnosis of Crohn's disease was established by colonoscopy and histopathological examination.

Laboratory studies disclosed the following values: iron-deficiency anemia (serum ferritin: 8.83; hematocrit: 36.8%; hemoglobin: 12 g/dL), inflammatory syndrome (ESR: 16 mm/1 h; CRP > 5 mg/dL), renal test (urea: 16.71 mg/dL, creatinine: 0.53, BUN: 8 mg/dL), and liver test (alkaline phosphatase: 288 IU/L).

As for celiac disease testing, antigliadin antibodies were within normal limits, and tissue transglutaminase IgG and IgA were positive.

A thyroid function test revealed the following: T3 (1.3 nmol/L), T4 (72 nmol/L), TSH (15.7 mIU/L). Antithyroid antibody: Anti-Tg antibody (96.14 IU/mL), TPO antibody (934.31 IU/mL), thyroglobulin (0.22 ng/mL).

Antinuclear antibody (ANA) profile and HIV and HCV antibody tests were negative.

The diagnoses were finally established: multiple autoimmune syndrome (vitiligo with Crohn's disease and thyroid disease) existing in a single patient, a variant type of multiple autoimmune syndrome.

DISCUSSION

Presumably, the link between various autoimmune diseases might be genetic and/or environmental exposures that trigger an aberrant immune response. Although various autoimmune diseases differ in their target organs and antigens, they share a common loss of self-tolerance [13].

The term *autoimmune tautology* is employed to describe the common physiopathological mechanisms and genetic factors shared by numerous autoimmune diseases, and clinically this is evident in the cases of polyautoimmunity and familial autoimmunity [14]. Polyautoimmunity is likewise significant for the flow conversation since it might impact the seriousness of immune system illnesses. As a matter of fact, some creators contend that there is a more extreme show of a specific promotion when polyautoimmunity is

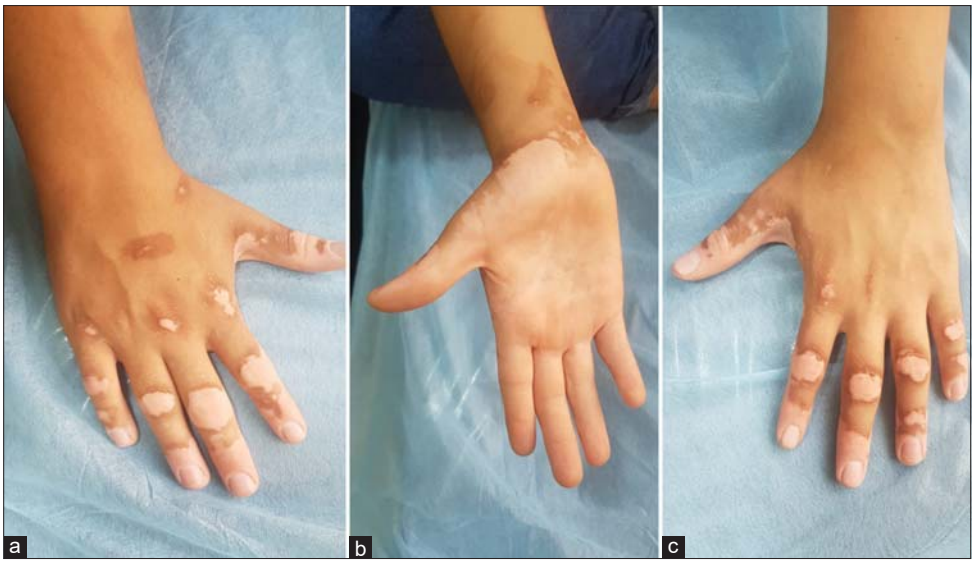


Figure 1: (a-c) Multiple depigmented patches on both hands.

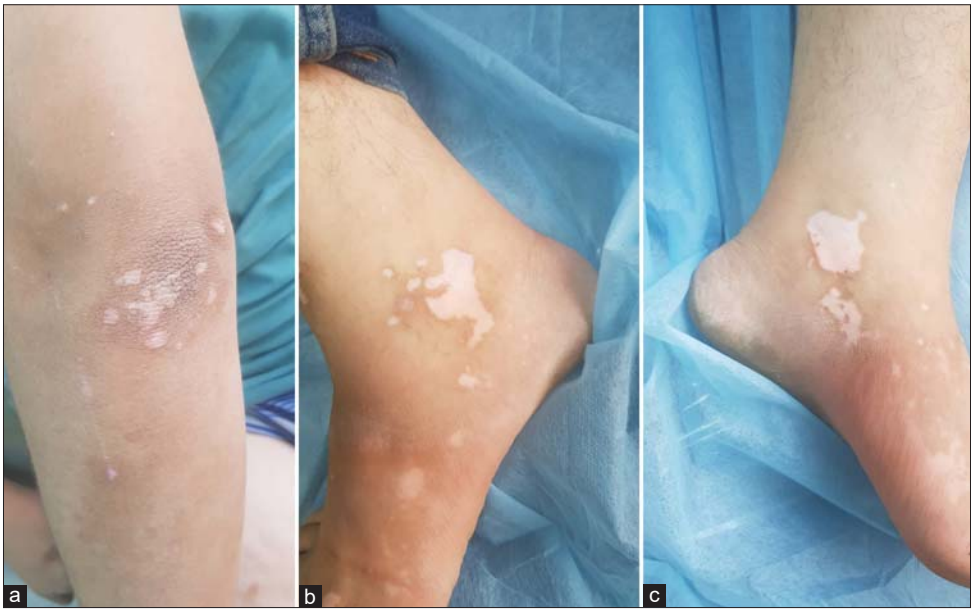


Figure 2: (a-c) Multiple depigmented patches on the elbows and knees.

available, while others have tracked down no impact or even a superior forecast in such cases [15].

The case described here was a typical form of MAS by three autoimmune disorders, including vitiligo, hypothyroidism, and Crohn's disease.

Pathogenesis in the immune system occurs more frequently in patients with a history of other immune system illnesses. The tendency to develop more diseases occurs in around 25% of these patients [16].

In a recent review of the literature, Manuel et al. revealed that MAS type I affected one case in two to three million newborns. Its prevalence in the general population is estimated to be 1/90,000 in Norway and 1/130,000 in Ireland. MAS is thought to be higher in Sardinians and Iranian Jews, with a prevalence of 1/14,000 and 1/9000, respectively. The female sex seems to be a risk factor for polyautoimmunity [17].

In a retrospective analysis of eleven patients with type 3 MAS, Klisnick et al. found that 63.6% of the patients had segmental or bilateral vitiligo, and 90% presented with autoimmune thyroid disease [18].

Cutaneous diseases related to Crohn's disease are erythema nodosum, pyoderma gangrenosum,

epidermolysis bullosa acquisita, polyarteritis nodosa, and vitiligo. The relationship between Crohn's disease and vitiligo has been observed in the literature. In research by Tanusin et al., the co-existence of vitiligo and Crohn's disease was seen in 10% of patients. McPoland and Moss revealed an instance of Crohn's disease and vitiligo. In the two examinations, vitiligo was correspondingly related [19]. Immune system peculiarities may be unmistakable in fiery gut sickness. Ulcerative colitis, specifically, shows a high rate of related immune system sicknesses, including hypothyroidism, essential sclerosing cholangitis, vitiligo, and alopecia areata [20].

CONCLUSION

The finding of MAS relies upon the doctor's exactness and the time that the principal immune system disease began. The presence of one immune system sickness ought to make one aware to watch for another. Therefore, early diagnosis and proper management are of great importance. As a rule, the presence of one issue in the immune system helps to lead to the revelation of other immunological conditions.

This case report illustrates the distinctive presentation of a case of the clinical coexistence of multiple autoimmune diseases (vitiligo with Crohn's disease and thyroid disease). The event of numerous immune system peculiarities in this situation shows the need for reconnaissance for the improvement of emerging immune system sicknesses in the inclined patients.

CONSENT

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. James DW, Elston MD, Treat RJ, Rosenbach AM, Neuhaus MI. Andrew's diseases of the skin clinical dermatology. Thirteen Edition. Elsevier; 2019: 871.
2. Weller BR, Hunter J.A Hamish, Mann W.M. Clinical dermatology. FIFTH EDITION. Blackwell Publishing; 2014: 271.
3. Habif PT. Clinical dermatology: A color guide to diagnosis and therapy. Seven Edition. Elsevier Inc. 2021: 774.
4. Malik FT, Aurelio MD. Extraintestinal manifestations of inflammatory bowel disease. Bioline International. March 9, 2022.:1989-2004.
5. Nakase H, Uchino M, Shinzaki S, Matsuura M, Matsuoka K, Kobayashi T. Evidence-based clinical practice guidelines for inflammatory bowel disease. J Gastroenterol. 2021;56:489-526.
6. Sindhu RK, Goyal A, Das J, Neha, Arora S. Crohn's disease: Symptoms, diagnosis, management by medical and alternative treatment. Pharm Sci Asia. 2021;48:204-23.
7. Malik S, Cohen RP. Vitiligo-Associated autoimmune disorders: A woman with vitiligo and incipient hypothyroidism. Cureus. 2021;13:e19164.
8. Alzahrani SA, Mourad AM, Hafez K, Almaghamsy MA, Alamri AF, Juhani RN. Diagnosis and management of hypothyroidism in Gulf Cooperation Council (GCC) Countries. Adv Ther. 2020;37:3097-111.
9. Alwasaidi AT, Mustafa W, Osman H, Hebshi AA, Sr AA. Multiple autoimmune syndrome with alopecia universalis and immune thrombocytopenic purpura. Cureus. 2021;13:e13033.
10. Mahdi M Sereshki A, Almasi S, Behnam B, Semnani F. Autoimmune haemolytic anaemia and multiple autoimmune syndrome. Eur J Case Rep Intern Med. 2019;6:001111.
11. González CC, Martínez AS, Guanes RJ. Ocular cicatricial pemphigoid, Sjögren's syndrome, and Hashimoto's thyroiditis as a multiple autoimmune syndrome: A case report. Eur J Ophthalmol. 2022;32:NP52-5.
12. Madan PM., Ramesh TC. Multiple autoimmune syndrome. Indian J Dermatol Venereol Leprol. 2003;69:298-9.
13. Greenberg MB, Casper CT, Jayne M N, Plumb P, Liang S, Goyal M. Familial history of autoimmune disorders among patients with pediatric multiple sclerosis. Neurol Neuroimmunol Neuroinflamm. 2021;8:e1049.
14. Prabhu SS, Ravi D, Shenoi DS, Pai K, Sudhir UK. Multiple autoimmune syndrome with isotopic phenomenon: Association of lichen planus, vitiligo and alopecia areata with autoimmune hepatitis. J Pak Assoc Dermatol. 2018;28:356-9.
15. Villarraga RA, Amaya AJ, Rodriguez RA, Mantilla DR, Anaya MJ. Introducing polyautoimmunity: Secondary autoimmune diseases no longer exist. Autoimmune Dis. 2012;2012:254319.
16. Setiyohadi BS, Mokoagow MI. Multiple autoimmune syndrome (Graves' disease, systemic lupus erythematosus, and systemic sclerosis) in a young woman in Jakarta. J Rheumatol.2020;3:41-4.
17. Niasse M, Kane SB, Dimitri A Mabom W, Makougang C, Dézoumbé M. Multiple autoimmune syndrome: A study of 25 Senegalese cases. Open J Rheumatol Autoimmune Dis. 2020;10:14-23.
18. Dourmishev L, Pozharashka J, Miteva L. Probable multiple autoimmune syndrome in a patient with vitiligo, autoimmune thyroiditis, and diabetes mellitus: A case report. J Skin Stem Cell. 2019;6:e103596.
19. Gargi R, Hita HM. Mehta, Jhamwar MM. Anogenital Crohn's disease with vitiligo. Indian J Sex Transm Dis AIDS. 2014;35;53-5.
20. Cojocaru M, Cojocaru MI, Silosi I. Multiple autoimmune syndrome. Mædica (Bucur). 2010;5;132-4.

Source of Support: This article has no funding source,

Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Case Report

Iatrogenic Kaposi's sarcoma in a patient with bullous pemphigoid treated with an oral corticosteroid

Muriel Sidnoma Ouédraogo[1,2], Nakougou Moï-Bohm Biatougou[3], Nomtondo Amina Ouédraogo[1,2], Angèle Ouangré/Ouédraogo[1], Gilbert Patrice Marie Louis Tapsoba[1,2], Adama Traoré[4], Fatimata Cissé[1], Nina Korsaga/Somé[2,5], Pascal Niamba[1,2], Jacques Simporé[3], Adama Traoré[1,2]

[1]Department of Dermatology-Venereology of Yalgado Ouédraogo University Hospital (YO UH), Ouagadougou, Burkina Faso, [2]Health Science Training and Research Unit, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso, [3]United of Formation and Research of Life and Land Sciences, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso, Laboratory of molecular biology and molecular genetic (Labiogène), Ouagadougou, Burkina Faso, [4]Department of Anatomy Pathology, Yalgado Ouédraogo University Hospital, Ouagadougou, Burkina Faso, [5]Department of Dermatology Venerology, Boulmiougou District Hospital, Ouagadougou, Burkina Faso

Corresponding author: Muriel Sidnoma Ouédraogo, MD, E-mail: sidnomam@yahoo.fr

ABSTRACT

Kaposi's sarcoma is a multifocal angiogenic tumor disease whose principal causal agent is human herpes virus 8 (HHV-8). Herein, we report a rare case of iatrogenic Kaposi's sarcoma developing during oral corticotherapy. A 76-year-old, HIV-negative male presented with papulous, angiomatous lesions on the trunk and limbs, which appeared three months after the beginning of oral corticotherapy for bullous pemphigoid. We suspected iatrogenic Kaposi's sarcoma given the time to lesion onset in relation to the immunosuppressive treatment, together with histological and virological confirmation of HHV-8. The lesions began to subside when corticosteroids were tapered down to 10 mg/day. This was the first case reported in our setting and it emphasized the need for the rigorous monitoring of patients receiving immunosuppressants to avoid overlooking the side effects or rare complications of these treatments.

Key words: Kaposi's sarcoma; Oral corticotherapy; HHV-8; Bullous pemphigoid

INTRODUCTION

Kaposi's sarcoma (KS) is a multifocal tumoral disease whose principal causal infectious agent is human herpes virus 8 (HHV-8), identified in 1994 [1]. Four clinical and epidemiological subtypes have been described: the classic or Mediterranean, endemic, epidemic AIDS-related, and iatrogenic. Iatrogenic KS occurs in patients exposed to long-term immunosuppressive treatments (topical or oral corticosteroids and/or other immunosuppressants) associated or not with organ transplantation [2-8]. It often raises the problem of managing the disease for which the immunosuppressant was prescribed because of the need to discontinue the drug or reduce the dose. Herein, we report a rare case of iatrogenic KS occurring during oral corticotherapy in a patient with bullous pemphigoid, who was followed at the dermatology department of Yalgado Ouédraogo University Hospital, Ouagadougou, Burkina Faso.

CASE REPORT

A 76-year-old male, married, a retired journalist, was followed for bullous pemphigoid confirmed by histology of a bullous lesion and by indirect immunofluorescence. Oral corticotherapy (prednisone) 60 mg/day (1 mg/kg/day) was prescribed. Arterial hypertension was discovered the

How to cite this article: Ouédraogo MS, Moï-Bohm Biatougou N, Ouédraogo NM, Ouangré/Ouédraogo A, Tapsoba GPML, Traoré A, Cissé F, Korsaga/Somé N, Niamba P, Simporé J, Traoré A. Iatrogenic Kaposi's sarcoma in a patient with bullous pemphigoid treated with an oral corticosteroid. Our Dermatol Online. 2023;14(1):73-76.

Submission: 05.07.2022; **Acceptance:** 13.11.2022

DOI: 10.7241/ourd.20231.15

day that the oral corticotherapy was initiated and he was given amlodipine 5 mg/day. He was HIV-negative.

Three months after the beginning of corticotherapy, reduced to 30 mg/day, he developed firm, angiomatous, nodular lesions measuring 0.5 to 2 cm in their greatest dimension, locally erosive and sensitive on the soles and sides of the feet, without lymphedema (Fig. 1a). These lesions then spread to the thighs and arms (Fig. 1b). There were no buccal lesions. The possible diagnoses considered were Kaposi's sarcoma, hypertrophic cutaneous lichen planus, and sarcoidosis. A pathological examination of a lesion biopsy specimen revealed an orthokeratotic, slightly acanthotic epidermis overlying a regular basal layer. The dermis revealed fusocellular tumoral proliferation with slit-like channels containing red cells, some of which were extravasated. Spindle cells were organized in twisted fascicles. Their nuclei were hyperchromatic and often mitotic. They were associated with inflammatory lymphoplasmacytic infiltrate (Figs. 2a and 2b). This morphological appearance was consistent with Kaposi's sarcoma. For confirmation, a blood sample and a swab from an erosive lesion were obtained for the molecular diagnosis of HHV-8 by real-time PCR. HHV-8 DNA was detected in plasma and in the lesion swab sample, confirming the diagnosis of KS. Lung radiography in search of interstitial infiltrates predominating in the two lung bases, nodules, mediastinal lymphadenopathy, and/or pleural effusions was normal. Abdominal and pelvic echography revealed no hepatic or splenic abnormality or lymphadenopathy.

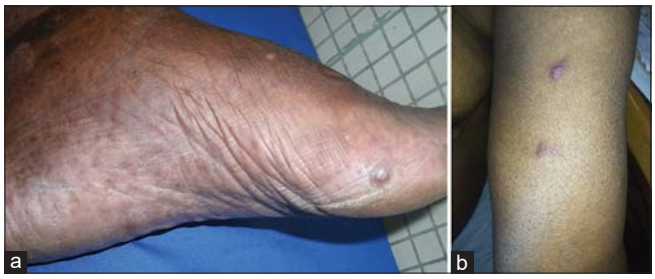


Figure 1: (a) Angiomatous papule on the internal side of the left foot. (b) Angiomatous plaques on the anterior aspect of the left arm.

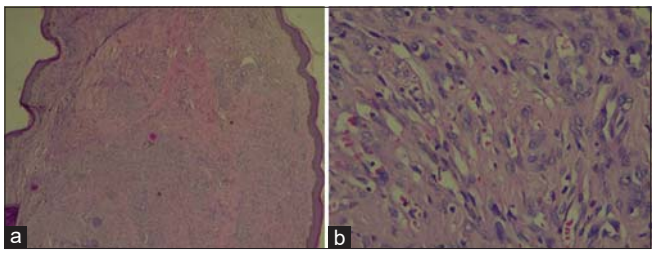


Figure 2: (a) Nodule biopsy specimen showing a regular epidermis overlying a dermis with vascular proliferation. (b) Vessels lined by an atypical endothelium with extravasated red cells.

As the disease progressed, the lesions increased in number to twenty. Prednisone was tapered first by 5 mg then by 10 mg every fourteen days. At a dose of 10 mg/day, the lesions began to subside. There was no recurrence of the bullous pemphigoid.

DISCUSSION

The iatrogenic subtype of KS was originally described in patients who had undergone organ transplantation, in particular kidney transplants followed by high-dose immunosuppressants [9]. Since then, several other cases have been reported in patients who have not had organ transplantation yet have been receiving immunosuppressants, including systemic and topical corticosteroids, for a variety of disorders (blood diseases, kidney diseases, atopic dermatitis, asthma, chronic inflammatory disease [8,10-14].

Herein, we report the first case of iatrogenic KS in a patient with skin phototype VI observed at the department of dermatology and venereology of Yalgado Ouédraogo University Hospital, the national reference center in Burkina Faso. This case occurred in a patient who had been receiving oral corticotherapy for bullous pemphigoid (pemphigoid diseases account for 4.6% of hospital admissions at our institution [15]). Some cases of KS in patients followed for an autoimmune bullous dermatosis (bullous pemphigoid or pemphigus vulgaris) treated with oral corticotherapy [10,14] and/or local corticotherapy [5,6] have previously been reported in the literature, yet not in sub-Saharan Africa.

The cases of iatrogenic KS described in the literature in patients with bullous pemphigoid occurred in elderly subjects, as in our patient (76 years), most seventy years old or older [2,5,14].

The time to onset of KS in our patient was 3 months after the start of corticotherapy. This corresponds to the time to onset (1-36 months) observed by other authors such as Tourlaki et al. [14] and Tremblay and Friedmann [2]. This time-lapse is in support of the iatrogenic nature of the disease in our patient, particularly as he had no sarcomatous lesions before oral prednisone was prescribed. His lesions developed at a prednisone dose of 30 mg/day, which is close to the dose of 8 to 25 mg/day recorded by Tourlaki et al. [14].

In addition to the oral corticosteroid (prednisone or methylprednisolone), which was the only drug taken by our patient, some reported cases had also received other associated immunosuppressants for the treatment of their bullous pemphigoid, either a dermal corticosteroid or mycophenolate mofetil [2]. Among the patients who applied a very strong topical dermal corticosteroid to their bullous lesions, without oral corticosteroids, some also took methotrexate [5].

In our patient, KS involved only the skin, with lesions on the limbs, as has been reported by some authors whose patients were followed for bullous pemphigoid [2,14]. However, in iatrogenic KS, mucosal involvement has frequently been described. Tourlaki et al. described duodenal involvement in one of their patients [14]. We did not perform gastrointestinal fibroscopy in our patient as he had no gastrointestinal warning signs.

Paraclinically, our patient's HHV-8 infection was confirmed by molecular diagnosis. However, such investigations are not routine as they are costly and performed in a research setting. HHV-8 is endemic in sub-Saharan Africa, where 30% to 60% of asymptomatic adults have markers of the infection [16]. In studies by other authors, patients did not always undergo HHV-8 serology and/or molecular biology techniques such as real-time PCR, yet the disease was confirmed histologically.

The modulation of the immunosuppressive treatment is the principal therapeutic weapon in controlling the progression of iatrogenic KS. In our patient, the lesions began to subside at the dose of 10 mg/day of oral corticosteroids. Some authors have reported complete remission of KS lesions when the immunosuppressant involved was decreased or discontinued [6,8,14]. Other authors, however, had to initiate specific treatment for KS (a course of bleomycin, intralesional injection of vincristine, intravenous vinblastine, radiotherapy) in order to obtain remission or stabilization of the lesions [4,5,14]. Worsening of the lesions and rare cases of death due to disseminated intravascular coagulation or septic shock have been reported [10].

With regard to the course of bullous pemphigoid in our patient, it did not recur during the tapering of corticotherapy. However, a longer follow-up period is required for the better evaluation of the course of the disease. We would also like to note that most authors report improvement of their patient's bullous pemphigoid with no recurrence on discontinuation of the immunosuppressive treatment over a longer period than in our case [5,6,14].

CONCLUSION

This rare case an HIV-negative patient with iatrogenic KS induced by long-term oral corticotherapy prescribed for the treatment of bullous pemphigoid highlights the need for rigorous and close patient monitoring in order to avoid overlooking the side effects or rare complications of such treatment. Decreasing the dose of the immunosuppressant or its complete discontinuation is generally followed by regression of KS.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Chang Y, Cesarman E, Pessin MS, Lee F, Culpepper J, Knowles DM, et al. Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. Science. 1994;266:1865-9.
2. Tremblay C, Friedmann D. Kaposi sarcoma associated with iatrogenic immunosuppression: A rare complication of bullous pemphigoid treatment. J Cutan Med Surg. 2017;21:449-51.
3. Saihi M, Jebali H, Breik N, Benfatma L, Mami I, Beji S, et al. Le sarcome de Kaposi iatrogène: à propos de trois observations. Rev Med Int. 2018;A199.
4. Lamchahab M, Oukkache B, Marouan S, Quessar A, Benchekroun S. [Kaposi sarcoma complicating aplastic anemia]. Pan Afr Med J. 2014;18:169.
5. Binois R, Nadal M, Esteve E, De Muret A, Kerdraon R, Gheit T, et al. Cutaneous Kaposi sarcoma during treatment with superpotent topical steroids and methotrexate for bullous pemphigoid: Three cases. Eur J Dermatol. 2017;27:369-74.
6. Boudhir H, Mael-Ainin M, Senouci K, Hassam B, Benzekri L. [Kaposi's disease: An unusual side-effect of topical corticosteroids]. Ann Dermatol Venereol. 2013;140:459-61.
7. Lazzarini R, Lopes ASA, Lellis RF, Brasil F. Iatrogenic Kaposi's sarcoma caused by corticosteroids. An Bras Dermatol. 2016;91:867-9.
8. El Jouari O, Chaymae J, Senhaji G, Douhi Z, Elloudi S, Baybay H, Mernissi FZ. Iatrogenic Kaposi sarcoma in an immune competent woman. Int J Cutaneous Disorders Med. 2018,1:180001.
9. Abi Rached H, Javed S, Lepesant P, Mortier L. Maladie de Kaposi. EMC 98-655-A-10-Dermatologie. 2018;13:1-12.
10. Lamchahab FE, Tadlaoui I, Beqqal K, Bouattar T, Ouzeddoun N, Bayahia R, et al. [Iatrogenic Kaposi's disease in Morocco in a non-transplant context]. Ann Dermatol Venereol. 2011;138:729-35.
11. Wall D, McMenamin M, O'Mahony D, Irvine AD. Kaposi sarcoma in a patient with atopic dermatitis treated with ciclosporin. BMJ

Case Rep. 2013;2013:bcr2013202171.
12. Zaraa I, Labbène I, El Guellali N, Ben Alaya N, Mokni M, Osman AB. [Kaposi's sarcoma: Epidemiological, clinical, anatomopathological and therapeutic features in 75 patients]. Tunis Med. 2012;90:116-21.
13. Duh E, Fine S. Human herpesvirus-8 positive iatrogenic Kaposi's sarcoma in the setting of refractory ulcerative colitis. World J Clin Cases. 2017;5:423-7.
14. Tourlaki A, Genovese G, Guanziroli E, Scoppio BM, Berti E, Brambilla L. Autoimmune bullous diseases in non-HIV Kaposi's sarcoma: a retrospective study in a large cohort of patients. J European Acad Dermatol Venereol. 2018;32:1777-83.
15. Korsaga/Somé N, Andonaba JB, Traoré F, Ouédraogo MS, Tapsoba GP, Barro/Traoré F, et al. Profil épidémiologique et clinique des patients hospitalisés dans le service de dermatologie-vénérologie du CHU Yalgado Ouédraogo de Ouagadougou. Burkina Médical. 2014;18:65-71.
16. Etta EM, Alayande DP, Ramarumo-Mavhandu LG, Gachara G, Bessong PO. HHV-8 seroprevalence and genotype distribution in Africa, 1998–2017: A systematic review. Viruses. 2018;10:1-17.

Source of Support: This article has no funding source.
Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Case Report

Abrikossoff's skin tumor: Report of two cases

Imane Gouzi[1], Layla Tahiri[1 2], Khaoula Abdellaoui[1], Sabrina Oujdi[3], Zakia Douhi[3], Sara Elloudi[3], Hanane Baybay[3], Meryem Soughi[3], Fatima Zahra Mernissi[3], Hinde El Fatemi[1,2], Laila Chbani[1,2], Nawal Hammas[1,2]

[1]Departement of Pathological Anatomy, CHU Hassan II Fez, Morocco, [2]Biomedical and Translational Research Laboratory, Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco, [3]Department of Dermatology, CHU Hassan II Fez, Morocco.

Corresponding author: Imane Gouzi, MD, E-mail: imane.gouzi@gmail.com

ABSTRACT

Abrikossoff's tumor, also known as granular cell tumor, is a rare tumor first described on the tongue by Ivanovich Abrikossoff in 1926. It is mainly located in the head and neck regions with preferential mucosal involvement and may occur at any age and in both sexes, although with a female predominance. Herein, we report two cases: the case of a nodule under the left breast in a 47-year-old female with a history of breast cancer and of a subcutaneous lesion on the right thigh in a 46-year-old female. The diagnosis of granular cell tumor was reached by biopsy with immunohistochemical staining, then treatment was completed by a large surgical excision.

Key words: Abrikossoff; Skin; Granular cell tumor

INTRODUCTION

Abrikossoff's tumor, also known as granular cell tumor, is an uncommon neoplasm of unclear etiology and histogenesis. It is thought to be of neural origin, probably derived from Schwann cells [1]. It tends to affect all races and sexes, although it is most frequently diagnosed in black-skinned individuals, females, and between the second and fifth decades of life [2]. Clinically, it presents itself as a solitary, slow-growing, asymptomatic nodule on the head or neck region with preferential mucosal involvement. In this paper, we report two new cases of a skin granular cell tumor and discuss their epidemiological, clinical, histopathological, and therapeutic aspects.

CASES REPORT

Case 1

A 47-year-old female with a history of thyroidectomy under levothyroxine and lumpectomy for infiltrating carcinoma of the left breast followed by radiochemotherapy presented ten months before admission with a nodule under the left breast, erythematous, well-limited, and gradually increasing in volume (Fig. 1).

Ultrasound was performed and objectified the presence of a superficial, heterogeneous, subcutaneous nodule 2 cm in size.

A cutaneous biopsy revealed a granular cell tumor with a dermal proliferation of large, non-atypical cells presenting a granular cytoplasm (Fig. 2a). An immunohistochemical study revealed positive staining for PS100 and eliminated the metastatic origin of the lesion with negative staining for pan-cytokeratin (Fig. 2b).

Case Two

A 46-year-old diabetic female presented with a seven-month history of a subcutaneous lesion on the right thigh progressively increasing in size, painless and non-pruriginous.

How to cite this article: Gouzi I, Tahiri L, Abdellaoui K, Oujdi S, Douhi Z, Elloudi S, Baybay H, Soughi M, Mernissi FZ, EL Fatemi H, Chbani L, Hammas N. Abrikossoff's skin tumor: Report of two cases. Our Dermatol Online. 2023;14(1):77-80.

Submission: 15.07.2022; **Acceptance:** 25.08.2022

DOI: 10.7241/ourd.20231.16

A physical examination revealed a subcutaneous, firm, painless nodule, 3 cm in size. It was movable relative to the deep plane, fixed to the skin; the skin was erythematously pigmented (Fig. 3). Ultrasound revealed a suspicious tissue mass. A biopsy followed by a large surgical excision was performed.

A histopathological examination revealed a dermal and subcutaneous neoplasm composed of nests of cells with abundant eosinophilic granular cytoplasm and small nuclei (Fig. 4a). Pseudoepitheliomatous hyperplasia was also visible. No cellular pleomorphism, mitosis, or necrosis were observed. In an immunohistochemical study, immunostaining for the S100 protein and CD68 was positive (Fig. 4b).

According to these histologic and immunohistochemical features, the lesion was diagnosed as a granular cell tumor.

DISCUSSION

A granular cell tumor, called also Abrikossoff's tumor, is a benign, conjunctival proliferation compound of large eosinophilic cells with granular cytoplasm. It was first described in 1926 by Russian pathologist Alexei Ivanovich Abrikossoff, who believed it to be of muscular origin because of the resemblance of its cells to muscle cells (or fibers), therefore calling it *myoblastenmyoma*, translated as *granular myoblastoma*. The term *myoblastoma* is now abandoned because of evidence of neurectodermal origin, probably schwanian, its close relationship with the nerves, its immunophenotype, and the presence of vacuoles containing myelin structures under electron microscopy [1-3].

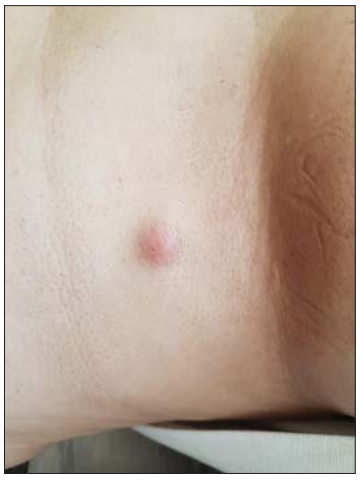


Figure 1: Subcutaneous, erythematous nodule 1.5 cm in size.

It commonly affects females between the second and fifth decades of life, most often black-skinned. Children and adolescents are rarely affected. Although it most frequently involves the head and neck regions, mainly the tongue [4,5], it has been found throughout the body: the skin, subcutaneous tissue, nerves, clitoris, vulva, glans, breast, and internal organs.

The skin lesions may present as subcutaneous nodules mimicking adnexal tumors with hyperpigmented or normal overlying skin or as a hyperkeratotic papule. It is a small lesion usually not larger than 3 cm in size, slowly-growing and firm in consistency. It is usually asymptomatic yet may be painful. Multiple granular cell tumors are not uncommon and are mainly seen in children. Solitary and multiple cutaneous granular cell tumors may be seen in association with neurofibromatosis and Noonan syndrome [6,7].

Histopathologically, the granular cell tumor reveals pseudoepitheliomatous hyperplasia, which is why care should be taken when evaluating a superficial biopsy sample to prevent the overdiagnosis of squamous cell carcinoma, because occasional tumors may be associated with mild to moderate cytological atypia in the pseudoepitheliomatous hyperplasic component. The dermis is infiltrated by cellular proliferation with syncytial, trabecular, or nested growth composed of

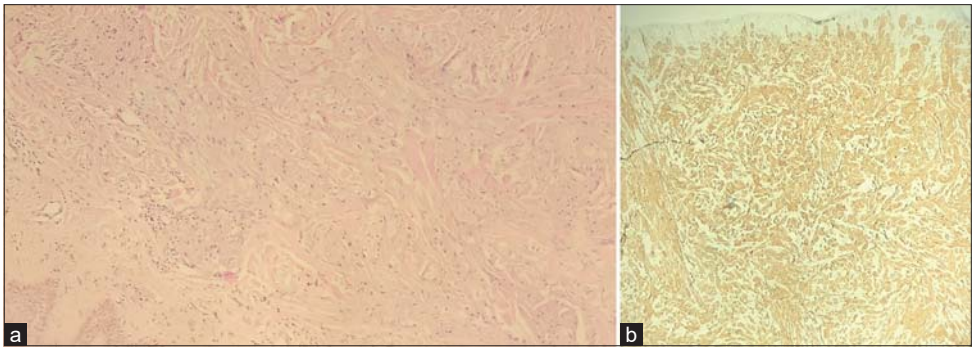


Figure 2: (a) Nets of cells with abundant granular cytoplasm (100×). (b) PS100 positive in granular cells (40×).

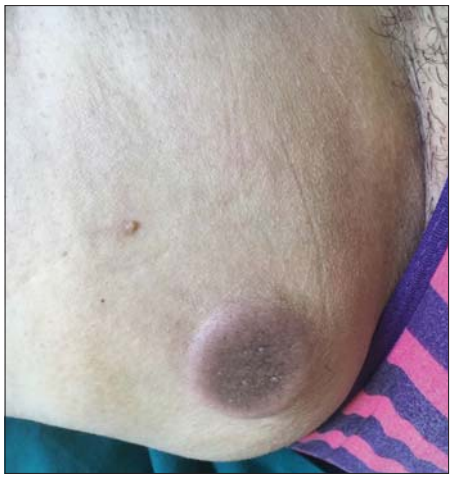


Figure 3: Well-limited, pigmented plaque with regular contours on the internal face of the right thigh.

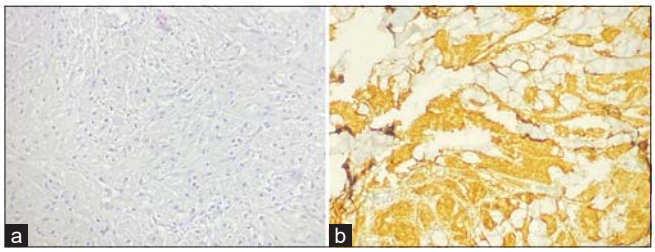


Figure 4: (a) Nets of cells with abundant granular cytoplasm (200×). (b) PS100 positive in granular cells (200×).

cells with round or oval nuclei and abundant, granular, eosinophilic cytoplasm. Vascular invasion reaching the level of subendothelial layers, without intraluminal cells, the infiltration of the erector pili muscles, and perineural extension may be seen. The latter are not criteria of malignancy, yet are just diagnostic features unrelated to prognosis. The cytoplasmic granules are positive for periodic acid–Schiff staining, the S100 protein, neuron-specific enolase, CD57, SOX10, and CD68 [8-10].

The histological diagnosis of malignancy is sometimes difficult and may be confirmed only by the existence of metastasis. Fanburg [11] described six criteria of malignancy: cells becoming fusiform, the presence of necrosis, large, nucleolus, vesicular nuclei, a high nucleocytoplasmic ratio, pleomorphism, mitotic activity (more than two mitoses per ten high-power fields).

The histologic differential diagnosis includes tumors with similar morphologic findings and with granular variants. Alveolar soft part sarcoma, atypical congenital granular cell epulis, epithelioid histiocytoma, hibernoma, rhabdomyoma, rhabdomyosarcoma, and tumors that may rarely have granular cell morphology, such as melanoma, ameloblastoma, benign fibrous histiocytoma, leiomyoma, leiomyosarcoma, angiosarcoma; undifferentiated pleomorphic sarcoma, and atypical fibroxanthoma are included [12-13].

The treatment consists of a large surgical excision with safe margins, which is not always easy given the poor limitation of the tumor. The few cases of recurrence are explained by incomplete excision. The Mohs surgical technique reduces excision margins, particularly in certain locations such as the external genitalia and extremities [14]. Regular and long-term overseeing is recommended to detect a possible recurrence or malignant transformation.

Our two patients benefited from the large excision of the nodules. Follow-up showed a good evolution with no recurrence or metastasis.

CONCLUSION

In this article, we have reported two new cases of Abrikossoff's skin tumor. The diagnosis of the granular cell tumor is established by a histological examination completed with immunohistochemical staining. The usual treatment is complete surgical excision.

CONSENT

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. López V, Santonja N, Jordá E. Granular cell tumor on the sole of a child: A case report. Pediatr Dermatol. 2011;28:473-4.
2. Abraham T, Jackson B, Davis L, Yu J, Peterson C. Mohs surgical treatment of a granular cell tumor on the toe of a child. Pediatr Dermatol. 2007;24:235-7.
3. Muscardin LM, Paradisi M, Provini A, Cota C, Marzetti G. Multiple cutaneous granular cell tumors, joint hypermobility and mild facial dysmorphism in a child. Int J Dermatol. 2006;45:847-50.
4. Gross VL, Lynfield Y. Multiple cutaneous granular cell tumors: A case report and review of the literature. Cutis. 2002;69:343-6.
5. Dimosthenous K, Righi A. Granular cell tumor of the parotid gland: An exceptionally rare occurrence. Int J Surg Pathol. 2008;16:213-4.
6. Martin RW 3rd, Neldner KH, Boyd AS, Coates PW. Multiple cutaneous granular cell tumors and neurofibromatosis in childhood:

A case report and review of the literature. Arch Dermatol. 1990;126:1051-6.
7. Moos D, Droitcourt C, Ranchere-vince D, Marec Berard P, Skowron F. Atypical granular cell tumor occurring in an individual with Noonan syndrome treated with growth hormone. Pediatr Dermatol. 2012;29:665-6.
8. WHO Classification of Head and Neck Tumours, 4th Edition, International Agency for Research on Cancer Lyon, 2017.
9. Battistella M, Cribier B, Feugeas JP, Roux J, Le Pelletier F, Pinquier L, et al.; Cutaneous Histopathology Section of the French Society of Dermatology. Vascular invasion and other invasive features in granular cell tumours of the skin: A multicentre study of 119 cases. J Clin Pathol. 2014;67:19-25.
10. Nasser H, Ahmed Y, Szpunar SM, Kowalski PJ. Malignant granular cell tumor: A look into the diagnostic criteria. Pathol Res Pract. 2011;207:164-8.
11. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, et al. Malignant granular cell tumor of soft tissue: Diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998;22:779–94.
12. Brenn T. Pleomorphic dermal neoplasms: A review. Adv Anat Pathol. 2014;21:108-30.
13. Neelon D, Lannan F, Childs J. Granular Cell Tumor. [Updated 2021 Nov 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563150
14. Gardner ES, Goldberg LH. Granular cell tumor treated with Mohs micrographic surgery: Report of a case and review of the literature. Dermatol Surg. 2001;27:772-4.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Report

Pigmented eccrine poroma in collision with seborrheic keratosis: Dermoscopic description and histological correlation

Ryme Dassouli[1], Zakia Douhi[1], Kenza Tahiri Joutei[1], Hanane BayBay[1], Sara Elloudi[1], Mouna Rimani[2], Fatima Zahra Mernissi[1]

[1]Department of Dermatology, University Hospital Hassan II, Fes, Morocco, [2]Hassan Anatomical Pathology Center – Rabat, Morocco

Corresponding author: Ryme Dassouli, MD, E-mail: dassouliryme@gmail.com

ABSTRACT

Poromas are rare, benign neoplasms arising from the terminal ductal portion of the sweat glands. They are mainly characterized by flesh-colored or pink papules or nodules, usually located at the extremities. The pigmented variant is rare. Collisions with other benign epithelial tumors have been reported. The clinical appearance may be confused with several benign or malignant tumor pathologies, yet thanks to dermoscopy, which is a non-invasive means of exploration, some signs are highly useful in the diagnosis and in suspecting the collision of two distinct tumors before proceeding to histological confirmation. Herein, we report the original case of a collision between pigmented eccrine poroma of the leg and seborrheic keratosis.

Key words: Pigmented poroma; Collision; Dermoscopy; Histology; Seborrheic keratosis

INTRODUCTION

Poromas were first described in 1956 by Pinkus, Goldman, and Login as tumors of eccrine sweat glands, although there are also reports of exocrine differentiation [1]. It is a rare pathological condition that usually appears between the fourth and sixth decades of life. Further studies on this rare pigmented variant of eccrine poroma may shed new light on the identification of specific dermoscopic features [2]. Collision tumors correspond to the coexistence of two histologically distinct tumors composing a single mass [3]. Herein, we report a tumor composed of pigmented eccrine poroma in collision with seborrheic keratosis.

Observation

A 62-year-old patient, without a notable pathological antecedent, presented a lesion of the right leg for two years increasing very gradually in size, becoming pruritic and not painful. No notion of trauma or bleeding was reported.

A dermatological examination revealed a pigmented nodule, roughly oval, with irregular contours and a firm consistency, 2 cm in length, located on the external surface of the right leg. The lower half of the lesion was surrounded by a detached epidermal collar on its inner side (Fig. 1).

A dermoscopic examination showed well-circumscribed, milky-red areas surrounded by brownish interlacing, reminding in its globality the aspect of frog eggs, vascular structures within it, poorly visualized with rounded ends, some of which had a globular aspect. There were also bright, whitish streaks in places, grayish-white areas without structure, and scattered, blackish dots and globules. This aspect was in collision with a homogeneous, brownish structure with a coral-like appearance and mordant borders, interspersed by some homogeneous, brownish globules (Fig. 2).

How to cite this article: Dassouli R, Douhi Z, Joutei KT, BayBay H, Elloudi E, Rimani M, Mernissi FZ. Pigmented eccrine poroma in collision with seborrheic keratosis: Dermoscopic description and histological correlation. Our Dermatol Online. 2023;14(1):81-84.

Submission: 02.12.2021; **Acceptance:** 04.05.2022

DOI: 10.7241/ourd.20231.17

The patient underwent an excisional biopsy. An anatomopathological study was in favor of a collision tumor associating a pigmented eccrine poroma with a hyperkeratotic and pigmented seborrheic keratosis. A microscopic study of the horizontal sections revealed an intraepidermal proliferation with endophytic development realizing wide, tongue-like trabeculae composed of round, monomorphic basaloid cells with focally enlarged nuclei without exaggerated mitotic activity, and thick columns extending and anastomosing at the level of the reticular dermis. The proliferation was rich in melanin pigments. There were also dilated ductular structures lined with cuboid cells with patchy squamous differentiation. The stroma was fibrous and richly vascularized (Figs. 3a and 3b). This lesion collided intimately with a seborrheic keratosis. The borders were non-tumoral. The patient had no recurrence after the excision on two years of follow-up.

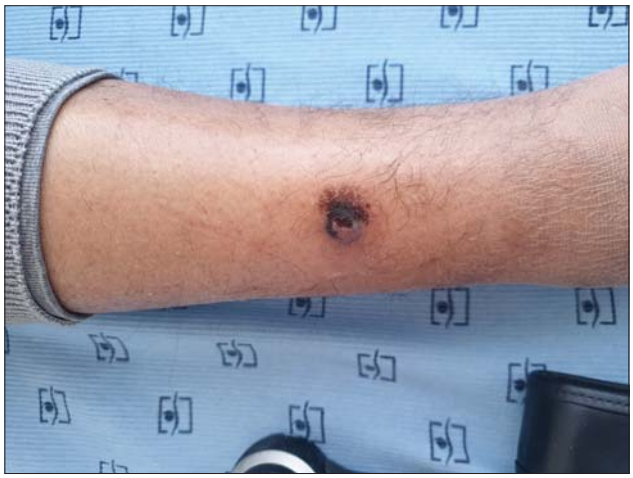


Figure 1: Pigmented nodule, roughly oval, with irregular contours surrounded by an epidermal collar, 2 cm in length, located on the external aspect of the right leg.

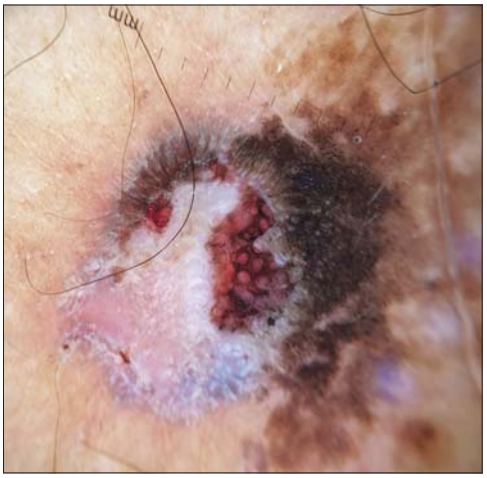


Figure 2: Dermoscopic image showing well-circumscribed, milky-red areas surrounded by brownish interlacing (frog's egg appearance), poorly visualized vascular structures within, bright, whitish streaks in places, with grayish-white areas without structure, blackish dots and globules. This aspect was in collision with a homogeneous, brownish structure with a coral-like appearance and mordant borders, dotted by some homogeneous, brownish globules.

DISCUSSION

Eccrine poroma (EP) is a relatively common benign adnexal tumor that accounts for 10% of all sweat gland tumors. EP usually occurs on the soles and lateral surfaces of the feet, which are the sites of a higher concentration of eccrine sweat glands, yet it may also be found on other anatomical sites. It appears more frequently in adults between the fourth and sixth decade of life. Its pathogenesis is unknown, yet may be related to trauma, radiation, or scarring [4].

The pigmented variant of EP often consists of a firm, pigmented nodule with a smooth or keratotic surface, sometimes slightly pedunculated, up to 2 cm in diameter [4,5]. It is frequently confused clinically with seborrheic keratosis, epithelialized pyogenic granuloma, pigmented basal cell carcinoma (BCC), squamous cell carcinoma (SCC), angiofibroma, and cutaneous melanoma [4-6].

Pigmented EP appears to be more common in darker phototypes and in non-acral locations. Indeed, it has been suggested that melanocytes in the palmar and plantar regions show reduced migration, proliferation, and survival activity [7]. Histologically and immunohistochemically, it has been observed that the expression of melanocyte-stimulating factors by tumor cells is associated with melanocyte colonization only by non-acral pigmented poromas [6].

Some articles describe the dermoscopic features of pigmented PE. As the number of published articles is

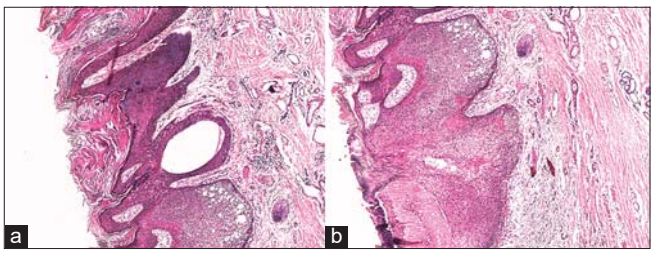


Figure 3: (a) Endophytic, intraepidermal proliferation with large basaloid cell tracts and thick columns extending and anastomosing into the reticular dermis. The proliferation was rich in melanin pigments with dilated ductal structures. The stroma was fibrous and richly vascularized. (b) Transition zone between poroma at the bottom and seborrheic keratosis at the top.

small, specific indices or patterns of non-pigmented PEs have not been established [4,8].

The main dermoscopic clues described in the literature of non-pigmented PE are the following: white, intertwining areas around vessels, areas without a pinkish-white structure, vascular structures composed of irregular glomerular or calyx vessels, hairpin vessels, irregular vessels, and branched vessels with rounded ends [9].

More recently, it has been shown that pigmented eccrine poroma may mimic several benign and malignant tumors also from a dermoscopic point of view [6-9]. Ovoid nests and bluish-gray dots were observed, in addition to tree-like vascular structures. a bluish-white central spot, which may occur in hairpin vessel melanoma in keratinized forms mimicking SKs [10]. In our case, the milky-red lagoons separated by brownish, intertwining, and poorly visualized vascular structures within it made us suspect pigmented eccrine poroma. These structures collided dermoscopically with a clear dermoscopic pattern of seborrheic keratosis with its well-demarcated appearance of bitten borders and coral-like fingerprints. The first diagnosis evoked in our case was pigmented eccrine poroma in collision with a KS, the histopathological study had confirmed our diagnosis.

Dermatopathologically it is a proliferation originating from the lower part of the epidermis from where it extends into the dermis forming large banded anastomoses, composed of epithelial cells of cuboidal appearance connected by intercellular bridges [9-11]. It has been observed that deeper tumors resembled pigmented BCC to a greater extent and that those with hyperkeratosis were similar to KS [10,11]. In our reported case, the grayish-white areas were consistent with hyperkeratosis. The black dots and globules were equivalent to aggregates of melanin pigments intra-epidermally and within the basaloid cells. The bluish-red lacunae were swollen dermal papillae and dilated vascular spaces in the papillary dermis. The brownish intertwining corresponded to the large, tongue-like trabeculae and columns arising from endophytic proliferation from the dermal–epidermal interface extending and anastomosing into the dermis. The whitish streaks corresponded to dermal lamellar fibroplasia [12].

The characteristic feature described was well-circumscribed, reddish lacunae with separation of the mesh bands, reminiscent of frog egg aggregates. This characteristic feature on dermoscopy was explained by the histopathological features observed in the horizontal sections: island-like, edematous stroma containing numerous microvessels embedded in a mass of melanin, pigment-rich poroid cells in a mesh-like pattern forming columns, realizing dermal and dermo-epidermal anastomoses.

The diagnosis of eccrine poroma is routinely reached by histopathology. Because of the diversity of findings, the surgical removal of the lesion is always recommended [7,12].

CONCLUSION

Although the diagnosis of eccrine poroma remains histopathologic, we highlight the role of dermoscopy as a non-invasive means in the diagnosis of poromas as well as its crucial usefulness in the suspicion of a collision with another distinct lesion.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Elboukhari K, El Kadiri S, Benkirane S, Mernissi FZ. Adnexal benign tumor with deroupting dermoscopy. Our Dermatol Online. 2020;11:e87.1-2.
2. Bloom BS, Kamino H, Hale CS, Pomeranz MK. Collision tumor of eccrine poroma, seborrheic keratosis, and a viral wart. Dermatol Online J. 2014;20:13030.
3. Chessa MA, Patrizi A, Baraldi C, Fanti PA, Barisani A, Vaccari S. Dermoscopic-histopathological correlation of eccrine poroma: An observational study. Dermatol Pract Concept. 2019;9:283-91.
4. Bombonato C, Piana S, Moscarella E, Lallas A, Argenziano G, Longo C. Pigmented eccrine poroma: Dermoscopic and confocal features. Dermatol Pract Concept. 2016;6:59-62.
5. Espinosa AE, Ortega BC, Venegas RQ, Ramírez RG. Dermoscopy of non-pigmented eccrine poromas: Study of Mexican cases. Dermatol Pract Concept. 2013;3:25-8.
6. Almeida FC, Cavalcanti SM, Medeiros AC, Teixeira MA. Pigmented eccrine poroma: Report of an atypical case with the use of dermoscopy. An Bras Dermatol. 2013;88:803-6.
7. Lallas A, Chellini PR, Guimarães MG, Cordeiro N, Apalla Z, Longo C, et al. Eccrine poroma: The great dermoscopic imitator. J Eur Acad Dermatol Venereol. 2016;30:e61-3.
8. Marchetti MA, Marino ML, Virmani P, Dusza SW, Marghoob AA,

Nazzaro G, et al. Dermoscopic features and patterns of poromas: A multicentre observational case-control study conducted by the International Dermoscopy Society. J Eur Acad Dermatol Venereol. 2018;32:1263-71.
9. Takada T. Diagnostic features of a non-pigmented eccrine poroma with a collarette: Histopathological and dermoscopic correlation. Clin Case Rep. 2021;9:1601-4.
10. Chong Y, Song D-H, Jang K-T, Park KH, Lee EJ. Concurrent occurrence of seborrheic keratosis and melanocytic nevus in the same lesion. Our Dermatol Online. 2014;5:179-82.
11. Zaballos P, Gómez-Martín I, Martin JM, Bañuls J. Dermoscopy of adnexal tumors. Dermatol Clin. 2018;36:397-412.
12. Rafiei R, Eftekhari H, Daryakar A, Nickhah N, Rafiee B. Eccrine porocarcinoma: A case report and brief review of the literature. Our Dermatol Online. 2016;7:391-3.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Report

Giant squamous cell carcinoma in a patient with epidermodysplasia verruciformis

Uzair Khursheed Dar, Yasmeen Jabeen Bhat, Shuhaab Ahmad Shah

Department of Dermatology, Venereology and Leprosy, Govt. Medical College Srinagar, J & K, India

Corresponding author: Uzair Khursheed Dar, MD, E-mail: uxairkhursheed@gmail.com

ABSTRACT

Epidermodysplasia verruciformis is an autosomal recessive skin disease usually presenting as multiple flat warts and pityriasis versicolor-like macules in early youth, possessing a great risk of developing skin cancer due to a lack of defense against beta HPV. Herein, we report the case of a 29-year-old female, a known case of EV, who presented with a verrucous growth on the forehead persistent for the previous one year. While clinical and dermoscopic examinations led to the suspicion of squamous cell carcinoma, it was confirmed by histopathological examination following a skin biopsy.

Key words: Epidermodysplasia verruciformis; SCC; Dermoscopy

INTRODUCTION

Epidermodysplasia verruciformis (EV) is a rare autosomal recessive genodermatosis that usually presents in early childhood as verrucous papules and plaques resembling pityriasis versicolor, verruca plana, or seborrheic keratosis, most commonly on the skin of the head, neck, and upper extremities, characterized by widespread infection with specific strains of human papillomavirus (beta HPV) [1]. There is a lack of defense against beta HPV in these individuals, which increases the likelihood of developing non-melanoma skin cancers, most commonly squamous cell carcinoma in these individuals [2]. These patients, therefore, serve as models for studying susceptibility to beta HPV and its carcinogenesis.

CASE REPORT

A 29-year-old female patient (Fitzpatrick skin type IV), normotensive, non-diabetic, belonging to a rural area, a diagnosed case of epidermodysplasia verruciformis with consanguinity in the parents' marriage (first degree) and the absence of such a condition in other family members, reported with a verrucous growth (5 × 6 cm) on the center of the forehead and multiple crusted plaques and ulcerations bilaterally on the forehead present for the last one year, which began as a small plaque on the pre-existing lesions of epidermodysplasia verruciformis one year previously and progressed to involve the central part of the forehead, with a rapid increase in size and pus discharge (Figs. 1a and 1b). The swelling was well-defined, firm, and not attached to the underlying structures. Diffuse swelling with crusted plaques was observed around the bilateral periorbital areas and the nasal bridge. An examination of other body areas revealed multiple seborrheic keratosis-like lesions on the face and neck. A general physical and system examinations were normal. The cervical lymph nodes were uninvolved. Hematological and biochemical investigations were within the normal limits.

Dermoscopy of the growth revealed multiple structureless, milky-white areas, yellowish, homogeneous areas, hemorrhages, and erosions on background erythema with short, linear, and polymorphic vessels (Fig. 2). An incisional biopsy taken from the lesion revealed poorly differentiated squamous cell carcinoma. The lesion was surgically excised followed by radiotherapy.

How to cite this article: Dar UK, Bhat YJ, Shah SA. Giant squamous cell carcinoma in a patient with epidermodysplasia verruciformis. Our Dermatol Online. 2023;14(1):85-87.

Submission: 08.06.2022; **Acceptance:** 30.08.2022

DOI: 10.7241/ourd.20231.18

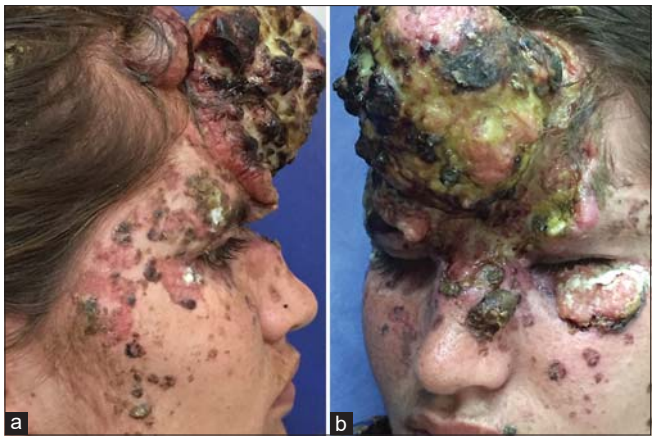


Figure 1: (a and b) Clinical image revealing a verrucous growth in the center and multiple crusted plaques and ulcerations bilaterally on the forehead in a patient with EV.

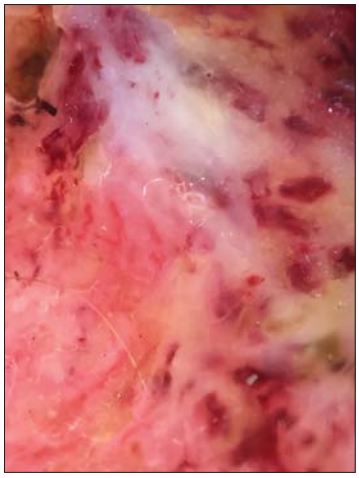


Figure 2: Dermoscopic image revealing multiple structureless, milky-white areas, yellowish, homogeneous areas, hemorrhages, and erosions on background erythema with short, linear, and polymorphic vessels, suggestive of SCC.

DISCUSSION

The clinical manifestations of EV begin in childhood, and up to 60% of patients with EV develop non-melanoma skin cancer, mainly squamous cell carcinoma (SCC) [3,4]. Such a skin cancer occurs usually in the fourth or fifth decade of life and is localized mainly in sun-exposed areas, indicating an important role of environmental factors, notably UV irradiation [5,6].

Beta HPV has a potential role in developing skin cancer in immunocompromised patients yet causes mainly unapparent skin infections in immunocompetent individuals, with types 5 and 8 being particularly more common forms in EV [7,8]. The inherited form of EV, which is caused by a mutation in TMC6/EVER1 or TMC8/EVER2 has a defect in the ability to mount an immune response to certain HPV types in keratinocytes [9]. However, there are normal immune capabilities against other infectious pathogens. The beta HPV types identified in patients with EV who develop skin malignancies are found throughout the general population. In persons without the EVER mutations or EV, these HPV types have not been shown to produce dysplasia or malignancy [10]. Patients with EV cannot appropriately control beta HPV replication and, therefore, have a strong antibody response against a broad variety of beta HPV types [11].

CONCLUSION

Patients with epidermodysplasia verruciformis are at a high risk of developing non-melanoma skin cancers, thus proper counseling and follow-up are needed for the timely management of dysplastic changes in any existing lesions. HPV is the viral agent clearly associated with the malignant transformation of cells.

CONSENT

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Fox SH, Elston DM. Epidermodysplasia verruciformis and the risk for malignancy. Cutis. 2016;98:E10-2.
2. Arnold AW, Burger B, Kump E, Rufle A, Tyring SK, Kempf W, et al. Homozygosity for the c.917A–>T (p.N306I) polymorphism in the EVER2/TMC8 gene of two sisters with epidermodysplasia verruciformis Lewandowsky-Lutz originally described by Wilhelm Lutz. Dermatology 2011;222:81-6.
3. Patel T, Morrison K, Rady P, Tyring S. Epidermodysplasia verruciformis and susceptibility to HPV. Dis Markers. 2010;29:199-206.
4. Hultgren TL, Srinivasan SK, DiMaio DJ. Epidermodysplasia verruciformis occurring in a patient with human immunodeficiency virus: A case report. Cutis. 2007;79:308-11.
5. Gewirtzman A, Bartlett B, Tyring S. Epidermodysplasia verruciformis and human papilloma virus. Curr Opin Infect Dis. 2008;21:141-6.
6. Orth G. Genetics of epidermodysplasia verruciformis: Insights into host defense against papillomaviruses. Semin Immunol. 2006;18:362-74.
7. Arnold AW, Hofbauer GF. Human papillomavirus and squamous cell cancer of the skin: Epidermodysplasia verruciformis-associated human papillomavirus revisited. Curr Probl Dermatol. 2012;43:49-56.

8. Lazarczyk M, Cassonnet P, Pons C, Jacob Y, Favre M. The ever proteins as a natural barrier against papillomaviruses: A new insight into the pathogenesis of human papillomavirus infections. Microbiol Mol Biol Rev. 2009;73:348-70.
9. Ramoz N, Rueda LA, Bouadjar B, Montoya LS, Orth G, Favre M. Mutations in two adjacent novel genes are associated with epidermodysplasia verruciformis. Nat Genet. 2002;32:579-81.
10. de Jong SJ, Imahorn E, Itin P, Uitto J, Orth G, Jouanguy E, et al. Epidermodysplasia verruciformis: Inborn errors of immunity to human beta-papillomaviruses. Front Microbiol. 2018;9:1222.
11. Dell'Oste V, Azzimonti B, De Andrea M, Mondini M, Zavattaro E, Leigheb G, et al. High beta-HPV DNA loads and strong seroreactivity are present in epidermodysplasia verruciformis. J Invest Dermatol. 2009;129:1026-34.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Report

Bardet–Biedl syndrome: Case report from a tertiary-care hospital in Srinagar, India

Saika Reyaz, Fozia Rehman, Shagufta Rather, Sheikh Javeed Sultan

Department of Dermatology, Venereology & Leprosy, Government Medical College Srinagar, Karan Nagar, Jammu and Kashmir, India

Corresponding author: Fozia Rehman, MD, E-mail: drfoziarehman16@gmail.com

ABSTRACT

Bardet–Biedl syndrome (BBS) is a rare autosomal recessive ciliopathic disorder affecting multiple organ systems. The main clinical features are marked central obesity, retinal dystrophy, polydactyly, mental retardation, hypogonadism, and renal dysfunction. It affects both males and females. Herein, we report an interesting case of BBS with features of the BBS yet without cone-rod dystrophy, which is considered one of the hallmark features of this condition. To the best of our knowledge, this is the first report of Bardet–Biedl syndrome with the absence of cone-rod dystrophy and a normal fundus examination on the Indian subcontinent.

Key words: Bardet–Biedl syndrome; Ciliopathic disorder; Polydactyly

INTRODUCTION

Bardet–Biedl syndrome (BBS) is a rare autosomal recessive ciliopathic disorder, first described by Bardet and Biedl in 1920, characterized principally by marked central obesity, retinal dystrophy, polydactyly, mental retardation, hypogonadism, and renal dysfunction [1]. Its frequency varies from country to country, the incidence being much higher in some populations with a high level of consanguinity or those geographically isolated, with a disease incidence of 1 in 13,000 in the isolated populations of Newfoundland and Kuwait, 1 in 17,000 live births [2]. Mutations in at least 21 BBS genes have been recognized as causative factors [3]. Herein, we report an interesting case of BBS presenting to the dermatology outpatient with hypogenitalism and features such as marked central obesity, acanthosis nigricans, polydactyly, and mental retardation, yet with the absence of cone-rod dystrophy, hence the relevance of reporting this case with the absence of the hallmark feature.

CASE REPORT

A ten-year-old boy was reported to the skin outpatient department with complaints of asymptomatic darkening and thickening of the neck and both axillae, excessive weight gain, and underdevelopment of the genital organs. His mother revealed that he began to gain excessive weight since the age of five years. His background problems included diminished vision in both eyes. Regarding the birth history, he was second in birth order, born out of a second-degree, consanguineous marriage through normal vaginal delivery at full-term without complications. According to the mother, he had delayed motor and developmental milestones, with the commencement of walking and speech at the age of three and five, respectively. He was enrolled in a school by his parents yet, due to difficulty in learning, withdrew. There was a history of the death of one of the older male siblings soon after birth due to an unknown reason.

A physical examination revealed a rounded face with retrognathia, a high-arched palate, bilateral gynecomastia, and a protuberant abdomen (Fig. 1).

How to cite this article: Reyaz S, Rehman F, Rather S, Sultan SJ. Bardet–Biedl syndrome: Case report from a tertiary-care hospital in Srinagar, India. Our Dermatol Online. 2023;14(1):88-91.

Submission: 31.07.2022; **Acceptance:** 01.09.2022

DOI: 10.7241/ourd.20231.19

Figure 1: Ten-year-old boy with a rounded face, retrognathia, gynecomastia, central obesity, and underdeveloped genitalia.

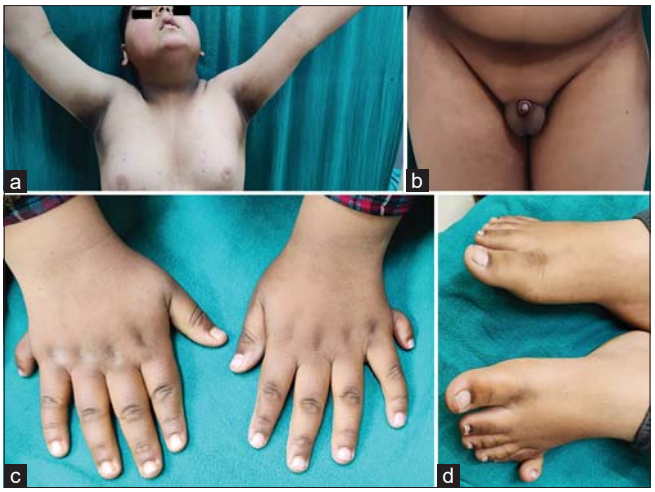


Figure 2: (a) Acanthosis nigricans in both axilla and neck regions. (b) Hypogonadism with a micropenis. (c) Polydactyly with hexadactyly of the hands (d) Hexadactyly of the right foot.

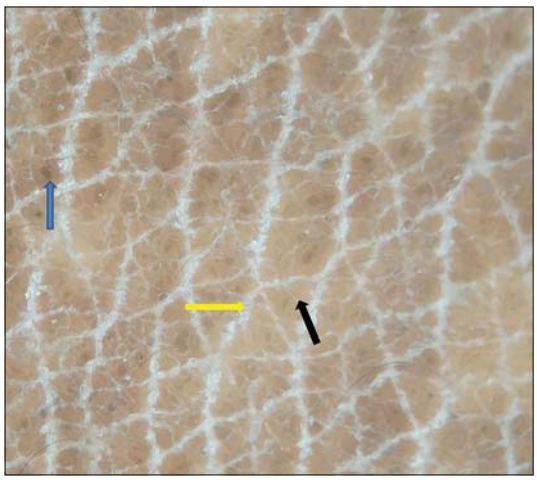


Figure 3: Dermoscopic image of acanthosis nigricans on the neck (DermLite; DL4; 10×) showing brown dots (blue arrow), linear crista cutis, and sulci cutis (yellow and black arrow, respectively) against a dark brown background.

The height and weight were 135 cm and 65 kg, respectively, with a resultant body mass index of 36, which indicated severe obesity according to the revised consensus guidelines for India [4]. Blood pressure and the pulse rate were 110/70 millimeters of mercury and 88 per minute, respectively. Acanthosis nigricans was present in the axillary and neck regions (Fig. 2a).

Dermoscopy of acanthosis nigricans in the neck region was performed, which demonstrated the presence of crista cutis and sulci cutis on a diffuse, dark brown background (Fig. 3).

Microtestis with a testicular volume of 1.5 mL (normal: 10–12 mL) as documented by ultrasonography and microphallus (< 2.5 cm) were observed (Fig. 2b).

Extra-axial-polydactyly was present in both upper limbs and the right foot with a normal digit number on the left foot (Figs. 2c and 2d).

A psychiatric consultation revealed that his mental development lagged behind the normal range, with an IQ below seventy.

On the ophthalmological examination, visual acuity was 18/36 in both eyes. However, a fundus examination was normal.

A neurological examination and auditory assessment were found to be normal.

Laboratory investigations, including a hemogram, liver function tests, renal function tests, urine analysis,

chest X-ray, electrocardiogram, and echocardiogram were normal. Ultrasound revealed grade-2 fatty liver disease. A fasting lipid profile revealed an increased level of triglycerides (TG)—200 mg/dL (normal: 32–100 mg/dL)—and a decreased level of high density lipoprotein (HDL)—24 mg/dL (normal for males: 40 mg/dL). Serum cortisol levels were normal. Genetic analysis was not conducted as it was not available in our hospital.

We diagnosed the case as BBS as our patient met four primary clinical features along with two secondary features based on the diagnostic criteria described below (Table 1).

As there is no definitive treatment for BBS, we counseled the child's parents about the genetic basis of the disease. We advised our patient to increase physical activity in the form of regular walks for thirty minutes a day at least four times per week, and a weight-reducing diet was advised as per the dietician's recommendations. Spectacles were advised by ophthalmology for low vision. The patient was advised to return for regular follow-up to observe any progressive ophthalmological changes and for behavioral therapy.

DISCUSSION

Bardet–Biedl syndrome is a rare autosomal recessive ciliopathic disorder named after George Louis Bardet, a French physician, and Arthur Biedl, a Hungarian pathologist and endocrinologist. There was a debate in the medical literature regarding the condition reported by Lawrence and Moon in 1886, referred to as Laurence–Moon syndrome (LMS). Laurence–Moon–Bardet–Biedl syndrome (LMBBS) is an abandoned term as patients with Laurence–Moon presented with spastic paraplegia with no polydactyly and obesity, which are the primary features of BBS. Hence, BBS and LMS are regarded as separate entities.

Table 1: Diagnostic criteria of BBS [1]

PRIMARY FEATURES	SECONDARY FEATURES
Cone-rod dystrophy (90–100%)	Speech delay (54–81%)
Obesity (72–92%)	Developmental delay (50–99%)
Polydactyly (63–81%)	Brachydactyly/syndactyly (46–100%)
Genital anomalies (59–98%)	Ataxia/poor coordination (40–86%)
Learning difficulties (50–61%)	Diabetes mellitus (6–48%)
Renal anomalies (20–53%)	Dental anomalies (51%)
	Anosmia/hyposmia (60%)
	Deafness (11–12%)
	Congenital heart disease (7%)
	Hepatic fibrosis
	Mild spasticity
	Strabismus/cataracts/astigmatism

The underlying pathology of BBS remains unclear. The basic reason for this pleiotropic disease originates from cilia dysfunction. Hence, the condition falls under the spectrum of "ciliopathies" [5]. Mutations in 21 BBS genes (BBS1–BBS20 and NPHP1) have been cloned, all of these genes having a relationship with cilia biogenesis or function [3].

According to these criteria, four primary or three primary and two secondary criteria are sufficient for the diagnosis. Four primary and two secondary features were present in our patient (shown in bold), thus fulfilling the diagnostic criteria of BBS.

The presence of cone-rod dystrophy is one of the hallmark clinical features of BBS. Decreased vision has been reported in the first decades of life in patients with BBS, as was in our case, with the majority legally blind (best corrected visual acuity < 6/60) by the second or the third decade of life [6].

Obesity is another cardinal feature in BBS, with a prevalence of 72–92%. The cause of obesity is 1) the deregulation of appetite; 2) impaired leptin receptor signaling; 3) a reduced number of cilia due to BBS gene mutations [7]. Obesity is usually noticed by parents within the first ten years of life in comparison to other children and playmates of similar age.

Limb anomalies such as polydactyly and syndactyly are seen since birth, thus providing a useful diagnostic clue for BBS as 63–81% of patients manifest the same [5].

Hypogonadism manifests as hypogenitalism in males and genital anomalies in females, with a delayed onset of puberty in both sexes. A small penis buried in the adipose tissue and a decreased testis volume are often seen in male patients.

Around 44% of cases with BBS have a learning disability, with an IQ level of 79 or below.

Renal anomalies seen in BBS include structural anomalies, hydronephrosis, vesicoureteral reflux, and progressive renal parenchymal disease, which is commonly associated with urinary concentration defects [8]. Chronic kidney disease (CKD) is a major contributor of morbidity and mortality in individuals with BBS.

An effective multidisciplinary approach is required to manage this pleiotropic condition. There should be an awareness of complications, for which BBS has laid the base and patients should be followed up in this respect. Both a proper diet (low in calories, low in protein), exercise programs, periodic vision evaluation, and up-to-date changing of their prescription lenses should be encouraged.

CONCLUSION

Bardet–Biedl syndrome is an autosomal recessive inherited disorder with wide variability in expression and a disease of genetic complexity. To the best of our knowledge, this is the first report of Bardet–Biedl syndrome with the absence of cone-rod dystrophy and a normal fundus examination on the Indian subcontinent. A timely and thorough management plan by a multidisciplinary team should allow these children to integrate better into society and thrive fully. Furthermore, both parents should undergo genetic counseling, especially those with a history of consanguineous marriages in the family.

CONSENT

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Beales PL,Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet–Biedl syndrome: Results of a population survey. J Med Genet. 1999;36:437-46.
2. Moore SJ, Green JS, Fan Y, Bhogal AK, Dicks E, Fernandez BA, et al. Clinical and genetic epidemiology of Bardet–Biedl syndrome in Newfoundland: A 22-year prospective, population-based, cohort study. Am J Med Genet.2005;132:352-6.
3. Suspitsin EN, Imyanitov EN. Bardet–Beidl syndrome. Molecular Syndromol.2016;7:6271.
4. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al; Concensus Group. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India. 2009;57:163-70.
5. E. Forsythe E, Beales P.L, Bardet–Biedl syndrome. Eur J Hum Genet.2013;21:8-13.
6. Mockel A, Perdomo Y, Stutzmann F, Letsch J, Marion V, Dollfus H. Retinal dystrophy in Bardet–Biedl syndrome and related syndromicciliopathies. Prog Retin Eye Res. 2011;30:258-74.
7. Guo DF, Rahmouni K. Molecular basis of the obesity associated with Bardet–Biedl syndrome. Trends Endocrinol Metab. 2011;22:286-93.
8. Putoux A, Attie-Bitach T, Martinovic J, Gubler M-C. Phenotypic variability of Bardet–Biedl syndrome: Focusing on the kidney. Paediatr Nephrol.2012;27:7-15.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Report

DRESS syndrome with carbamazepine and Epstein–Barr virus reactivation

Sokaina Chhiti, Zakia Douhi, Imane Kacimi Alaoui, Sara Elloudi, Hanane Baybay, Fatima Zahra Mernissi

Department of Dermatology, University Hospital Hassan II Fez, Morocco

Corresponding author: Sokaina Chhiti, MD, E-mail: sokaina.chhiti@usmba.ac.ma

ABSTRACT

DRESS syndrome is a serious toxidermia, most often caused by anticonvulsants, including carbamazepine, which is responsible for a formidable clinical picture and which may be accompanied by viral reactivations, in particular of the herpes group. Herein, we report the case of a young girl affected by DRESS syndrome with the reactivation of EBV, in whom the evolution was favorable. Recurrent EBV infection is demonstrated by the presence of IgM antibodies to anti-EBV early antigen and IgG antibodies to anti-EBV nuclear antigen. Its pathogenesis suggests that viral reactivation is the consequence of a T-immune response directed against the causative drug in some patients. It is an unpredictable entity requiring immediate treatment, namely stopping the drug in question, monitoring the patient, searching for viral reactivation and notifying pharmacovigilance.

Key words: Dress syndrom, carbamazepine, EBV, rash, reactivation

INTRODUCTION

DRESS syndrome (*drug reaction with eosinophilia and systemic symptoms*) is a serious drug eruption most commonly associated with carbamazepine and other drugs. Its pathophysiology has been clarified by the demonstration of reactivations of herpes viruses. It has been postulated that virus infection may play a role in the development of this syndrome. Herein, we report carbamazepine-induced hypersensitivity syndrome with Epstein–Barr virus (EBV) infection in a nineteen-year-old girl with a favorable evolution.

CASE REPORT

A nineteen-year-old girl was hospitalized for diffuse pruritic erythematous rash with facial edema progressing one month after taking carbamazepine for an epileptic seizure. An examination found a febrile patient with diffuse maculopapular rash with facial erythro-edema (Fig. 1a and 1b) associated with a declining purpura. A blood test revealed hepatic cytolysis and eosinophilia. A skin biopsy revealed an inflammatory infiltrate rich in neutrophils and eosinophils. A pharmacovigilance declaration incriminated carbamazepine. The patient was put on topical corticosteroid with the discontinuation of the drug. Two days later, she presented a fever at 39.5°C with otitis put on amoxicillin, worsening of the rash, the appearance of basophilia with monocytosis, worsening of cytolysis hepatic, negative blood culture, negative CMV serology, positive MNI test, and positive EBV serology. Viral hepatitis serologies were negative. The patient was put on antihistamines and a topical corticosteroid, and amoxicillin was withdrawn, with good clinical and biological improvement. After one week the otitis was treated with amoxicillin without any complications or reactions.

DISCUSSION

DRESS syndrome, initially described by Bocquet et al. [1], is an acute and severe drug eruption that

How to cite this article: Chhiti S, Douhi Z, Alaoui IK, Elloudi S, Baybay H, Mernissi FZ. DRESS syndrome with carbamazepine and Epstein–Barr virus reactivation. Our Dermatol Online. 2023;14(1):92-94.

Submission: 20.08.2022; **Acceptance:** 01.10.2022

DOI: 10.7241/ourd.20231.20

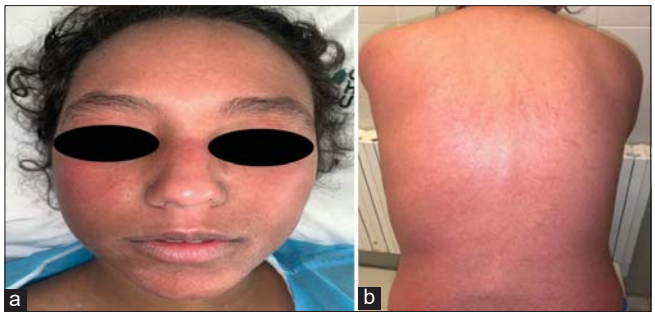


Figure 1: (a) Facial erythredema with desquamation.(b) Diffuse maculopapular rash on the body.

may be life-threatening [2]. The diagnosis is now well known and is based on a set of arguments associating, in a variable way, a generalized rash resembling a maculopapular exanthema, fever, periorbital facial edema, bilateral superficial polyadenopathy, hyperleukocytosis, blood hypereosinophilia, and multi-visceral failure, including the liver, kidney and lungs [2,3]. Recently, its physiopathology has been clarified by the demonstration of reactivations of herpes viruses, including Epstein–Barr virus (EBV), as well as cytomegalovirus (CMV) [4], human herpes virus-6 (HHV-6), and human herpes virus-7 (HHV7) [5-6], which explains the seriousness of the clinical manifestations, in particular, the systemic attacks, as well as the biological modifications of DRESS syndrome [7].

In our case, the delay, the clinical and biological data, the viral reactivation of EBV, and the aggravation by amoxicillin were in favor of DRESS syndrome with carbamazepine and EBV reactivation. In our patient, the reintroduction of amoxicillin did not modify the evolution of clinical or biological data. This is why it is necessary to know how to distinguish between a simple cutaneous reaction, infectious mononucleosis, and a true drug eruption with the reactivation of EBV [8].

The pathogenesis of this viral reactivation during this type of toxidermia remains poorly understood [9]. Several arguments exist to consider DRESS syndrome a mainly viral disease induced by a drug on a ground of genetic predisposition not yet determined: a similarity between the clinico-biological picture of DRESS syndrome and infections with herpes viruses, a demonstration viral reactivation, a possible immunomodulatory action of drugs associated with DRESS syndrome, favoring viral reactivation as well as a T-lymphocyte response directed against viral antigens with a T repertoire profile close to that observed in EBV infections. Some authors consider that viral reactivation is the consequence of a T-immune response directed against the causal drug [10].

The management of DRESS syndrome aims to monitor and possibly control the immune response. In some cases, no treatment is necessary while, in other cases, the immune response is deleterious requiring corticosteroid therapy [11].

Amoxicillin may be responsible for DRESS syndrome, yet may especially worsen it in the absence of a previous allergy to betalactamines [12].

CONCLUSION

DRESS syndrome is a rare and unpredictable entity, which is important to be aware of because of its potential seriousness, its progressive risk, and the necessary therapeutic sanction, namely the discontinuation of the drug in question and the search for a viral reactivation. The notification of these cases to the pharmacovigilance centers in addition to helping in identifying the suspected drug allows an inventory of these attacks and contributes to a better understanding of this iatrogenic pathology.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudo-lymphoma and drug hypersensitivity syndrome (drug rash with eosinophilia and systemic symptoms: DRESS. Semin Cutan Med Surg. 1996;15:250-7.
2. Shiohara T, Lijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the basis of typical clinical features and viral reactivations. Br J Dermatol. 2007;156:1083-4.
3. Kardaun SH, Sidoroff A, Valeyrie-Allanore L. Variability in the clinical pattern of cutaneous side effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? Br J Dermatol. 2007;156:609-11.
4. Aihara, M, Sugita, Y, Takahashi, S, Nagatani, T, Arata, S, Takeuchi, K, et al. Anticonvulsant hypersensitivity syndrome associated with reactivation of cytomegalovirus. Br J Dermatol. 2001;144:1231-4.
5. Descamps V, Ben Saïd B, Sassolas B, Avenel-Audrane M. [Management of drug reaction with eosinophilia and systemic symptoms (DRESS)]. Ann Dermatol Venereol. 2010;137:703-8.

6. Eshki M, Allanore L, Musette P. Twelve-year analysis of severe cases of drug reaction with Eosinophilia and systemic symptoms: A cause of severe of unpredictable multiorgan failure. Arch Dermatol. 2009;145:67-72.
7. Shiohara T, Kano Y. A complex interaction between drug allergy and viral infection. Clin Rev Allergy Immunol. 2007;33:124-33.
8. Pullen H, Wright N, Murdoch JM. Hypersensitivity reactions to antibacterial drugs in infectious mononucleosis. Lancet. 1967;ii:1176-8.
9. Descamps, V, Mahe, E, Houhou, N, Abramowitz, L, Rozenberg, F, Ranger-Rogez S, et al. Drug-induced hypersensitivity syndrome associated with Epstein–Barr virus infection. The British journal of dermatology. 2003;1485;1032-4.
10. Descamps V, Mardvirin L, Janela B. Le syndrome d'hypersensibilité (DRESS) n'est qu'une maladie virale. Rev Fr Allergol. 2010;50:171-3.
11. Sellami, W, Mrad, I. B, Hajjej, Z, Gharssallah, H, Labbène, I, Ferjani, M. Syndrome DRESS à la carbamazépine avec réactivation virale à cytomégalovirus. Médecine Intensive Réanimation. 2018;1:86.
12. Sussman S, Devlin V, amp Dimitriades, VR. A teenager with sulfasalazine-associated DRESS syndrome after the introduction of amoxicillin. Clin Pediat. 2017;56:290-1.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Image

Eccrine poroma on the forearm in a child: A rare presentation

Fatima Azzahra El Gaitibi[1], Hind Palamino[1], Kaoutar Znati[2], Laila Berbich[1], Karima Senouci[1]

[1]Department of Dermatology, Mohammed V University in Rabat, Ibn Sina University Hospital, Rabat. Morocco, [2]Department of Histopathology, Mohammed V University in Rabat, Ibn Sina University Hospital, Rabat. Morocco

Corresponding author: Fatima Azzahra El Gaitibi, MD, E-mail: elgaitibi.fatimaazzahra@gmail.com

Eccrine poroma (EP) is a benign adnexal tumor arising from the terminal duct of the sweat gland. It represents 10% of all sweat gland tumors and is most commonly found on the sole or the side of the foot [1]. Herein, we report a case of EP on the right forearm in a child.

A thirteen-year-old female with no past medical history presented with an asymptomatic nodule on the right forearm (Fig. 1). The nodule had gradually increased in size and was not associated with pain, pruritus, or bleeding from the lesion. A physical examination revealed a firm, mobile flesh-colored nodule on the right forearm 7 × 6 mm in size. A dermoscopic examination revealed chalice-like vessels, whitish-pink areas, and yellow structureless areas (Fig. 2). The nodule was completely excised and histopathological findings showed a tumor proliferation connecting to the epidermis, organized on thick, cellular cords and composed of small, cohesive, round cells forming homogeneous layers. These cellular cords were separated by fibrous interstitial tissue, not especially inflammatory, and traversed by regularly distributed capillaries (Figs. 3 and 4). Based on these histological findings, a diagnosis of EP was reached.

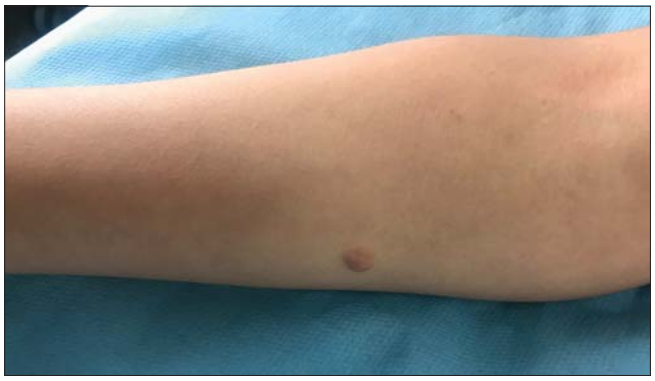


Figure 1: Flesh-colored nodule located on the right forearm.

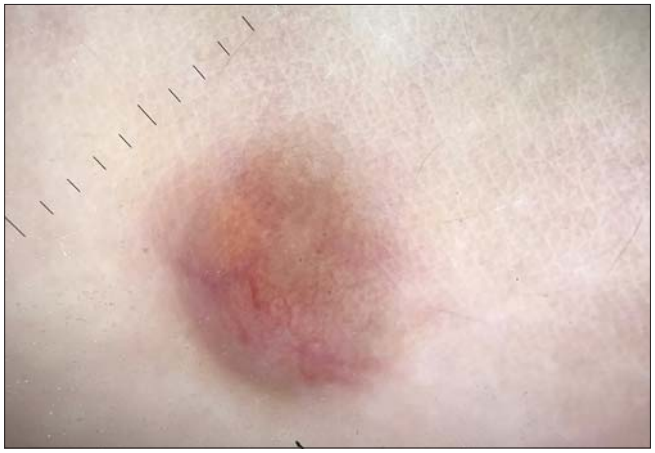


Figure 2: Dermoscopic image revealing chalice-like vessels, whitish-pink areas, and yellow structureless areas.

Although the pathogenesis of EP is unknown, it has been associated with trauma, scarring, and X-ray radiation [2]. EP occurs in middle-aged individuals, with only around ten cases reported in children. EP typically presents as a solitary, asymptomatic papule, nodule, or plaque gradually enlarging, with colors varying from flesh-colored to red, and brown, and bluish. The palm and sole are the most common localizations of this tumor. The main dermoscopic features are vascular structures, a white-to-pink halo

How to cite this article: El Gaitibi FZ, Palamino H, Znati K, Berbich L, Senouci K. Eccrine poroma on the forearm in a child: A rare presentation. Our Dermatol Online. 2023;14(1):95-96.

Submission: 03.03.2021; **Acceptance:** 08.05.2021

DOI: 10.7241/ourd.20231.21

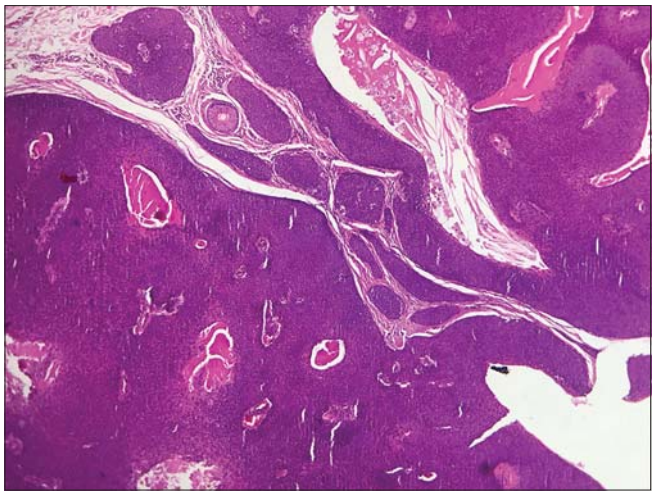


Figure 3: Histological image showing a tumor proliferation connecting to the epidermis, organized on thick, cellular cords separated by fibrous interstitial tissue (H&E, 20×).

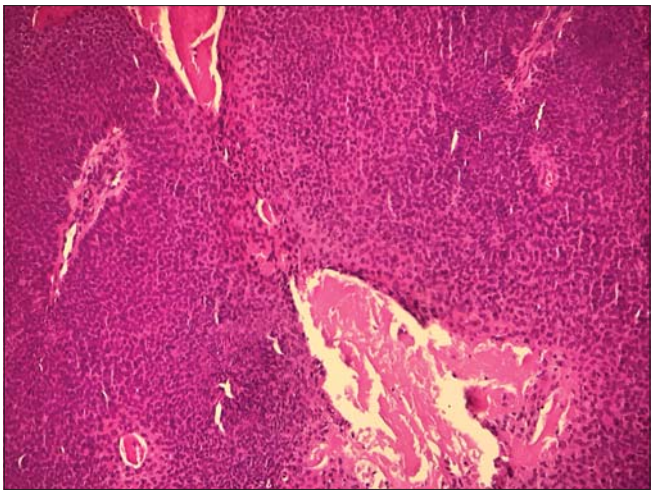


Figure 4: Histological image showing cellular cords composed of small, cohesive, round cells forming homogeneous layers (H&E, 40×).

surrounding vessels, pink-white structureless areas, and yellow structureless areas [2]. Pigmented EP may resemble basal cell carcinoma clinically and dermoscopically. Routinely, the diagnosis is reached by histopathology. Surgical excision is the treatment of choice. EP does not recur after excision. Malignant transformation rarely occurs [3].

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Ahmed jan N, Masood S. Poroma. 2020 Jul 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–.
2. Bombonato C, Piana S, Moscarella E, Lallas A, Argenziano G, Longo C. Pigmented eccrine poroma: Dermoscopic and confocal features. Dermatol Pract Concept. 2016;6:59-62.
3. Mantri MD, Dandale A, Dhurat RS, Ghate S. Pedunculated poroma on forearm: A rare clinical presentation. Indian Dermatol Online J. 2014;5:469-71.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Image

Pearly-white patches reminiscent of juvenile morphea

Sara Kerroum, Nadia Ismaili, Mariame Meziane, Laila Benzekri, Karima Senouci

Department of Dermatology, Mohammed V University in Rabat, Ibn Sina University Hospital, Rabat, Morocco

Corresponding Author: Sara Kerroum, MD, E-mail: kerroums1992@gmail.com

Morphea is a sclerotic condition limited to the skin corresponding to various clinical entities depending on the extension of the lesions, their linear nature, and their depth [1]. It is a relatively rare condition in children. Although almost never life-threatening, it may in some cases be responsible for functional and/or esthetic disability [2] with a major impact on quality of life, hence the importance of its early diagnosis and treatment. Herein, we report the case of juvenile morphea in plaques.

A ten-year-old child with a history of the first-degree consanguinity of the parents and a family atopic condition presented with four oval, hyperpigmented plaques on the thorax with a pearly-white center (Fig. 1), which were sclerotic on palpation. Dermoscopy revealed an appearance resembling a white cloud (Fig. 2). The rest of the clinical examination was unremarkable. Raynaud's phenomenon was absent, the genital tract was intact, and no visceral involvement was noted. A skin biopsy was performed confirming the diagnosis of morphea. The child was treated with dermocorticoids with good evolution.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki. The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

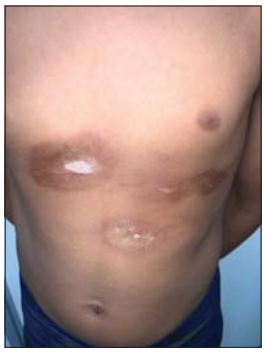


Figure 1: Plaques with a blurred contour and a pearly-white center.

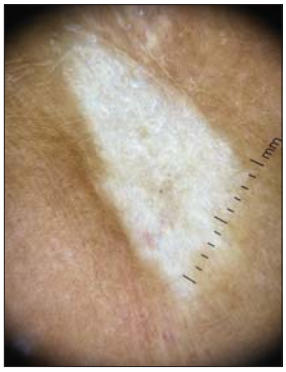


Figure 2: Dermoscopic appearance of a white cloud.

REFERENCES

1. Bono W, Dupin N. [Localized scleroderma (morphea)]. Presse Med. 2006;35:1923-8.
2. Elloudi S, Baybay H, Gallouj S, Mernissi FZ. [Localized scleroderma: About 24 cases]. Pan African Med J. 2017;29:53.

Source of Support: Nil, **Conflict of Interest:** None declared.

How to cite this article: Kerroum S, Ismaili N, Meziane M, Benzekri L, Senouci K. Pearly-white patches reminiscent of juvenile morphea. Our Dermatol Online. 2023;14(1):97.

Submission: 29.05.2022; **Acceptance:** 27.07.2022

DOI: 10.7241/ourd.20231.22

Clinical Image

Intravenous cannula for sterile ear piercing

Shazia Zubair[1], Hamza Ejaz[1], Moizza Tahir[2]

[1]Dermatology Department, City hospital Multan, Pakistan, [2]Combined Military Hospital Military Hospital Gujranwala, Pakistan

Corresponding author: Dr. Shazia Zubair MBBS, MCPS, FCPS, E-mail: mrsshaziazubair@yahoo.com

Ear piercing is highly popular globally. The traditional methods of ear piercing include passing a wire, followed by jewelry, piercing guns, intravenous cannula (18G) employed to pierce the ear lobule [1]. Other methods include the eyelet-type Teflon tube, angiocatheter, magnetic earrings, and a 14- or 16-gauge trocar needle antrum [2]. Other safe options for body piercing include solid gold of 14 or 18 karats, niobium, titanium, and platinum [3]. We feel that the cannula method is effective, as piercing is globally popular and the technique is easy and single staged. We made little modification to the technique, which is convenient and friendly to the patient.

The site was marked on the ear. It was anesthetized with topical lignocaine. A surgical clamp was employed to reduce blood flow to the site pierced. A 16-gauge intravenous cannula was passed from the anterior to posterior direction. After removing the stylet, the head of the cannula was cut with scissors (Figs. 1a and 1b), leaving a plastic tube. The stud was passed directly through the plastic tube (Fig. 1c). The tube was removed and a stopper was attached to the stud. Antiseptic cleaning was performed and topical fusidic acid was applied. The ear piercing technique was shown on a video clip available at the editorial office.

The intravenous cannula is a cheap and sterile solution for body piercing.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

Figure 1: (a and b) Stylet removed and the cannula head cut with scissors. (c) Stud passed through the plastic tube.

How to cite this article: Zubair S, Ejaz H, Tahir M. Intravenous cannula for sterile ear piercing. Our Dermatol Online. 2023;14(1):98-99.

Submission: 26.06.2022; **Acceptance:** 09.10.2022

DOI: 10.7241/ourd.20231.23

REFERENCES

1. Lamba S, Gupta AK. A novel technique for piercing of ear lobule suited to Indian subcontinent. Indian J Plast Surg Plasti Surg. 2013;46:594.
2. Landeck A, Newman N, Breadon JZS. A simple technique for ear piercing. J Am Acad Dermatol. 1998;39:795-6.
3. Martini L, Brzezinski P. A simplest method to avoid inflammation and infection after the insertion of a piercing (even using the safest metal), by using quaternium-15. Our Dermatol Online. 2018;9:393-6.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Image

Anterior cervical hypertrichosis: A rare location

Hanane Chahoub[1], Ibtissam Al Faker[2], Farah Marraha[2], Najlaa Rahmani[2], Younes Benyamna[2], Salim Gallouj[2]

[1]Department of Dermatology University hospital center of Tangier, Tetouan, Al Hoceima, Morroco, [2]Faculty of Medicine and Pharmacy Tangier, Abdelmalek Essaadi University, Tangier, Morocco

Corresponding author: Hanane Chahoubb, MD, E-mail: drchahoubhanane@gmail.com

We report the case of a twelve-year-old male who presented with isolated anterior cervical hypertrichosis persistent since birth. No notion of trauma or local inflammation or the use of a topical treatment was noted. The patient had no other clinical symptoms and no similar family history.

A clinical examination found a tuft of hair, approx. 6 × 3 cm in size, at the level of the mid-neck region, consisting of fine, brown hairs, 3 cm in length (Fig. 1a), with a dermoscopic appearance showing terminal hair and fluffy hair without other associated signs. (Fig. 1b). The rest of the somatic examination was unremarkable. A laser hair removal treatment was offered to the patient with a good response.

Anterior cervical hypertrichosis is a rare form of congenital localized hypertrichosis. To date, around forty cases have been reported worldwide [1]. Clinically, it is characterized by a tuft of terminal hairs located in the anterior cervical region.

It may sometimes be associated with neurological, orthopedic, or ocular abnormalities. The most common association is with motor and sensory neuropathy, followed by hallux valgus, optic atrophy, chorioretinopathy, mental retardation, and localized dorsal hypertrichosis. Familial and sporadic cases have been reported [2].

The management of isolated anterior cervical hypertrichosis is cosmetic. Laser hair removal is the best recommended treatment, with an estimated response of 70% [3].

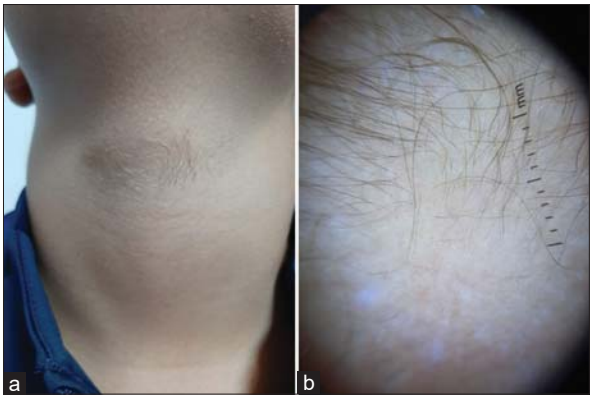


Figure 1: (a) Tuft of hair, 6 × 3 cm in size, at the level of the mid-neck region. (b) Dermoscopy showing terminal hairs measuring 3 cm in length.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Blasco-Morente G, Sánchez-Carpintero I. Isolated Anterior cervical hypertrichosis. Actas Dermosifiliogr. 2017;108:672.
2. Nalluri R, Gilmour E, Brooke R. Anterior cervical hypertrichosis. Eur J Dermatol. 2010;20:393-4.
3. Bostan S, Yaşar Ş, Serdar ZA, Gizlenti S. Anterior cervical hypertrichosis: A sporadic case. Turk Pediatri Ars. 2016;51:49-51.

Source of Support: Nil, **Conflict of Interest:** None declared.

How to cite this article: Chahoub H, Al Faker I, Marraha F, Rahmani N, Benyamna Y, Gallouj S. Anterior cervical hypertrichosis: A rare location. Our Dermatol Online. 2023;14(1):100.

Submission: 13.07.2022; **Acceptance:** 02.10.2022

DOI: 10.7241/ourd.20231.24

Our Dermatology Online

Case Letter

Erythrodermic psoriasis eruption following COVID-19 vaccination

Khadija Oujennane[1,2], Ouafa Hocar[1,2], Said Amal[1,2], Maryem Aboudourib[1,2]

[1]Dermatology Department, CHU Mohammed VI, Marrakech, Morocco, [2]Bioscience and Health Laboratory, FMPM Caddi Ayyad University, Marrakech, Morocco

Corresponding author: Khadija Oujennane, MD, E-mail: khadija.oujennane1@gmail.com

Sir,

Psoriasis is a chronic inflammatory skin condition affecting roughly 2% of the population. Erythrodermic psoriasis (EP) is its rare and severe variant [1]. It is characterized by acute flare-ups induced by various factors, yet some reports have described the onset or flare-up of EP induced by vaccination. To our knowledge, only two such cases following COVID-19 vaccination have been reported. Herein, we report a case of an EP flare-up after COVID-19 vaccination.

A 47-year-old male was referred by our emergency department with diffuse erythema, desquamation, fever, and a poor general condition, arising ten days after the reception of the first dose of the Sinopharm vaccine. He had a history of plaque psoriasis, yet used only topical treatments. He denied any past vaccination-related reaction, recent medication changes, or recent infection. A physical examination revealed diffuse erythema and desquamation on the entire body (Fig. 1a). Initial laboratory investigation revealed hyperglycemia and incidentally discovered diabetes. A COVID-19 PCR test was negative and the peripheral blood smear was normal. He had no history of malignancy and the tumor marker tests were negative. Histopathology was also compatible with erythrodermic psoriasis. He was, thus, diagnosed with the exacerbation of erythrodermic psoriasis associated with the administration of CoronaVac. We commended methotrexate and local treatment with very good improvement (Fig. 1b).

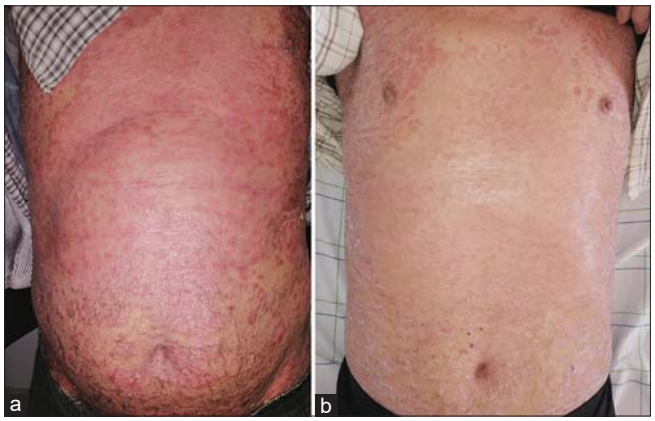


Figure 1: (a) Erythrodermic psoriasis. (b) Improvement after the treatment.

Erythrodermic psoriasis is a rare, chronic, highly inflammatory, and potentially life-threatening variant of psoriasis. Its acute flare-ups are associated with significant morbidity and mortality if not adequately treated. The onset or flare-up of EP is frequently induced by infection, pregnancy, and medications, including systemic corticosteroids. However, flare-ups induced by vaccination are highly rare. Reports of COVID-19 vaccines associated with the exacerbation of psoriasis have emerged. In an international registry of 414 individuals with cutaneous reactions after Pfizer–BioNTech and Moderna vaccines, two patients experienced the exacerbation of psoriasis [2].

To date, four case reports of patients with psoriatic erythroderma and COVID-19 infection have been published [3]. Onsun et al. reported the case of a 72-year-old patient with psoriasis who had developed a flare of generalized pustular psoriasis after the administration of CoronoVac (Sinopharm).

How to cite this article: Oujennane K, Hocar O, Amal S, Aboudourib M. Erythrodermic psoriasis eruption following COVID-19 vaccination. Our Dermatol Online. 2023;14(1):101-102.

Submission: 05.06.2022; **Acceptance:** 16.10.2022

DOI: 10.7241/ourd.20231.25

Recently, Erick Daniel et al. have reported the acute exacerbation of erythrodermic psoriasis one week after the administration of the second dose of the Pfizer COVID-19 vaccine in a 58-year-old male [3].

Our patient had not recently changed his medication and the interval from vaccination to the onset of the disease was relatively long (ten days).

To the best of our knowledge, this is the second reported case of *de novo* EP following the first dose of the Sinopharm COVID-19 vaccine and the third case after COVID-19 vaccine in general. We believe it is important to be aware of potential adverse side effects implicated by COVID-19 vaccinations and to enquire about any recent vaccinations in a patient with a new onset or flare-up of a skin disease.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Singh RK, Lee KM, Ucmak D, Brodsky M, Atanelov Z, Farahnik B, et al. Erythrodermic psoriasis: Pathophysiology and current treatment perspectives. Psoriasis (Auckl). 2016;6:93-104.
2. Huang YW, Tsai TF. Exacerbation of psoriasis following COVID-19 vaccination: Report from a single center. Front Med (Lausanne). 2021;8:812010.
3. Lopez ED, Javed N, Upadhyay S, Shekhar R, Sheikh AB. Acute exacerbation of psoriasis after COVID-19 Pfizer vaccination. Proc (Bayl Univ Med Cent). 2021;35:199-201.

Source of Support: Nil, **Conflict of Interest:** All authors declare no conflicts of interest

Our Dermatology Online

Research Letter

Cutaneous manifestations associated with COVID-19 in 24 cases from Fez, Morocco

Sokaina Chhiti, Hanane Baybay, Fatima Zahra Hashas, Zakia Douhi, Sara Elloudi, Fatima Zahra Mernissi

Department of Dermatology, University Hospital Hassan II Fès, Morocco

Corresponding author: Sokaina Chhiti, MD, E-mail: sokaina.chhiti@usmba.ac.ma

Sir,

Various cutaneous manifestations occurring during SARS- CoV-2 infection have been reported since March 2020. Their exact incidence remains to be estimated, their pathophysiological mechanisms are largely unknown, and the role of SARS-CoV-2 in their pathogenesis—direct or indirect—is still being debated.

This was a prospective study conducted since the beginning of the pandemic including 24 patients with cutaneous manifestations associated with COVID-19.

The diagnosis of COVID-19 was confirmed (by RT-PCR and/or positive serology) in 23 cases. One case was negative for COVID-19 by serology and RT-PCR. This included 11 women, 11 men, and 2 children, with an average age of 35 years (1 – 70 years). Only one patient had a skin biopsy revealing leukocytoclastic vasculitis. Among these patients, thirteen were treated as outpatients, nine were hospitalized in the COVID-19 unit, and two were admitted to the intensive care unit (ICU). The main skin manifestations were as follows: four maculo-papular eruptions (Fig. 1a), one case of maculo-vesicular eruption, seven patients with Chilblain-like lesions (Fig. 1b), four cases of urticaria, one case of Raynaud's phenomenon (Fig. 1c), two cases of erythema multiforme (Fig. 1d), two cases of Kawasaki-like syndrome (Fig. 1e), two cases of acral vasculitis, three cases of acral necrosis (Fig. 1f), and four cases of the reactivation of oral herpes in intensive-care patients (Fig. 2). Six patients had two concomitant skin manifestations.

Skin manifestations remain rare in SARS-CoV-2. Cases have been reported sporadically. The first data was collected by Recalcati et al. Among 88 patients who tested positive, 20.4% developed skin manifestations [1]. However, in our experience, it is difficult to determine a true incidence of infection and, thus, the incidence of skin manifestations as only patients with severe respiratory symptoms were screened at the beginning of the pandemic. Therefore, the observed incidence is underestimated.

The incidence of skin rashes appears to be low, with no more than six hundred reported cases of skin manifestations out of more than four million SARS-CoV-2 patients in a study by Paulo Ricardo Criado et al. This may be explained by the underreporting of skin manifestations due to their lesser severity.

The manifestations are varied and polymorphous: exanthema, urticaria, livedo, purpura, vasculitis, necrosis, erythema multiforme, Kawasaki-like disease, Sweet-like with a predominance of Chilblain-like lesions unusually frequent this season and of late appearance in young subjects often asymptomatic in PCR, mostly negative, thus some authors consider them a delayed reaction of COVID-19 infection [2,3]. One patient in our series presented with Chilblain-like lesions fifteen days after her stay in intensive care and only one case had negative RT-PCR.

A recent article concluded that infection with COVID-19 could be a risk factor for the reactivation of *Herpesviridae* in seriously ill patients [4], such as in the four of our cases. In erythema multiforme, a drug origin has often been discussed in view of the late appearance of post-infectious lesions and after negative PCR [5],

How to cite this article: Chhiti S, Baybay H, Hashas FZ, Douhi Z, Elloudi S, Mernissi FZ. Cutaneous manifestations associated with COVID-19 in 24 cases from Fez, Morocco. Our Dermatol Online. 2023;14(1):103-104.

Submission: 06.05.2022; **Acceptance:** 23.07.2022

DOI: 10.7241/ourd.20231.26

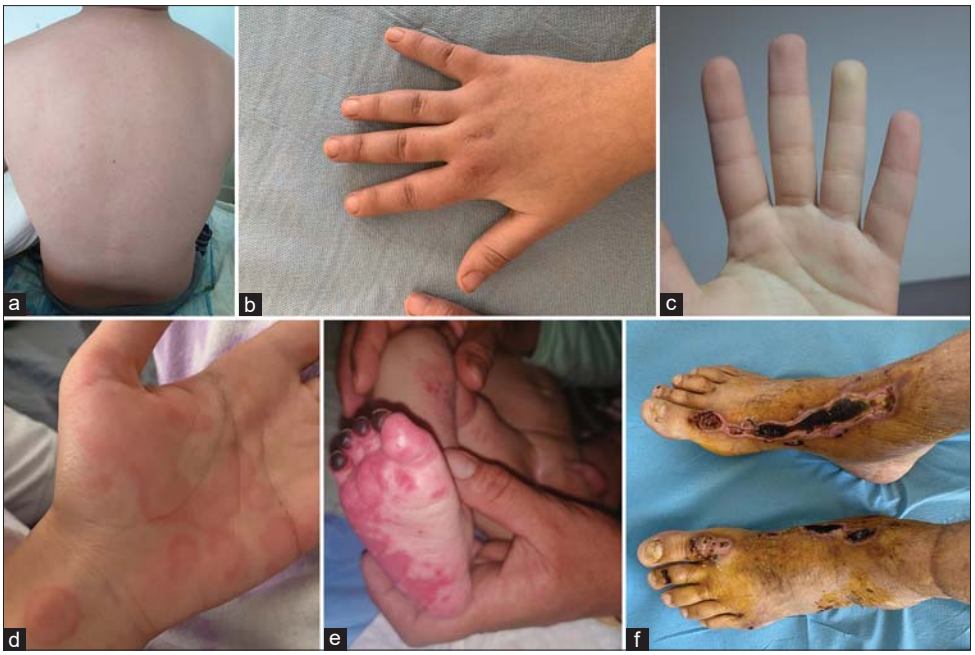


Figure 1: (a) Generalized papular macular rash. (b) Chilblain-like lesions on the hands. (c) Raynaud's phenomenon. (d) Palmar blackouts and pseudo-blackouts. (e) Kawasaki-like syndrome in a child. (f) Vasculitis with acral skin necrosis.

Figure 2: Oral herpes lesion.

such as in the case of one of our patients. Children constituted only a small proportion of patients with COVID-19, which was reported in 1.7% [6]. In our series, two children presented Kawasaki-like syndrome with a favorable evolution.

Therefore, physicians must be vigilant and aware of these skin signs, which may constitute an early indication of the severity of infection as well as retrospectively correct its diagnosis.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

REFERENCES

1. Hedou M, Carsuzaa F, Chary E, Hainaut E, Cazenave-Roblot F, Masson Regnault M. Cutaneous manifestations in COVID-19: A first perspective by Recalcati S. J Eur Acad Dermatol Venereol. 2020:34:299-300.
2. Estébanez A, Pérez-Santiago L, Silva E, Guillen-Climent S, García-Vázquez A, Ramón MD. Cutaneous manifestations in COVID-19: A new contribution. J Eur Acad Dermatol Venereol. 2020;34:e250-1.
3. Sachdeva M, Gianotti R, Shah M, Bradanini L, Tosi D, Veraldi S, et al. Cutaneous manifestations of COVID-19: Report of three cases and a review of literature. J Dermatol Sci. 2020;98:75-81.
4. Genovese G, Moltrasio C, Berti E, Marzano AV. Skin manifestations associated with COVID-19: Current knowledge and future perspectives. Dermatology. 2021;237:1-12.
5. Jimenez-Cauhe J, Ortega-Quijano D, Carretero-Barrio I, Suarez-Valle A, Saceda-Corralo D, Moreno-Garcia Del Real C, et al. Erythema multiforme-like eruption in patients with COVID-19 infection: Clinical and histological findings. Clin Exp Dermatol. 2020;45:892-5.
6. CDC COVID-19 Response Team. Coronavirus disease 2019 in children. Morb Mortal Wkly Rep. 2020;69:422-6.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Letter

A case of idiopathic granulomatous vasculitis with phlebitis and underlying subcutaneous necrotizing venulitis

Toshiyuki Yamamoto[1], Reiko Orikasa[2], Ko-Ron Chen[3]

[1]Department of Dermatology, Fukushima Medical University, Fukushima, Japan, [2]Department of Dermatology, Ohta Nishinouchi General Hospital, Fukushima, Japan, [3]Meguro Chen Dermatology Clinic, Tokyo, Japan

Corresponding author: Prof. Toshiyuki Yamamoto, M.D., Ph.D, E-mail: toyamade@fmu.ac.jp

Sir,

Granulomatous vasculitis in skin lesions is rarely seen in non-infectious granulomatous diseases and other systemic disorders. Herein, we report a unique case of cutaneous vasculitis in which granulomatous phlebitis was observed in a muscular vein at the dermal–subcutaneous junction and necrotizing granulomatous venulitis in the underlying subcutaneous tissues.

A 74-year-old female was referred to the dermatology clinic at Ota Nishinouchi General Hospital complaining of a painful, ulcerative lesion and numbness of the lower right extremity, which appeared one year earlier. She had hyperlipidemia, yet did not suffer from either diabetes mellitus or thyroiditis. A physical examination revealed an ulcer with an elevated, brownish border and ill-circumscribed, reddish infiltrated erythemas surrounding the concaved healed ulcerative lesion on the right shin (Fig. 1). A biopsy was taken from the erythematous plaque. The histopathological features found revealed degenerated collagen with surrounding vessels in the mid-dermis and a number of infiltrated inflammatory cells around the vessels at the dermal–subcutaneous junction (Figs. 2a and 2b). Higher magnification revealed several multi-nucleated giant cells and infiltration of inflammatory cells in the vascular wall (Fig. 2c). Elastica van Gieson stain confirmed that the vessel was a muscular vein with the partial destruction of the muscular layer, which was consistent with the features of granulomatous phlebitis (Fig. 2d). Naked epithelioid granulomas were additionally observed near granulomatous phlebitis. Immunohistochemistry revealed that histiocytes in and around the affected vessel wall were immunoreactive for CD68. In the subcutaneous tissue, the feature of necrotizing granulomatous venulitis was characterized by marked angiocentric infiltrate of histiocytes in and around the affected vessel wall mixed with neutrophils and lymphocytes and vessel wall fibrinoid necrosis (Fig. 2e). There was no eosinophil infiltration, and a dermal mucin deposition was not detected. On laboratory examination, the eosinophil ratio in the peripheral blood and the serum level of angiotensin-converting enzyme (ACE) were normal, and neither PR3-ANCA nor MPO-ANCA was detected. Ophthalmological and pulmonary examinations excluded sarcoidosis. Tuberculosis was excluded by chest X-ray, a chest CT scan, and a tuberculin test. In addition, the patient had no previous history of inflammatory bowel disease or intestinal symptoms. She was treated with topical difluprednate ointment, and the ulcer was completely epithelialized in three months.

The present case exhibited granulomatous phlebitis with naked epithelioid cell granulomas in the dermal–subcutaneous junction and subcutis. Furthermore, necrotizing granulomatous venulitis with fibrinoid necrosis and a predominantly angiocentric infiltration of histiocytes and giant cells in and around the vessel wall mixed with neutrophils and lymphocytes was observed in the underlying subcutis. Several cutaneous disorders that histologically show granulomatous vasculitis,

How to cite this article: Yamamoto T, Orikasa R, Chen K-R. A case of idiopathic granulomatous vasculitis with phlebitis and underlying subcutaneous necrotizing venulitis. Our Dermatol Online. 2023;14(1):105-106.

Submission: 27.07.2022; **Acceptance:** 28.09.2022

DOI: 10.7241/ourd.20231.27

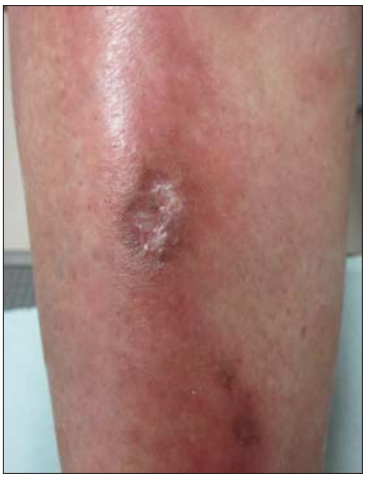


Figure 1: Ill-defined, infiltrative, erythematous plaque with an elevated, brownish border surrounding the small ulcer on the right shin.

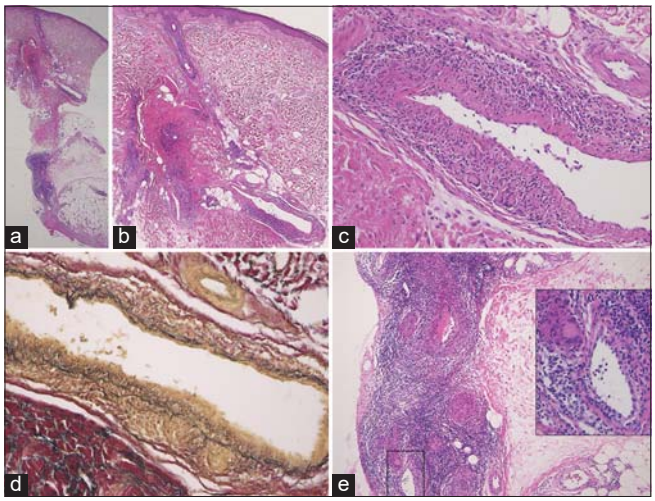


Figure 2: (a) Histological features showing vasculitis at the dermal–subcutaneous junction and subcutaneous tissues. (b) Higher magnification revealing vasculitis with multinuclear giant cells at the dermal–subcutaneous junction (arrows). (c) Granulomatous phlebitis at the dermal–subcutaneous junction characterized by a marked angiocentric infiltrate of histiocytes and multi-nucleated giant cells in and around the vessel wall. (d) Elastiva van Gieson stain revealing the affected vessel wall with the partial destruction of the muscular layer. (e) Necrotizing granulomatous venulitis in the underlying subcutis characterized by a marked angiocentric infiltrate of histiocytes and multi-nucleated giant cells in and around the affected venule mixed with neutrophils in the infiltrate and vessel wall fibrinoid necrosis (H&E stain; a: 20×, b: 40×, c: 200×, d: 200×, e: 100×) (insert: higher magnification of the enclosed square: 400×).

including granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, rheumatoid arthritis, giant cell arteritis, Crohn's disease, granulomatous phlebitis, and the non-infectious granulomatous diseases appearing in pretibial sites such as sarcoidosis and necrobiosis lipoidica, should be differentiated from one another [1-5]. Although this case clinically resembled necrobiosis lipoidica and the histopathological findings of granulomatous phlebitis could also be found in necrobiosis lipoidica [4], the key histopathological findings, such as dermal collagen necrobiosis changes surrounded by histiocytes and giant cells suggesting necrobiosis lipoidica, were absent in this case. Both features of pretibial plaque lesion clinically and subcutaneous naked granuloma with granulomatous vasculitis histopathologically could be found in sarcoidosis [5], yet neither extracutaneous examinations nor serological findings suggesting sarcoidosis were observed. Other systemic disorders such as ANCA-associated granulomatous vasculitis, rheumatoid arthritis, and inflammatory bowel disease were excluded. The examination of tuberculosis revealed no abnormal findings. Thus, none of the possible triggers or associated diseases could be identified in this case. The patient is today under careful follow-up for the appearance of possible associated diseases.

Consent

The examination of the patient was conducted according to the Declaration of Helsinki principles.

REFERENCES

1. Ackerman AB, Boer A, Bennin B, Gottlieb GJ. Histologic diagnosis of inflammatory skin diseases: an algorithmic method based on pattern analysis. Ardor Scribendi, 3rd Ed. pp425-431, Lea&Febiger, Philadelphia.
2. Sharma A, Dogra S, Sharma K. Granulomatous vasculitis. Dermatol Clin. 2015;33:475-87.
3. Marzano AV, Balice Y, Tavecchio S, Desimine C, Colombo A, Berti E. Granulomatous vasculitis. G Ital Dermatol Venereol. 2015;150:193-202.
4. Yamamoto T, Chen KR. Granulomatous phlebitis in necrobiosis lipoidica. Am J Dermatopathol. 2020;42:307-8.
5. Yamamoto T, Chen KR. Perforating plaque-type pretibial sarcoidosis with granulomatous phlebitis. Am J Dermatopathol. 2020;42:225-6.

Source of Support: This article has no funding source,
Conflict of Interest: The authors have no conflict of interest to declare.

Case Letter

Pruritic papular eruption revealing HIV

Chaymae Jroundi[1], Hanane Baybay[1], Hajar El Bennaye[1], Imane Couissi[1], Zakia Douhi[1], Sara Elloudi[1], Fatima Zahra Mernissi[1], Mouna Rimani[2]

[1]Department of Dermatology, University Hospital Hassan II, Fes, Morocco, [2]Hassan Center of Pathology, Rabat, Morocco

Corresponding author: Chaymae Jroundi, MD, E-mail: chaymaejr92@gmail.com

Sir,

Pruritic papular eruption (PPE) described in HIV is a skin disease often encountered in HIV-positive patients. It is most often a sign of severe immunodeficiency and is commonly reported in African, Southeast Asian, and Indian populations [1,2]. It affects both adult females and males and may also be seen in children. The elementary lesion is a discrete, firm, erythematous, urticarial, very itchy papule of the extremities, face, and trunk, sparing the palms and soles. Painful excoriations in the genital mucosa are sometimes described. The $CD4^+$ lymphocyte count (CD4) is usually below 250 cells/mm^3. Histopathology reveals a lymphohistiocytic, inflammatory, perivascular, and periannexal infiltrate with a variable number of eosinophils. According to the World Health Organization (WHO), it is recommended to all HIV patients with antiretroviral therapy (ART), regardless of the staging and the CD4 count [3]. However, an elective treatment for PPE has not yet been found. Regression has been noted in some cases after the initiation of antiretroviral therapy. UVB therapy seems to be the most successful method in cases not improving with antiretroviral therapy [4]. Herein, we report the case of a patient who presented with PPE revealing HIV.

A 42-year-old patient presented with itchy, papular eruption persistent for over one year, worsening with topical steroids. A clinical examination revealed erythematous papules and urticarial plaques, some of which were purpuric and located on the trunk, limbs, and face (Fig. 1). Also, the presence of pustules on the nose, forehead, and arms, without palmoplantar involvement was noted. A mucosal examination showed hairy leukoplakia of the tongue (Fig. 2) and two erosions on the penis. The patient also had recurrent episodes of bronchitis and diarrhea. A blood examination was performed, which returned positive for HIV. A skin

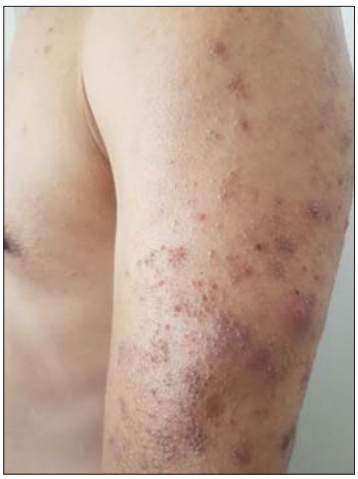


Figure 1: Erythematous papule and urticarial plaques of the limbs.

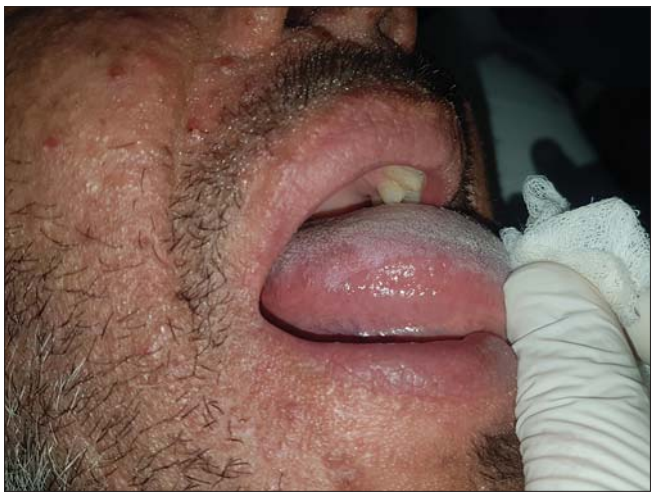


Figure 2: Hairy leukoplakia of the tongue.

How to cite this article: Jroundi C, Baybay H, El Bennaye H, Couissi I, Douhi Z, Elloudi S, Mernissi FZ, Rimani M. Pruritic papular eruption revealing HIV. Our Dermatol Online. 2023;14(1):107-108.

Submission: 27.10.2021; **Acceptance:** 05.01.2022

DOI: 10.7241/ourd.20231.28

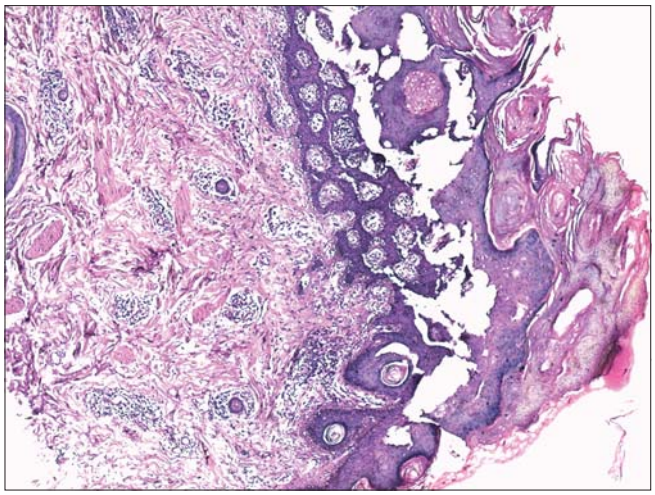


Figure 3: Marked hyperkeratosis with parakeratosis and keratotic, follicular plugs, also mild to moderate inflammatory infiltrates of the perivascular dermis, including eosinophils, lymphocytes, and histiocytes (H&E; 50×).

biopsy was performed showing marked hyperkeratosis with parakeratosis and keratotic, follicular plugs, also mild to moderate inflammatory infiltrates of the perivascular dermis, including eosinophils, lymphocytes, and histiocytes (Fig. 3), confirming the diagnosis of PPE related to HIV. A biological assessment showed a CD4 count of 234, and antiretroviral therapy was initiated.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Resneck JS, Van Beek M, Furmanski L, et al. Etiology of pruritic papular eruption with HIV infection in Uganda. JAMA. 2004;292:2614-21.
2. Ekpe O, Forae GD, Okpala CI. Pruritic papular eruption of HIV: A review article. Our Dermatol Online. 2019;10:191-6.
3. Rajput PS, Das AK, Paudel U, Parajuli S. Mucocutaneous disorders in HIV/AIDS at a tertiary care hospital in Nepal: An observational study. Our Dermatol Online. 2021;12:101-5.
4. Bellavista S, D' Antuono A, Infusino SD, Trimarco R, Patrizi A. Pruritic papular eruption in HIV: A case successfully treated with NB-UVB. Dermatol Ther. 2013;26:173-5.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Letter

Iatrogenic Kaposi's sarcoma in the anovulvar area

Asmae Abdelmouttalib, Hamich Soumaya, Mariame Meziane, Nadia Ismaili, Leila Benzekri, Karima Senouci

Dermatology and Venereology Department, Mohamed V University in Rabat, Morocco

Corresponding author: Asmae Abdelmouttalib, MD, E-mail: abdelmouttalibasmae@gmail.com

Sir,

Kaposi's sarcoma (KS) is an indolent angioproliferative tumor that depends on viral replication (HHV-8) and inflammatory cytokines produced by infected immune and endothelial cells [1]. It is a multifocal disease, with its evolutionary spectrum varying from a locoregional "indolent" form to a disseminated and fulminant form. KS lesions are rarely limited to unusual mucocutaneous areas. To our knowledge, there have been no reports of iatrogenic KS confined to the female external genitalia. Herein, we report the first case of iatrogenic KS restricted to the vulva and anus in an HIV-negative patient.

An 85-year-old female presented with violaceous nodules on the external genitalia. Her past medical history was significant for post-hepatitis C cirrhosis treated with sofosbuvir and daclatasvir for six months (the viral load of the control was negative). The patient developed bullous pemphigoid two weeks after the initiation of the anti-viral treatment. Thereafter, corticotherapy was started at the dose of 1 mg/kg/day. During follow-up, the patient had a complete healing of the pemphigoid lesions. On control, four months after the initiation of corticotherapy, a physical examination revealed several brownish-violaceous angiomatous nodules and slightly raised plaques on both labia majora and minora reaching up to the anus. The labia majora were swollen and painful with lymphatic edema (Figs. 1 and 2). No other significant mucocutaneous lesions were observed, and there was no evidence of inguinal lymphadenopathy. Fibroscopy showed no involvement of the digestive mucosa. A chest X-ray and abdominal and pelvic CT showed no visceral lesions. HIV serology was negative. A histological study revealed dermal proliferation of spindle cells, slit-like vascular spaces, and extravasated red blood cells. A PCR assay revealed HHV-8 DNA sequences in the lesional skin tissue. For our patient, we suggested bleomycin intramuscularly 5 mg per day for three days in a row every four weeks, and a faster reduction in corticosteroid therapy.

Kaposi's sarcoma (KS) is a spindle-shaped vascular cell tumor that may be located in the skin, the gastrointestinal and respiratory tract, or the lymphoid organs [2]. Four types of histologically indistinguishable KS exist: classic, endemic, immunosuppressive-therapy-related, and epidemic [1]. Each form seems to be connected with HHV-8 infection.

The iatrogenic form is caused by immunosuppressive drugs used after an organ transplantation. This form may also appear following the use of systemic corticosteroids and dermocorticoids [3]. The majority of cases of KS limited to the external genitalia are observed in males, especially on the penis. In females, it is highly uncommon and is observed mainly in HIV-positive females (up to five times more frequently than in HIV-negative females) [4,5]. In fact, to our knowledge, one case of classic KS confined to the female external genitalia not associated with HIV infection has been reported [6]. Clinically, it presents itself as a tumor mass, papilloma, or abscess. Confirmation of the diagnosis is based on biopsy and virological tests showing the presence of KSHV in the lesional tissues [4,5]. Cryotherapy, surgical excision, and radiotherapy are the main local treatments in the case of solitary lesions. The use of interferon alpha has also produced good results. In the case of iatrogenic MK, there is no uniform treatment regimen for KS. Immunosuppression must be reduced to the lowest levels while preserving allograft function in the case of an organ transplantation. Cyclosporine A should

How to cite this article: Abdelmouttalib A, Soumaya H, Meziane M, Ismaili N, Benzekri L, Senouci K. Iatrogenic Kaposi's sarcoma in the anovulvar area. Our Dermatol Online. 2023;14(1):109-110.

Submission: 01.06.2021; **Acceptance:** 09.10.2021

DOI: 10.7241/ourd.20231.29

Figure 1: Edematous labia with several brownish-violaceous nodules and slightly raised plaques on both the labia majora and minora.

Figure 2: Brownish-violaceous nodules and slightly raised plaques around the anus.

be converted to mycophenolate mofetil or mTOR inhibitors. Sirolimus appears to inhibit the growth of established vascularized tumors and this effect is best achieved with relatively low immunosuppressive doses of the drug [2].

Kaposi's sarcoma must be considered in the case of vulvar or anal tumor masses. Strict skin surveillance is necessary in patients treated with corticosteroid therapy or other immunosuppressive drugs.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Hinojosa T, Lewis DJ, Liu M, Garza G, Vangipuram R, Ramos E, et al. Nonepidemic Kaposi sarcoma: A recently proposed category. JAAD Case Rep. 2017;3:441-3.
2. Zmonarski SC, Boratyńska M, Puziewicz-Zmonarska A, Kazimierczak K, Klinger M. Kaposi's sarcoma in renal transplant recipients. Ann Transplant. 2005;10:59-65.
3. Baykal C, Atci T, Buyukbabani N, Kutlay A. The spectrum of underlying causes of iatrogenic Kaposi's sarcoma in a large series: A retrospective study. Indian J Dermatol. 2019;64:392-9.
4. van Bogaert LJ. Anogenital lesions: Kaposi's sarcoma and its mimics. ISRN AIDS. 2012;31:486425.
5. Chokoeva A, Tchernev G, Wollina U. [Kaposi's sarcoma of the vulva]. Akush Ginekol (Sofiia). 2015;54:24-8.
6. Errichetti E, Stinco G, Pegolo E, Patrone P. Primary classic Kaposi's sarcoma confined to the vulva in an HIV-negative patient. Ann Dermatol. 2015;27:336-7.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Letter

Basosquamous cell carcinoma: A specific finding of a basaloid squamous cell transition

Shohei Igari[1], Takako Miura[1], Osamu Yamamoto[2], Toshiyuki Yamamoto[1]

[1]Department of Dermatology, Fukushima Medical University, Fukushima, Japan, [2]Department of Dermatology, Tottori University, Tottori, Japan

Corresponding author: Prof. Toshiyuki Yamamoto, MD, E-mail: toyamade@fmu.ac.jp

Sir,

Basosquamous cell carcinoma is a relatively rare tumor with unique histopathological features of both basal and squamous cell carcinoma [1]. Herein, we report a case of basosquamous cell carcinoma on the face of an elderly male.

An 85-year-old male visited a local dermatology clinic complaining of a nodule on the face, which enlarged one month prior. He was a farmer and a never smoker, and his medical history included cerebral infarction, prostatic hypertrophy, and myocardial infarction. On physical examination, a relatively well-circumscribed, keratotic nodule measuring 15 × 12 mm in size was observed on the right cheek (Fig. 1). A biopsy specimen revealed a central basophilic area and an eosinophilic area surrounding the center of the dermis (Fig. 2). The peripheral eosinophilic area displayed anastomosing islands of atypical squamous cells with polygonal cytoplasm and intercellular bridges. The tumor cells had a keratinization tendency represented by cancer pearls. On the other hand, the central area exhibited smaller, solid or cord-like nests composed of basaloid cells, showing peripheral palisading and mucinous clefts between the nests and surrounding stroma. Both areas continued to the epidermis. In addition, some nests of both areas directly continued each other as transitional zones (Figs. 3a and 3b). Immunohistochemistry revealed the expression of AE1/AE3 (pancytokeratin) and CAM 5.2 (cytokeratin 8) in both areas, yet stronger in the squamous area (Fig. 4a), whereas the expression of BerEp4 was detected only in the basaloid cell areas (Fig. 4b). Epithelial membrane antigen was negatively stained. The patient was referred

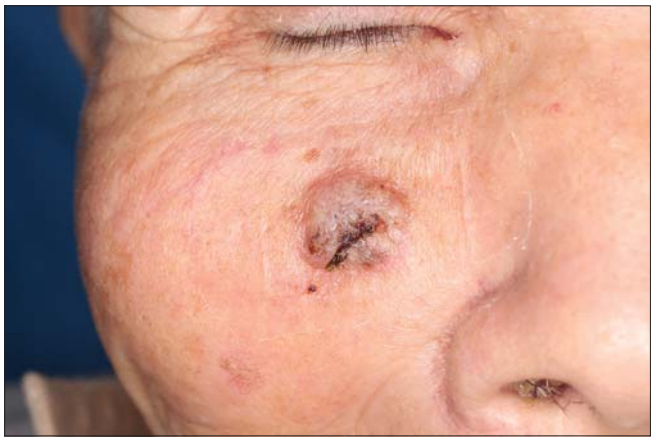


Figure 1: Clinical appearance showing a well-circumscribed, keratotic nodule on the right cheek.

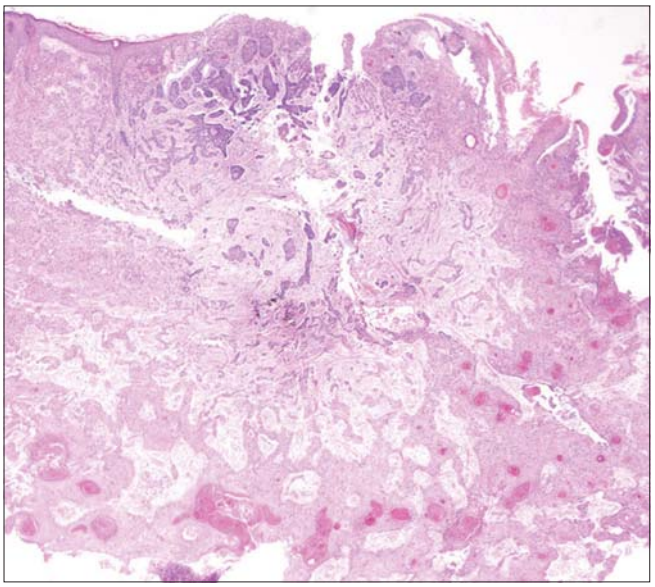


Figure 2: Biopsy specimen showing two types of neoplasms composed of squamous and basaloid cells (H&E, 40×).

How to cite this article: Igaria S, Miuraa T, Yamamotob O, Yamamotoa T. Basosquamous cell carcinoma: A specific finding of a basaloid squamous cell transition. Our Dermatol Online. 2023;14(1):111-113.

Submission: 27.04.2022; **Acceptance:** 29.07.2022

DOI: 10.7241/ourd.20231.30

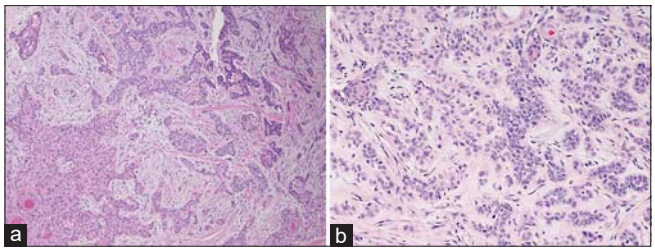


Figure 3: (a-b) Higher magnification showing areas of SCC and BCC with a direct transition (H&E; a: 100×, b: 200×).

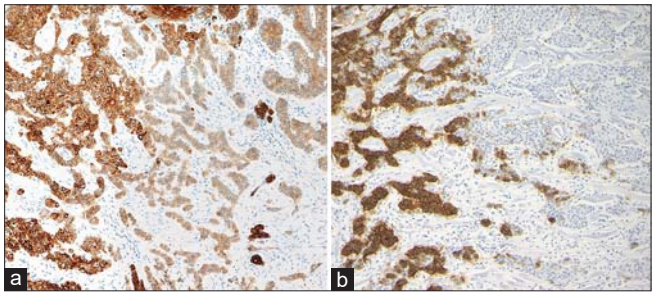


Figure 4: Immunohistochemistry showing that pancytokeratin expression was (a) much stronger in the SCC areas, (b) whereas BerEp4 was positive only in the BCC areas (a: 100×, b: 100×).

to our clinic for a surgical operation. Examination by computed tomography revealed lymph node metastasis. The remaining nodule was removed completely with a 6-mm margin, and covered with a full-thickness skin graft from the abdomen. Post-operative radiation therapy was not performed. Neither local recurrence nor lymph node metastasis was observed during a three-year follow-up period.

The definition of basosquamous cell carcinoma remains controversial. Some consider basosquamous cell carcinoma to be a variant of basal cell carcinoma (BCC), while others suggest a biological similarity to squamous cell carcinoma (SCC) with a metastatic potential [2]. In addition, the diagnosis of basosquamous cell carcinoma is often established when the collision of BCC and SCC is recognized in the same specimen, whereas other reports have defined basosquamous cell carcinoma only after the recognition of direct continuity between the areas of SCC and BCC [3]. It was highlighted that basosquamous cell carcinoma is neither a collision tumor nor a coincidental finding of adjacent BCC and SCC [1]; however, cases such as ours, exhibiting the direct transition between BCC and SCC, are extremely rare. Mitsuhashi et al. reported the concomitant occurrence of basosquamous cell carcinoma and spindle cell SCC. Their case also had a transitional zone between SCC and BCC, showing diminished BerEp4 staining in the former. In the present case, BerEp4 was detected only in the basaloid area. Furthermore, the expression fashion of cytokeratin was clearly different in the transitional zones. The mucinous stroma was prominent in the BCC areas. Recent studies have genetically defined basosquamous cell carcinoma and demonstrated that basosquamous cell carcinoma likely originates as BCC through the accumulation of ARID1A mutations and RAS/MAPK pathway activation, suggesting that basosquamous cell carcinoma resembles BCC more closely than SCC [4].

Basosquamous cell carcinoma has a significantly more frequent site of occurrence in sun-exposed areas. In a report collecting seventy-six cases of basosquamous cell carcinoma, the head and neck regions were the most common (76.3%), followed by the trunk (10.5%), lower limbs (7.9%), and upper arm (5.2%) [5]. A recent multi-center, prospective cohort study revealed that basosquamous cell carcinomas were localized on the head and neck in over 70% of cases, followed by the trunk (14.2%), arms (8%), and legs (7.3%) [6].

Basosquamous cell carcinoma is occasionally invasive and bears a high recurrence rate, suggesting its highly aggressive behavior [1]. Therefore, careful and long-term follow-up is necessary. The treatment of basosquamous cell carcinoma is performed according to SCC, and surgery with a wide and deep margin or Mohs surgery is the first-line option, with or without postoperative radiation therapy. A recent systematic review showed a high recurrence rate of basosquamous cell carcinoma after Mohs surgery and wide local excision [7]. Because the facial tumor was removed completely with a negative margin, additional therapies were not performed in the present case. Under the careful follow-up period, the patient has been free from either local recurrence or lymph node metastasis. In conclusion, our case was not a collision, yet a direct transition between BCC and SCC, and basosquamous cell carcinoma should be defined as such cases.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Shukla S, Khachemoune A. Reappraising basosquamous carcinoma: A summary of histologic features, diagnosis, and treatment. Arch Dermatol Res. 2020;312:605-9.
2. Garcia C, Poletti E, Crowson AN. Basosquamous carcinoma. J Am Acad Dermatol 2009;60:137-43.
3. Mitsuhashi T, Itoh T, Shimizu Y, Ban S, Ogawa F, Hirose T, et al. Squamous cell carcinoma of the skin: Dual differentiations to rare basosquamous and spindle cell variants. J Cutan Pathol. 2006;33:246-52.
4. Chiang A, Tan CZ, Kuonen F, Hodgkinson LM, Chiang F, Cho RI, et al. Genetic mutation underlying phenotypic plasticity in basosquamous carcinoma. J Invest Dermatol. 2019;139:2263-71.
5. Betti R, Crosti C, Ghiozzi S, Cerri A, Moneghini L, Menni S. Basosquamous cell carcinoma: A survey of 76 patients and a comparative analysis of basal cell carcinomas and squamous cell carcinomas. Eur J Dermatol. 2013;23:83-6.
6. Gualdi G, Soglia S, Fusano M, Monari P, Giuliani F, Porreca A, et al. Characterization of basosquamous cell carcinoma: A distinct type of keratinizing tumour. Acta Derm Venereol. 2021;101:adv00353.
7. Tan CZ, Rieger KE, Sarin KY. Basosquamous carcinoma: Controversy, advances, and future directions. Dermatol Surg. 2017;43:23-31.

Source of Support: Nil, **Conflict of Interest:** None declared.

Our Dermatology Online

Case Letter

A case of delayed diagnosis of Dowling–Degos disease

Servet Topal[1], İlteriş Oğuz Topal[1], Hülya Bilgi[2]

[1]*University of Health Sciences, Department of Dermatology, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Turkey,*
[2]*University of Health Sciences, Department of Histopathology, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Turkey*

Corresponding author: Servet Topal, MD, E-mail: dr.servettopal@gmail.com

Sir,

Dowling–Degos disease (DDD) is a rare genodermatosis characterized by acquired reticular hyperpigmentation of flexural sites, comedo-like lesions, and pitted facial scars. The classic disease is inherited by the autosomal dominant pattern. Herein, we present here the case of a fifty-year-old female diagnosed with Dowling–Degos disease.

A fifty-year-old female was admitted to our outpatient clinic with a fifteen-year history of brown spots on the neck, face, axilla, wrist, and vulva. Dermatological examination revealed pitted, periorbital scars and pigmented brown macules on the face, axilla, dorsum of the hands, inner face of the wrists, inguinal folds, external genitalia, and multiple, small, brown papules with variable hyperkeratosis on the chest (Figs. 1 and 2). The mucosal membranes, hair, and nails were normal. There were similar pitted lesions in the patient's two children as well. Routine laboratory parameters, including the blood glucose level, lipids, and insulin, were in the normal range. Two punch biopsy specimens were taken from the trunk and axilla. Histopathology of the skin biopsy revealed orthokeratosis on the superficial layer, keratin horns in the epidermis, an elongated and increased melanin pigment on the rete ridges, and mild dermal infiltration (Fig. 3). Based on the clinical and histopathological features, a diagnosis of Dowling–Degos disease was established and referred to the genetics department.

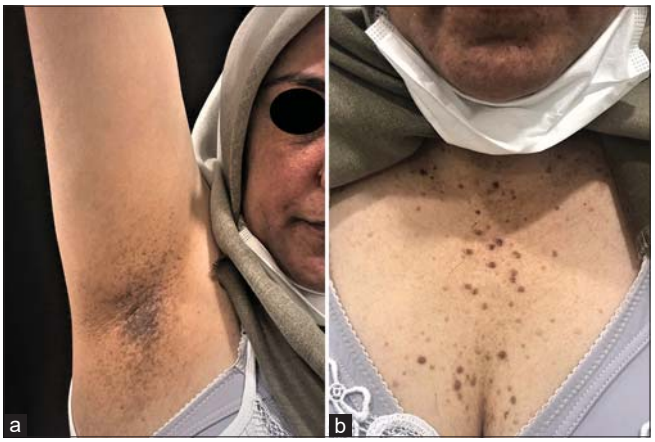


Figure 1: (a) Reticulate hyperpigmentation on the axilla. (b) Multiple, small, brown papules with variable hyperkeratosis on the chest.

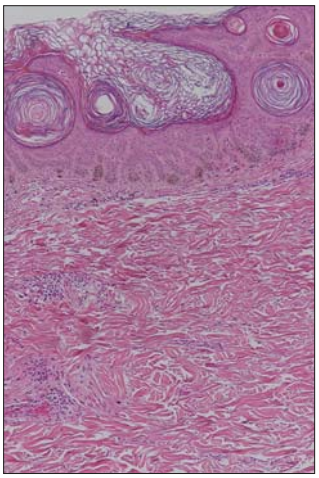


Figure 2: Histopathology revealing keratin horns in the epidermis and an elongated and increased melanin pigment on rete ridges (H&E; 10×).

Dowling–Degos disease, also known as the reticular hyperpigmented anomaly of the flexures, is a rare genodermatosis first described by Dowling and Freudenthal in 1938 distinguished by acanthosis nigricans [1]. DDD is characterized by acquired reticulate pigmentation of the flexures, neck, groin, wrist, face, vulva, and scrotum. Other associated skin manifestations are pitted, perioral, acneiform scars, comedo-like, hyperkeratotic papules, epidermal, trichilemmal cysts, and hidradenitis suppurativa [2,3]. The onset of the disease is typically after puberty and

How to cite this article: Topal S, Topal IO, Bilgi H. A case of delayed diagnosis of Dowling–Degos disease. Our Dermatol Online. 2023;14(1):114-115.

Submission: 18.09.2022; **Acceptance:** 02.12.2022
DOI: 10.7241/ourd.20231.31

the third to fourth decade of life. Mutations in the keratin-5 gene affecting the transfer of melanosomes to melanocytes and keratinocyte differentiation have been found in the pathogenesis of the disease. Atypical clinical presentations are fingernail dystrophy, dyschromatosis universalis hereditaria-like lesions; localized areas such as vulva have been reported in the literature so far [4]. There are several defined dermoscopic features in Dowling–Degos disease, which are irregular, brown pigmentations surrounding a hypopigmented center in a reticular pattern [5]. Pigmented lesions of genital involvement, especially on the vulva, may be rarely seen. Our patient has also genital involvement along with other sites (Fig. 2). Ho Song Kang et al. presented a case of Dowling–Degos disease with vulva involvement [6]. Histopathologically, the disease is characterized by increased pigmentation of the basal layer, thinning of the underlying suprapapillary epithelium, and downward elongation of the rete ridges [7]. Involvement of the infundibulum of the hair follicle is the unique and distinctive feature of the reticular pigmented anomaly [6]. A differential diagnosis should be made from Galli–Galli disease, Haber syndrome, reticulate acropigmentation of Kitamura, dyschromatosis symmetrica hereditaria (acropigmentation of Dohi), and acanthosis nigricans [7]. The most closely related disease is Galli–Galli disease (GGD), which is also an autosomal dominant genodermatosis with loss of function in KRT-5. GGD is clinically indistinguishable from DDD and histologically differentiated with the presence of acantholysis. GGD may also be considered an acantholytic variant of DDD [4]. Reticulate acropigmentation of Kitamura was excluded because of acral involvement and childhood onset. Furthermore, epidermal atrophy was not present in our case, as in Kitamura [7].

DDD is diagnosed based on clinical and histological findings. Numerous treatment options, such as topical hydroquinone, tretinoin, adapalene, and corticosteroids, have been tried for DDD, yet no treatment options have been completely successful in eliminating the lesions. Er: YAG lasers have been proven to be effective by some case reports [7]. Our patient is being followed up with topical tretinoin and methylprednisolone. The results of the genetic samples taken from the patient and her two children have not been concluded yet.

Since Dowling–Degos disease is a rare dermatosis, an average of a hundred familial cases have been reported in the literature so far. We present this case in order to review its diagnosis, emphasize genital involvement, and review its distinction from diseases with reticular pigmentation, particularly in familial cases.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Dowling GB, Freudenthal W. Acanthosis nigricans. Proc R Soc Med. 1938;31:1147-50.
2. Kim YC, Davis MD, Schanbacher CF, Su WP. Dowling–Degos disease (reticulate pigmented anomaly of the flexures): A clinical and histopathologic study of 6 cases. J Am Acad Dermatol. 1999;40:462-7.
3. Mancy A. Dowling–Degos disease: An association with hidradenitis suppurativa. Our Dermatol Online. 2022;13:445-8.
4. Stephan C, Kurban M, Abbas O. Dowling–Degos disease: A review. Int J Dermatol. 2021;60:944-50.
5. El Kadiri S, Bay Bay H, Chaoui R, Douhi Z, Elloudi S, Mernissi FZ. A rare classic case of Dowling–Degos disease with dermoscopy description. Our Dermatol Online. 2020;11:e71.1-e71.2.
6. Kang HS, Hur J, Lee JW, Oh DH, Yeo KY, Kim JS, et al. A case of Dowling–Degos disease on the vulva. Ann Dermatol. 2011;23:205-8.
7. Rice AS, Cook C. Dowling–Degos disease. 2022 Jul 26. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–.

Source of Support: This article has no funding source.

Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Case Letter

Green nail syndrome: Contribution of dermoscopy in two cases

Boularbah Siham, Meryem Soughi, Kawtar El Fid, Zakia Douhi, Sara Elloudi, Hanane Bay Bay, Fatima Zahra Mernissi

Department of Dermatology, CHU Hassan II, Fez, Morocco

Corresponding author: Siham Boularbah, MD, E-mail: sihamboularbah1902@gmail.com

Sir,

Green nail syndrome (GNS) is a nail disorder that may be caused by several etiologies, among which *Pseudomonas aeruginosa* is the main factor that produces pyocyanin and pyoverdine, causing green discoloration. This infection may be confused with etiologies, such as co-infection with onychomycosis [1]. Herein, we report the dermoscopic models of GNS observed in two cases.

A 42-year-old female presented with painless nail discoloration of the right thumb (Fig. 1a). The patient reported that there was only white and yellowish coloring in the same area present for around three years and that the green color had been returning for the last five months. The patient had no similar lesions elsewhere. A dermoscopic examination revealed a polychrome pattern consisting of areas of greenish and yellowish coloring, giving the aspect of aurora borealis (Fig. 1b) with a yellowish-white, jagged edge and subungual hyperkeratosis (Fig. 1c). Microbiological examinations confirmed the presence of *Pseudomonas* infection and *T. rubrum* dermatophytosis.

A thirty-year-old housekeeper female with a history of insulin-treated diabetes presented to our dermatology department with a four-year history of asymptomatic nail discoloration affecting the thumb of the right hand (Fig. 2a), repeatedly treated with oral fluconazole by her general practitioner yet without clinical improvement. An onychoscopic examination revealed a multicolored pattern on the nail plate consisting of areas of homogeneous, blackish-gray and greenish coloration (Fig. 2b). and pachyonychia without subungual hyperkeratosis (Fig. 2c). The direct microscopic preparation of potassium hydroxide was negative, yet a microbiological examination confirmed the presence of *Pseudomonas* infection.

Pseudomonas aeruginosa is the most common pathogen causing bacterial nail infections [3]. However, other saprophytic germs such as *Candida albicans* [2], some species of *Aspergillus*, and *Proteus mirabilis* may also cause chloronychia. Very often, it is a mixed infection.

Pseudomonas aeruginosa is a strictly aerobic, ubiquitous, saprophytic, Gram-negative bacterium that may become an opportunistic pathogen. In humans, moist regions (folds, anogenital regions, external auditory canal) are places of natural colonization. This bacterium may produce green nail syndrome by the accumulation of pyocyanin according to two modes of contamination [3].

On the one hand, *Pseudomonas* may develop immediately in the ungueal tablet. On the other, it may develop by cuticular weakening favored by several risk factors such as [6]:

- repeated immersions, thus being common among housekeepers, hairdressers, and beauticians;
- repetitive strain injuries, such as excessive manicure and onychophagia.

The results of our study confirmed the previously reported risk factors, such as frequent water exposure. The first finger injury in both cases meant that trauma is likely an important risk factor for chloronychia.

How to cite this article: Boularbah S, Soughi M, El Fid K, Douhi Z, Elloudi S, Baybay H, Mernissi FZ. Green nail syndrome: Contribution of dermoscopy in two cases. Our Dermatol Online. 2023;14(1):116-118.

Submission: 25.07.2022; **Acceptance:** 24.09.2022

DOI: 10.7241/ourd.20231.32

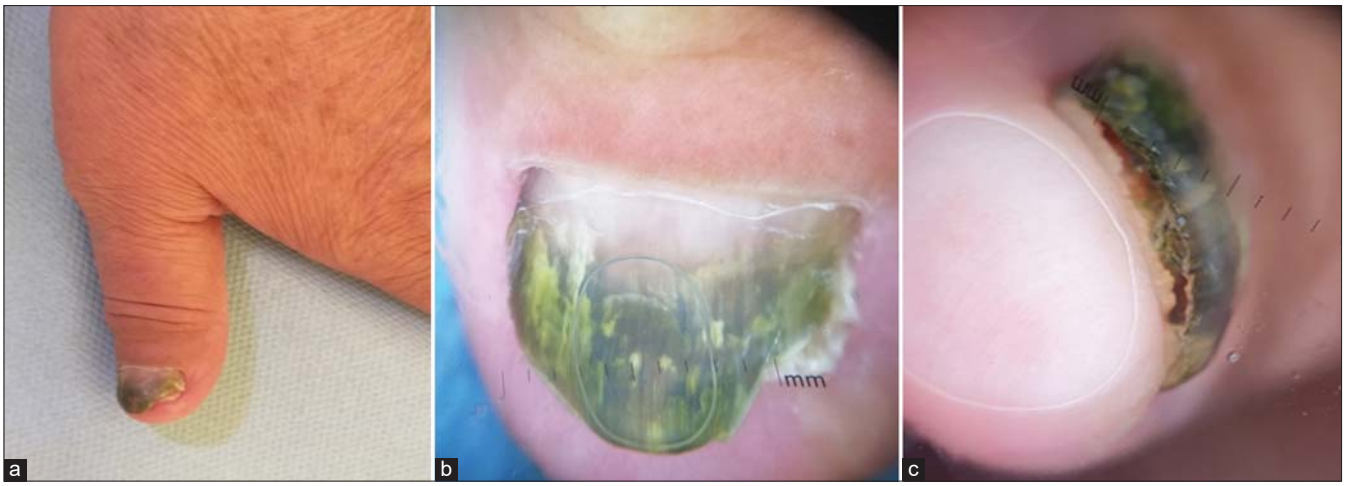


Figure 1: (a) Right thumb green nail: the mycological and bacteriological examinations were in favor of co-infection with *Pseudomonas* and *T. rubrum*. (b) Polychrome pattern consisting of zones of greenish and yellowish coloration. (c) Free edge dermoscopy revealing hyperkeratosis under the nail.

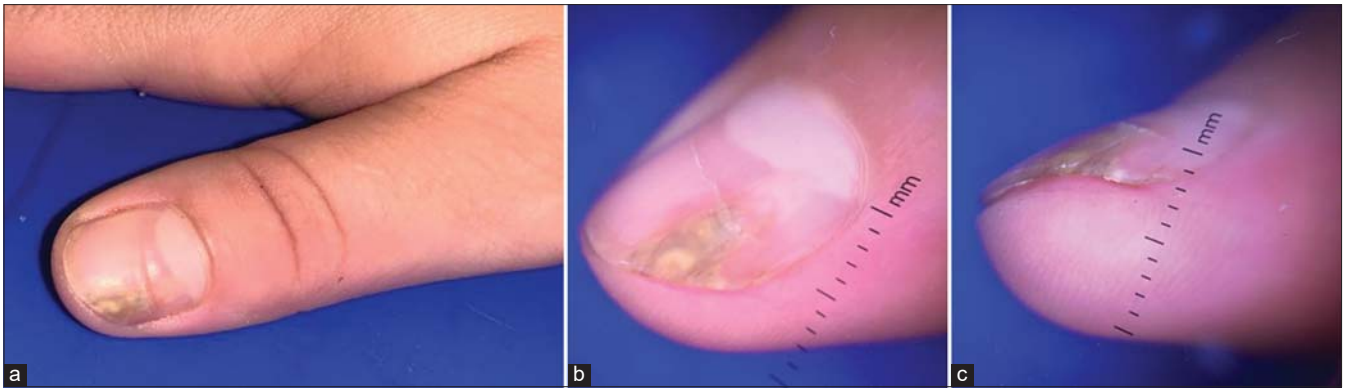


Figure 2: (a) Left thumb green nail: the mycological examination was negative and the bacteriological examination was in favor of *Pseudomonas*. (b) Polychrome pattern consisting of areas of greenish and yellowish coloration. (c) Free edge dermoscopy revealing the absence of subungual hyperkeratosis.

Concomitant nail pathology, essentially onychomycosis [4], is another risk factor for infection with this bacterium. Indeed, concomitant onycholysis constitutes a space for humidity and, therefore, a bed for *P. aeruginosa*. The mixed infection may be confused with isolated *Pseudomonas* infection. It is already known that the isolation of the causative fungus is highly difficult due to the fungicidal properties. In our cases, a greenish pattern without structure or polychrome with the absence of hyperkeratosis under the nail should guide the clinician toward isolated infection with *P. aeruginosa*, while onycholysis and the greenish pattern without structure or polychrome with the presence of subungual hyperkeratosis may direct the diagnosis toward a mixed infection.

Dermoscopy may, therefore, help in the etiological diagnosis of green nails by distinguishing infections with *Pseudomonas aeruginosa* isolated from co-infection with onychomycosis. Our study corroborated a Spanish report published in 2021 [5]. We also suggest reserving the term *aurora borealis* for the dermoscopic appearance of green nails observed in *P. aeruginosa* infection and the term *green aurora sign* for that observed in onychomycosis.

Consent

The examination of the patient was conducted according to the Declaration of Helsinki principles.

REFERENCES

1. Benati E, Ribero S, Longo C, Piana S, Puig S, Carrera C, et al. Clinical and dermoscopic clues to differentiate pigmented nail bands: An International Dermoscopy Society study. J Eur Acad Dermatol Venereol. 2017;31:732-6.
2. Romaszkiewicz A, Slawinska M, Sobjanek M, Nowicki RJ. Nail dermoscopy (onychoscopy) is useful in diagnosis and treatment

follow-up of the nail mixed infection caused by *Pseudomonas aeruginosa* and *Candida albicans*. Postepy Dermatol Alergol. 2018;35:327-9.
3. Kristina DM, Charles PG. Risk assessment of *Pseudomonas aeruginosa* in water. Rev Environ Contam Toxicol. 2009;201:71-115.
4. Chiriac A, Brzezinski P, Foia L, Marincu I. Chloronychia: green nail syndrome caused by *Pseudomonas aeruginosa* in elderly persons. Clin Interv Aging. 2015;10:265-7.
5. Miguel D-S, Borja D-G, Juan J-C, Ana S-V. Dermoscopy of green nail syndrome: The "green aurora sign." Dermatol Pract Concept. 2021;11:e2021093.
6. Solomon G, Shari RL. Retrospective case series on risk factors, diagnosis and treatment of pseudomonas aeruginosa nail infections. Am J Clin Dermatol. 2020;21:297-302.

Source of Support: This article has no funding source,

Conflict of Interest: The authors have no conflict of interest to declare.

Our Dermatology Online

Case Letter

Rapidly fatal metastatic melanoma arising from a congenital nevus in a young female

Jihad Kassel[1], Sara Elloudi[1], Kaoutar Soussy[2], Soukaina Chhiti[1], Hanane Baybay[1], Zakia Douhi[1], Touria Bouhafa[2], Fatima-Zahra Mernissi[1]

[1]Department of Dermatology, University Hospital Hassan II, Fes, Morocco, [2]Radiation oncology department, Oncology hospital, University Hospital Hassan II, Fes, Morocco

Corresponding author: Jihad Kassel, MD, E-mail: kassel.jihad@gmail.com

Sir,

Melanoma is an aggressive and potentially fatal tumor of melanocytic origin. It may occur at any age yet more rarely at a young age [1]. Melanomas in young patients have overall a more favorable prognosis than in older. However, progression to the metastatic stage and the death of the patient are not exceptional [2]. One of the major risk factors for the development of melanoma in children and young adults is the congenital melanocytic nevus (CMN) [3]. The risk of malignant transformation of all congenital nevi ranges from 0.05% to 10.7%. The risk of malignant degeneration is correlated with size and location [4]. The size of the CMN above 40 cm as well as the presence of satellite nevi and the location in the trunk seem to increase the risk of developing MM. The role of surgical removal in inducing melanomas is controversial. In anatomopathology, melanomas arising from CMNs are usually located in the dermis and hypodermis, while melanocytic proliferation in a melanoma without a CMN starts in the epidermis [3]. Given the differences in the anatomical involvement of the disease, melanoma arising from congenital nevi may be considered a separate entity from the conventional case of melanoma and management may differ. Large excision may not be sufficient to remove all neoplastic cells from the nevi, and adjuvant aggressive systemic therapies may be essential to avoid a fatal outcome [4]. A recent study revealed that congenital nevi preferentially harbor NRAS mutations rather than BRAF mutations commonly seen in other types of nevi, indicating an altered molecular basis of nevogenesis in congenital nevi [3]. Herein, we report the case of a rapidly fatal metastatic melanoma in a young female arising from a congenital nevus of the trunk.

A young female 24 years of age presented with a pigmented, congenital, 5 cm lesion of the abdomen. The patient underwent surgical excision of the lesion without histological assessment. A painful angiomatous nodule appeared over the existing lesion evolving for the last year (Fig. 1). The evolution was then marked three months later by the appearance of numerous erythematous and angiomatous cutaneous and subcutaneous nodules disseminated over the entire body (Figs. 2a and 2b). We also noted inguinal and axillary bilateral lymph nodes associated with asthenia, dyspnea, headaches, and dizziness. A biopsy of the angiomatous nodule adjacent to the nevus

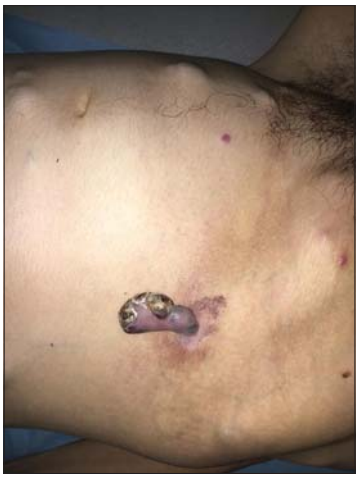


Figure 1: The pigmented angiomatous nodule above an asymmetric pigmented macule in the abdominal area.

How to cite this article: Kassel J, Elloudi S, Soussy K, Chhiti S, Baybay H, Douhi Z, Bouhafa T, Mernissi FZ. Rapidly fatal metastatic melanoma arising from a congenital nevus in a young female. Our Dermatol Online. 2023;14(1):119-120.

Submission: 06.01.2022; **Acceptance:** 03.03.2022

DOI: 10.7241/ourd.20231.33

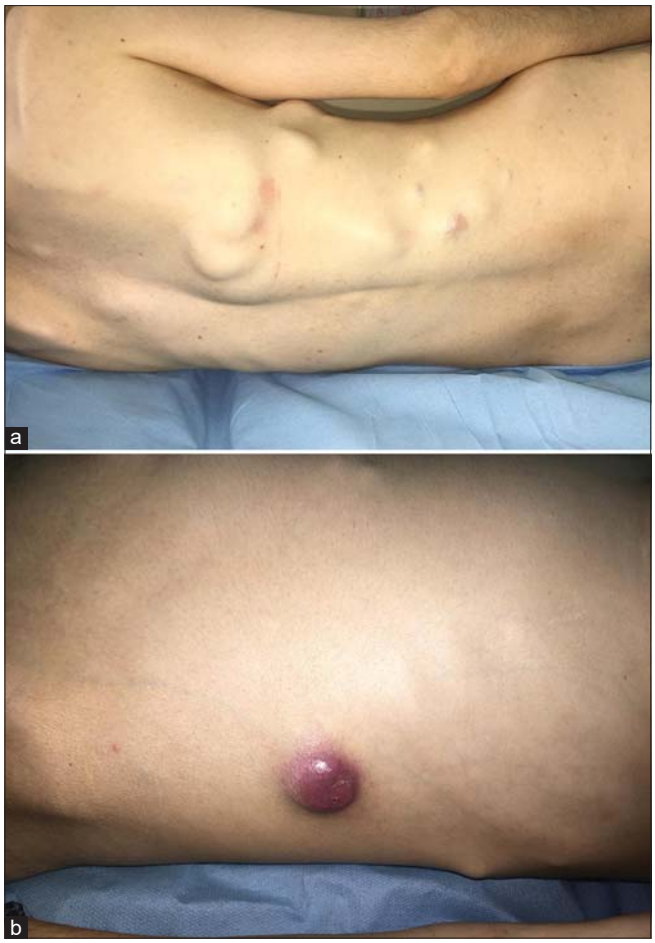


Figure 2: (a) Multiple subcutaneous nodules on the back. (b) The angiomatous nodule at the abdominal level.

was performed and showed a predominant dermal proliferation with some intraepidermal nests of atypical melanocytic cells with foci of tumor necrosis and ulceration. IHC showed a positive marking of HMB45 and Melan A. A total body CT scan was performed showing metastases of the brain, lungs, soft tissue, pancreas, and bone with peritoneal calcinosis. The patient was transferred to the oncology and radiotherapy department and deceased two weeks later.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Bebe FN, Hu S, Brown TL, Tulp OL. Metastatic melanoma in Florida, 1996-2010: Racial, demographic, occupational and tumor characteristics, and burden of metastasis. Our Dermatol Online. 2018;9:369-79.
2. Limam SAM, Erebih CE, Beyrouk A, Boye KI, Didi EH, Ely SO, et al. [Acral melanoma of the foot: A study of 9 cases and guidelines update]. Our Dermatol Online. 2019;10:23-9.
3. Lacoste C, Avril MF, Frassati-Biaggi A, Dupin N, Chrétien-Marquet B, Mahé E, et al. Malignant melanoma arising in patients with a large congenital melanocytic naevus: Retrospective study of 10 cases with cytogenetic analysis. Acta Derm Venereol. 2015;95:686-90.
4. Wei CH, Shoo BA, Zedek DC, Kashani-Sabet M, Sagebiel RW, Leong SP. Rapidly lethal metastatic melanoma arising from a large congenital melanocytic naevus. BMJ Case Rep. 2009;2009:bcr09.2008.0981.

Source of Support: Nil, **Conflict of Interest:** None declared.

On behalf of our **Scientex family** and **Conference committee**, we are happy to invite all our professional scholars, researchers, doctors and beloved students to be a part of the **"International Conference on Dermatology and Cosmetology"** on **May 18-19, 2023** at **Tokyo, Japan.**

The **Dermatology 2023** consists of several sessions to present researches in the category of keynote, plenary, poster, exhibitor, workshop, video presentation, e-poster and YRF.

The gathering will be oriented on the theme **"Investigate skin care issues and new technologies for better treatment".**

It is a Global platform for business delegates, B2B meetings, poster presentations, workshops, symposia, networking and more. It will offer a platform wherein you can ensure enormous exposure and networking by exhibiting products and services. Grab the opportunities and share your innovative ideas, new technologies and recent researches.

With the great support of our conference committee members and we are expecting huge response and support from the **Dermatologist,** Aesthetic and Ageing, Medicine Physicians, Trichologists and Students, Dermatology Associations and Societies, Journal Publishing Groups, Healthcare Industries, Cosmetics Companies and Clinics etc. Young Researchers, Students, Delegates, Directors and other Skin Care companies to have your gracious presence at our Dermatology and to make this congress a great successful event of the year 2023.

This Conference will be a **Hybrid event** (Physical conference as well as Virtual conference) As some attendees may not be able to fly due to the pandemic or its economic impacts.

In Japan, dermatological care is likely to receive special attention. A nationwide study was carried out by the Japanese Dermatological Association, and statistics on 67,448 cases that took part was analysed.

Tokyo, Japan is the excellent place to discuss skin care advancements in dermatology and cosmetology, so join us as we experience this stunning city.

With Thanks
Rowena Gilbert
Conference Manager | Dermatology 2023
1309 Coffeen Avenue, STE 1200,
Sheridan, Wyoming 82801, USA
T: +1-307-445-0640

Our Dermatology Online

www.odermatol.com

1.2023 (02.January.2023)