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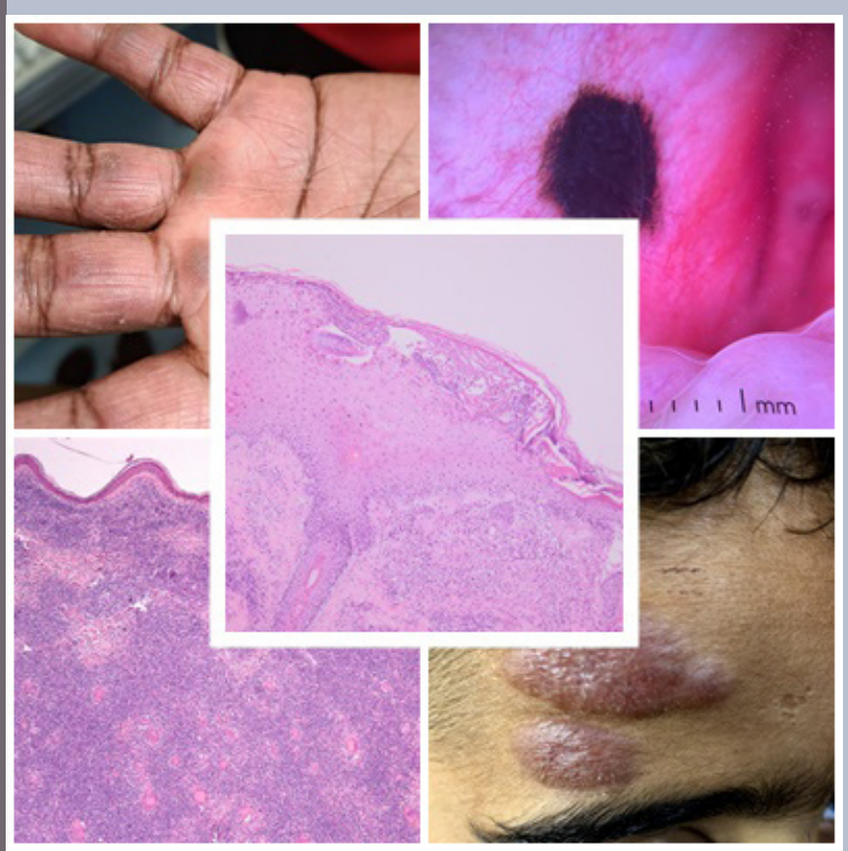

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Original Article

Androgenetic alopecia and metabolic syndrome: A cross-sectional study in Northeast India

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a multifactorial progressive disorder due to excessive response to androgens. Its association with metabolic syndrome still has conflicting results. **Aim:** The aim was to assess the association between androgenetic and metabolic syndrome and to study the clinico-epidemiological profile of AGA in Northeast India. **Materials and Methods:** A hospital-based, cross-sectional study was conducted on 150 patients with AGA within the age group of 20–65 years. The degree of hair loss was assessed and classified according to the Hamilton and Norwood classification in males and the Ludwig classification in females. The diagnosis of metabolic syndrome (MetS) was based on criteria defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Analysis was performed with IBM SPSS Statistics 21. The chi-squared test was used to assess the associations. The unpaired *t*-test was used to compare continuous variables. A p value < 0.05 was considered statistically significant. **Results:** The prevalence of MetS in the study was 36% (54 patients). HDL was significantly ($p = 0.03$) lower among MetS cases than those without MetS. The components of MetS such as high WC, low-level HDL, and hypertension were significantly ($p < 0.05$) associated with cases of AGA with MetS. Hypertension was present among all males of grades VI and VII and all females of grade III. **Conclusion:** AGA could be considered a predictor of metabolic syndrome. Patients with an early onset and higher grades of AGA should be routinely screened for MetS, which will help in preventing long-term complications such as cardiovascular diseases.

Key words: Androgenetic alopecia, Metabolic syndrome, Cardiovascular diseases

INTRODUCTION

Androgenetic alopecia (AGA) is a multifactorial disorder with progressive hair loss in specific patterns depending on circulating androgens in genetically predisposed individuals. It is characterized by stepwise miniaturization of the hair follicle, resulting from an alteration in the hair cycle dynamics, leading to vellus transformation of terminal hair follicle. Metabolic syndrome (MetS) is a group of metabolic disorders such as glucose intolerance, insulin resistance (IR), central obesity, dyslipidemia, and hypertension associated with increased risk of cardiovascular disease [1].

A previously reported association between AGA and chronic diseases, including hypertension, abnormal serum lipid profiles, obesity, insulin resistance, and cardiovascular disease (CVD) remains poorly understood [2]. Corroborating the association between metabolic syndrome and AGA may provide another clue to the clinical signs and symptoms related to both diseases [1]. Therefore, the present study was conducted to assess the association between AGA and metabolic syndrome and to study the clinico-epidemiological profile of AGA in Northeast India.

MATERIALS AND METHODS

A cross-sectional study was conducted on 150 patients with AGA attending the outpatient department of dermatology at the Regional Institute of Medical

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Sciences in Imphal, Manipur, for 24 months from September 2017 to August 2019. All patients presenting with AGA within the age group of 20–65 years were included, and those suffering from other types of alopecia and on glucocorticoid treatment within the previous six months were excluded. Proforma was filled and general physical examination and relevant systemic and clinical examinations were performed after obtaining informed consent. The degree of hair loss was assessed and classified according to the Hamilton and Norwood classification in males and the Ludwig classification in females. The diagnosis of MetS was based on criteria defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Subjects were required to have three or more of the following: i) waist circumference (WC) > 90 cm in men and > 80 cm in women, ii) serum triglycerides (TG) ≥ 150mg/dL, (iii) high-density lipoprotein (HDL) ≤ 40 mg/dL, iv) fasting blood glucose ≥ 110 mg/dL, v) blood pressure ≥ 130/85 mmHg.

Analysis was done with IBM SPSS Statistics 21 (IBM Corp. 1995, 2012). Descriptive statistics such as frequencies, percentages, means with standard deviations, and medians were used. The chi-squared test was used to assess the associations. The unpaired *t*-test was used to compare continuous variables. A p value < 0.05 was considered statistically significant.

Ethics Statement

Ethical approval was obtained from the institute ethics committee.

RESULTS

The study included 150 patients. More than one-third of the cases were between 31–40 years of age (44%), followed by 20–30 (35.3%), 41–50 (12%), and 51–65 (8.7%) years, with a mean age of 32.92 ± 7.98. More than half of the cases were males (65.3%).

Grade III was the most common (27.6%), and grade VIII was the least common type of hair loss (5.1%) among the males (Hamilton Norwood classification), and grade I (55.8%) was the most common and grade III was least among the females (Ludwig classification) (Table 1).

A family history for AGA was the most common (91 cases; 60.7%) family history noted in patients with AGA, followed by hypertension in 53 patients (35.3%) and dyslipidemia in 39 (26%).

The prevalence of MetS in the study was 36% (54 patients). HDL was significantly ($p = 0.03$) lower among MetS cases than those without MetS. However, there was no significant ($p > 0.05$) difference in other biochemical parameters between AGA cases with and those without MetS (Table 2).

The components of MetS such as high WC, low-level HDL, and hypertension were significantly ($p < 0.05$) associated with cases of AGA with MetS. None of the other components of MetS were significantly ($p > 0.05$) associated with AGA (Table 3).

There was no significant ($p > 0.05$) association of AGA grades with the prevalence of MetS among both males and females.

When we compared the prevalence of the components of metabolic syndrome and other associated systemic diseases in the men and women with AGA grades, hypertension was present among all men of grades VI and VII and all women of grade III (Table 4).

DISCUSSION

In androgenetic alopecia, there is androgen dependent conversion of the terminal scalp hairs into miniaturized vellus hairs [3]. It is usually observed on the vertex and fronto-temporal area in men and central thinning

Table 1: Distribution of type of hair loss depending on sex

Type of Hair Loss	Males ($n = 98$)		Females ($n = 52$)		p value[1]
	No.	%	No.	%	
I	13	13.3	29	55.8	NA
II	26	26.5	17	32.7	
III	27	27.6	6	11.5	
IV	10	10.2	0	0.0	
V	7	7.1	0	0.0	
VI	10	10.2	0	0.0	
VII	5	5.1	0	0.0	

[1]: Chi-squared test, NA: Not applicable

Table 2: Comparison of the biochemical profile between AGA cases with and without MetS ($n = 150$)

Biochemical Profile	With MetS	Without MetS	p value[1]
Total cholesterol (mg/dL)	165.50±50.21	171.77±50.38	0.46
S. triglycerides (mg/dL)	128.83±32.17	137.84±31.50	0.09
HDL (mg/dL)	52.18±17.68	58.48±16.22	0.03*
FBS (mg/dL)	92.52±22.50	97.34±25.11	0.24
TSH (mu/L)	3.34±3.32	2.54±2.34	0.08
CRP (mg/L)	2.16±0.92	2.37±1.02	0.21
ESR (mm/hr)	10.68±4.76	10.38±4.88	0.72

[1]: Unpaired *t*-test

Table 3: Components of MetS in patients of AGA with and without metabolic syndrome (National Cholesterol Education Program: Adult Treatment Panel III)

Biochemical Parameter#	Total No. of Cases (n = 150)		With MetS (54)		Without MetS (94)		*p* value[1]
	No.	%	No.	%	No.	%	
WC (> 90 cm in men, > 80 cm in women)	46	30.7	37	80.4	9	19.6	0.005*
Hypercholesterolemia > 200 mg/dL	58	38.7	18	31.0	40	69.0	0.31
Hypertriglyceridemia > 150 mg/dL	64	42.7	18	28.1	46	71.9	0.08
Low-level HDL < 40 md/dL	43	28.7	33	76.7	10	23.3	0.03*
Diabetes mellitus FBS > 100 mg/dL	46	30.7	13	28.3	33	71.7	0.18
Hypertension > 130/85 mmHg	53	35.3	43	81.1	10	18.9	0.001*

[1]: Chi-squared test, *: Significant, #: Multiple response

Table 4: Prevalence of the components of metabolic syndrome and other systemic diseases in the men and women with AGA (Hamilton Norwood and Ludwig classifications)

Sex	AGA Grade	HTN	DM	WC (cm)	BMI >25	Dyslipidemia	Heart disease	Others	No. of Cases (%)
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Males	I	0 (0.0)	0 (0.0)	2 (15.4)	2 (15.4)	8 (61.5)	0 (0.0)	0 (0.0)	13
	II	10 (38.5)	4 (15.4)	5 (19.2)	5 (19.2)	12 (46.2)	0 (0.0)	0 (0.0)	26
	III	7 (25.9)	4 (14.8)	5 (18.5)	5 (18.5)	15 (55.6)	0 (0.0)	0 (0.0)	27
	IV	9 (90.0)	10 (100.0)	9 (90.0)	8 (80.0)	2 (20.0)	0 (0.0)	0 (0.0)	10
	V	1 (14.3)	2 (28.6)	1 (14.3)	2 (28.6)	3 (42.9)	0 (0.0)	0 (0.0)	7
	VI	10 (100.0)	9 (90.0)	8 (80.0)	8 (80.0)	5 (50.0)	1 (10.0)	0 (0.0)	10
	VII	5 (100.0)	5 (100.0)	4 (80.0)	5 (100.0)	0 (0.0)	4 (80.0)	0 (0.0)	5
								TOTAL	98
Females	I	0 (0.0)	0 (0.0)	5 (17.2)	5 (17.2)	8 (27.6)	0 (0.0)	2 (6.9)	29
	II	5 (29.4)	6 (35.3)	5 (29.4)	5 (29.4)	7 (41.2)	0 (0.0)	1 (5.9)	17
	III	6 (100.0)	6 (100.0)	2 (33.3)	2 (33.3)	3 (50.0)	1 (16.7)	1 (16.7)	6
								TOTAL	52

of the crown with preserved frontal hairline seen in women. Increased 5 alpha-reductase activity with dihydrotestosterone (DHT) levels are implicated in the pathogenesis [4,5]. Hyperinsulinemia found in AGA patients favors vasoconstriction resulting in nutritional deficit in scalp hair follicles which is an important component of MetS also [6].

In the present study, the majority of AGA cases was between 31 and 40 (44%) years of age, with a mean age of 32.92 ± 7.98 years. This was in contrast to a study conducted by Wang et al. [7], in which the majority of the AGA patients belonged to the age group of 40 to 49 years (38.66%), followed by 20 to 29 years, and the mean age of presentation was 42.6 years (SD = 8.03 years).

In our study, more than half of the cases were males 98 (65.3%), compared to a study conducted by Devi et al. [8], in which 53.33% were males. In the present study, grade II hair loss of the Hamilton Norwood scale was the most common type of hair loss (28.7%). Grade I was the second most common type of hair loss (28%) and grade VII was the least common type of hair loss (3.3%). This study was in conformity with a study done by Wang et al. [7] and Shankar et al. [9], who also found grade II AGA to be the commonest type. In a study done by Batra et al. [10], more severe grades III and IV were the most common types (32% each).

In the present study, when each component of metabolic syndrome was considered individually, statistical association ($p < 0.05$) was identified for waist circumference, blood pressure, and HDL. Associations for the other components (TG, blood glucose, total cholesterol) were not statistically significant. Waist circumference was increased in 37 (80.4%) cases of AGA with MetS and 9 (9.6%) without MetS. This was in agreement with a study done by Devi et al. [8], who found that a high prevalence of abdominal obesity was in 25 (33.3%) cases of AGA and 11 (14.6%) controls with a significant *p* value (0.007). Similar findings were seen in studies done by Banger et al. [11] and Acibucu et al. [12].

In this study, hypertension was present in 81.1% of AGA cases with MetS and 18.9% of AGA without MetS with significant ($p = 0.001$) association. This was in conformity with studies done by Devi et al. [8] and Banger et al. [11]. The androgen-mediated receptors in the arterial wall endothelium and high serum androgen levels in AGA cases contribute to the proliferation

of smooth muscle cells in vessels and increase the tendency for hypertension. Another explanation for this association is the binding of androgens to mineralocorticoid receptors, favoring increased BP or increased peripheral sensitivity to androgens despite their normal circulating levels [5].

Low-level HDL was significantly associated ($p < 0.03$) with 33 (76.7%) cases of AGA with MetS and 10 (23.3%) cases without MetS in our study, which was in concordance with Devi et al. [8] and Arias-Santiago et al. [13]. However, the low HDL levels may be part of the general Indian population, as found in studies by Enas et al. [14] and Sawant et al. [15].

Androgens were proven to decrease HDL levels in experimental studies. High values of TGs and low values of HDL were associated with a transition from atheroma to atherothrombosis. A negative gradient relationship between the level of HDL and the risk for moderate or severe AGA (i.e., the higher the HDL level, the lower the risk for moderate or severe AGA) was demonstrated. Therefore, investigation and control of lipid profiles in patients with AGA may be important to reduce this risk.

Regarding the family history, in the present study, we found a significant association between the presence of AGA and a family history of AGA in 91 (60.7%) cases of AGA, followed by hypertension 57 (38%), dyslipidemia 39 (26%), diabetes mellitus 37 (24.7%), thyroid disorder 19 (12.7%). This was in agreement with a study done by Bas et al. [16] who also reported that AGA was the most common family history among cases of AGA.

In this study, higher fasting blood sugar levels and hypertriglyceridemia showed an insignificant association with AGA, which was in contrast with a study by Devi et al. [8], who reported a statistical significance of high fasting blood sugar and hypertriglyceridemia with AGA.

In the present study, the prevalence of MetS in AGA patients was 36%. It was seen in 35.7% of the males and 36.5% of the females. This finding was in agreement with a study by Devi et al. [8], in which the prevalence of MS was found in 25 cases (33.3%) (18 males and 7 females). Chronic inflammation occurring in AGA with the associated increase in proinflammatory cytokines in the arterial wall may contribute to the associated cardiovascular disease [6].

In the present study, we were unable to find any significant ($p > 0.05$) association of AGA grades with the prevalence of MetS among both males and females.

The limitations of our study included small sample size, a cross-sectional design of the study, and lack of control groups in the study.

CONCLUSION

AGA could be considered a predictor of MetS. Patients with an early onset and higher grades of AGA should be routinely screened for MetS, which will help in preventing long-term complications such as cardiovascular diseases.

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. Fulop T, Tessier D, Carpentier A. The metabolic syndrome. Pathol Biol. 2006;54:375-86.
2. Sawaya ME, Price VH. Different levels of 5 alpha-reductase type I and II, aromatase, and androgen receptor in hair follicles of women and men with androgenetic alopecia. J Invest Dermatol. 1997;109:296-300.
3. Birch MP, Lashen H, Agarwal S, Messenger AG. Female pattern hair loss, sebum excretion and the end-organ response to androgens. Br J Dermatol. 2006;154:85-9.
4. Otberg N, Finner AM, Shapiro J. Androgenetic alopecia. Endocrinol Metab Clin North Am. 2007;36:379-98.
5. Fujimoto R, Morimoto I, Morita E, Sugimoto H, Ito Y, Eto S. Androgen receptors, 5 alfa-reductase activity and androgen-dependent proliferation of vascular smooth muscle cells. J Steroid Biochem Mol Biol. 1994;50:169-74.
6. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: A potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol. 1999; 19:972-8.
7. Wang TL, Zhou C, Shen YW, Wang XY, Ding XL, Tian S, et al. Prevalence of androgenetic alopecia in China: A community-based study in six cities. Br J Dermatol. 2010;162:843-7.
8. Devi MM, Raju PVK, Gopal KVT, Rao TN. Study of prevalence of metabolic syndrome in androgenetic alopecia. Int J Res Dermatol. 2018;4:522-6.
9. Shanka r KD, Chakravarthi M, Shilpakar R. Male androgenetic alopecia: Population-based study in 1005 subjects. Int J Trichol. 2009;1:131-3.

10. Batra J, Khunger N, Maan KK. A study of the association of premature androgenetic alopecia with metabolic syndrome and coronary artery disease. Int J Res Dermatol. 2017;3:523-6.
11. Gopinath H, Upadya GM. Metabolic syndrome in androgenic alopecia. Indian J Dermatol Venereol Leprol. 2016;82:404-8.
12. Chakrabarty S, Hariharan R, Gowda DG, Suresh H. Association of premature androgenetic alopecia and metabolic syndrome in a young Indian population. Int J Trichol. 2014;6:50-4.
13. Agamia N. Risks for metabolic syndrome and cardiovascular diseases in both male and female patients with androgenetic alopecia. Egypt J Dermatol Venerol. 2015;35:49-55.
14. Enas EA, Mohan V, Deepa M, Farooq S, Pazhoor S, Chennikkara H. The metabolic syndrome and dyslipidemia among Asian Indians: A population with high rates of diabetes and premature coronary artery disease. J Cardiometab Syndr. 2007;2:267-75.
15. Sawant AM, Shetty D, Mankeshwar R, Ashavaid TF. Prevalence of dyslipidemia in young adult Indian population. J Assoc Physicians India. 2008;56:99-102.
16. Bas Y, Seckin HY, Kalkan G, Takci Z, Citil R, Onder Y, et al. Prevalence and types of androgenetic alopecia in north Anatolian population: A community-based study. J Pak Med Assoc. 2015;65:134-41.

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Our Dermatology Online

Original Article

Cutaneous leishmaniasis: The frequency according to geographical distribution in Al-Ramadi, Iraq

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ABSTRACT

Background: Cutaneous leishmaniasis (CL) is a protozoal disease endemic in most cities of Iraq. The disease is caused by different species of the *Leishmania* genus via the bite of an infected female sandfly. Different species of the sandfly act as a vector for the parasite to the different mammalian host, and the human is considered as an incidental host for these parasites. This study was arranged to clarify the distribution of the disease in different regions of Al-Ramadi, Iraq. **Materials and Methods:** An observational descriptive study for cutaneous leishmaniasis in Al-Ramadi was conducted for two years (2020 thru 2021). The disease was diagnosed depending on its cutaneous manifestations, while tissue smear and histopathology were done as a confirmatory test especially in atypical cases. Geographically, the city was divided into four regions: region A, region B, region C, and region D, each consisting of numerous districts. All patients were asked about their residence, houses construction, living within their farms, and animal breeding. **Results:** Three hundred and ninety-one patients were examined at the Dermatology Clinic of Al-Ramadi Teaching Hospital during a period of two years (2020 thru 2021). There was a variation in the number of cases during the two years. 53.70% and 46.30% of the cases occurred during the year 2020 and 2021, respectively. The mainly affected part of the city was along the left side of the Euphrates River (region A, constituting 36.57%). Within this region, Albu-Ali Jassim district was mostly involved (29%). On the right side of the river, the City Centre, region C, was the least one affected (16.88%). The Al-Thalia district within the region C was mostly involved (14.3%). **Conclusion:** CL is an endemic disease in Al-Ramadi and represents a public health problem. A high rate of infection was recorded alongside the Euphrates River, especially the rural district, while it was low in the urban side of the city. Any parts of the city may be affected, yet Albu-Ali Jassim, Al-Tamim, Al-Sufia, and Al-Thalia were the most frequently involved regions of the city.

Key words: Leishmaniasis, Old World, Sandfly, Amastigote, Ramadi

INTRODUCTION

Leishmaniasis is a disease caused by obligate intracellular parasites of the genus *Leishmania* [1]. These parasites are transmitted by the bite of an infected female sandfly [2]. They exist in two forms: the amastigote and the promastigote [3].There are mainly three clinical types of leishmaniasis: visceral, cutaneous an, mucocutaneous [4,5].

The incidence of cutaneous leishmaniasis (CL) is estimated to be 1.0 – 1.5 million cases a year [6]. The disease possesses a substantial risk for residents, military personnel, and those working or traveling to the endemic areas [7]. CL is classified geographically into the old-world and new-world leishmaniasis [8]. Old-world CL is caused by *L. tropica*, *L. major*, and *L. aetiopica* [9]. New-world leishmaniasis is caused by *L. mexicana complex* species and L. *brasiliensis complex* [8]. Regarding CL in Iraq, the main species of Leishmania are *L. tropica* and *L. major*, which cause the anthroponetic and the zoonotic type, respectively [10]. The virulence of the parasite, the host defense mechanisms, and some environmental factors determine the clinical features and the course of infection [11].

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The disease has been endemic in Iraq since a long time, yet from now and then, runs outbreaks or epidemics according to environmental factors. The frequency of the disease has increased so it may be seen in many cities from north to south of Iraq [12]. CL manifests with various morphologies that range from small papules with a central crater to large and disfiguring ulcers [13]. The lesion usually appears on the exposed parts of the body, especially the face and extremities [14] (Figs. 1a – 1d). In endemic regions, the diagnosis of the infection may be established easily depending on its clinical presentation [15]. In unusual cases, tissue smear, culture, histopathological examination, and polymerase chain reaction (PCR) tests may be performed for confirmation of the infection [16]. CL is an endemic disease in Al-Ramadi [1]. This study was arranged to shed light on the distribution of the disease in different regions of the city.

MATERIALS AND METHODS

This study was an observational, descriptive study on CL in Al-Ramadi. This city is the capital of Al-Anbar governorate that lies west of Iraq. The city is divided by the Euphrates River into two halves, right and left. The right side is subdivided into two parts by a water drain that originates from the right side of the Euphrates. This water drain evacuates excess water from that river.

Geographically, the city was divided into four regions. Region A is the part that lies on the left side of the Euphrates River. The area on the right side of the Euphrates is further subdivided into three regions. Region B lies to the west of the water drain. Region C includes the part to the east of this drain, which resembles the city center. Region D is the east of the city. Each one of these regions consists of numerous districts (Fig. 2).

Throughout the city and its surroundings, there are numerous agriculture farms. Also, animal breeding is distributed alongside the Euphrates River and about periphery of the city. The inhabitants of Al-Ramadi are around 900,000 people [1]. Patients affected with CL were examined at the Dermatology Department of Al-Ramadi Teaching Hospital.

Three hundred and ninety-one patients infected with CL were included in this study during the period from the first of January 2020 to the end of December 2021. Depending on at least two dermatologists, the patient who had clinical manifestations of CL was included in the study. In an uncertain infection, a tissue smear was taken from the affected site, and if the amastigotes were not seen, it was excluded from the study. Full information was obtained from all patients regarding their social state, lifestyle, cultural behavior, housing construction, farming, and animal breeding. Informed consent was taken from all patients. An approval for the study was obtained from the ethical committee.

Statistical Analysis

We depended on SPSS, version 22. Statistical analysis of efficacy was completed by chi-squared test. p values < 0.05 were considered significant, while p values < 0.01 were considered highly significant.

RESULTS

A total of 391 patients affected by CL were examined at the Dermatology Clinic for a period of two years (2020 thru 2021). Most cases of CL were found in region A (36.57%) while the least were recorded in region C (16.88%) (Table 1). Within region A, the most commonly affected area was Albu-Ali Jassim (29%)

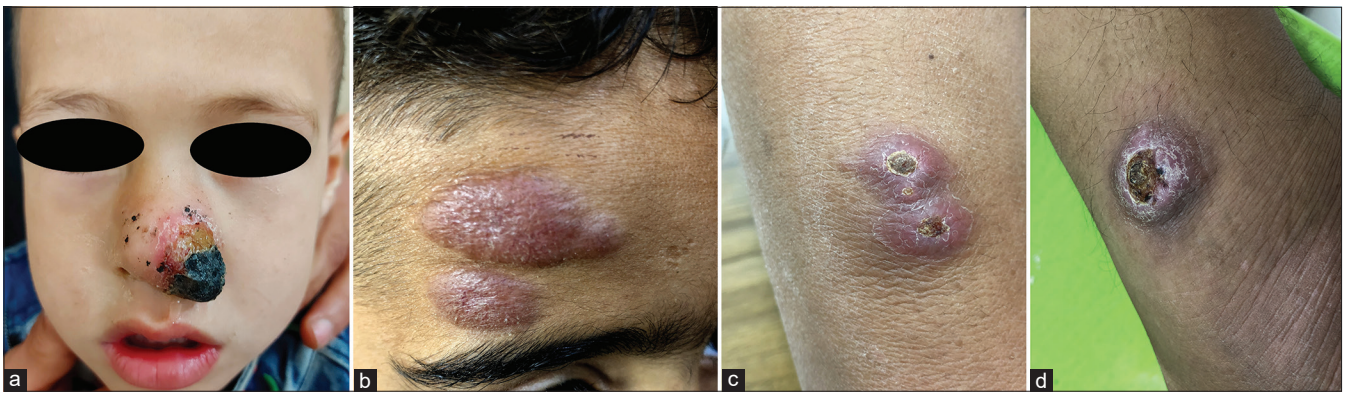

Figure 1: Cutaneous leishmaniasis: a) left side of the nose, b) the forehead, c) the forearm, d) the lower leg.

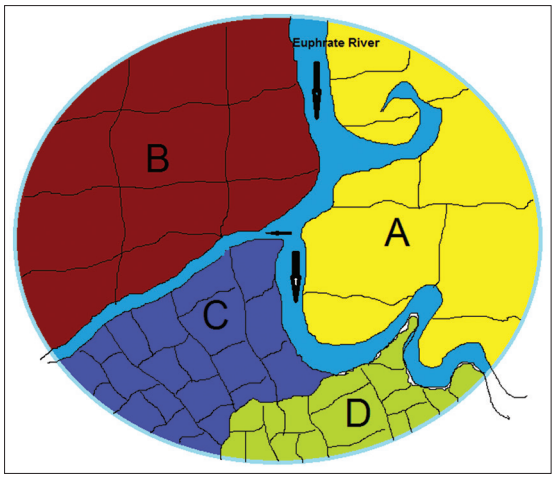

Figure 2: A diagram of the different regions of Al-Ramadi.

Table 1: Patients affected with cutaneous leishmaniasis in different regions of Al-Ramadi during the two-year period (2020 thru 2021).

Region of City	2020	2021	Total
A	90**	53**	143 (36.57%)**
B	68	42	110 (28.13%)
C	24	42	66 (16.88%)
D	28	44	72 (18.42%)
Chi-squared	58.2	14.5	39.5

(p value < 0.01), and the least commonly affected was Albunimr (1%) (Fig. 3).

In region B, Al-Tamim district was the most involved (24.6%) (p value < 0.01), and Al-Angor district was the least affected (1%) (Fig. 4). Al-Thaila district was mostly involved in region C (14.3%) (p value < 0.05), while Al-Aziziya was the least involved (1%) (Fig. 5). Al-Sufia was the most involved in region D (50%) (p value < 0.01), while Al-Nassaf was the least involved (Fig. 6).

DISCUSSION

CL has been one of the communicable diseases endemic in Iraq since a long time ago, yet its frequency varies according to numerous environmental factors that affect the breeding of the sand fly as a vector and reservoir animals. This disease represents a major public health problem [17]. The disease was reported in most cities of the country from south to north [18]. In the south (Al-Diwaniya and Al-Rhamania), 300 and 400 cases, respectively, were recorded in 2009 [7,19]. In the north (Kirkuk and Rabeea), 571 and 1482 cases, respectively, were recorded for one year [17]. In Kurdistan provinces, 228 and 257 cases of CL were reported during 2015 and 2017, respectively [7]. Thus, the infections were spread all over Iraqi cities,

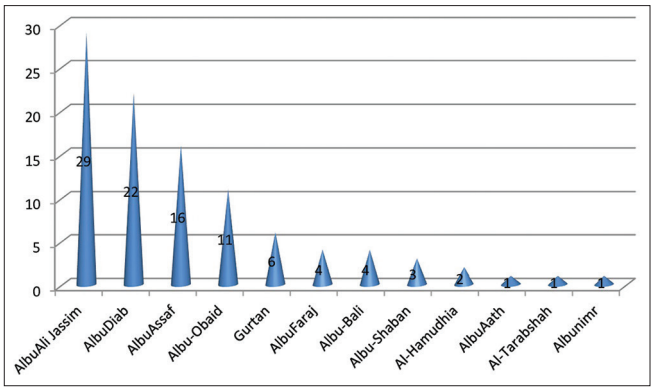

Figure 3: Distribution of cutaneous leishmaniasis in region A of Al-Ramadi city during the two-year period. Chi-squared = 64.1 **. ** sig. at 0.01, * sig at 0.05. Significantly high in Albu Ali Jassim (p value < 0.01).

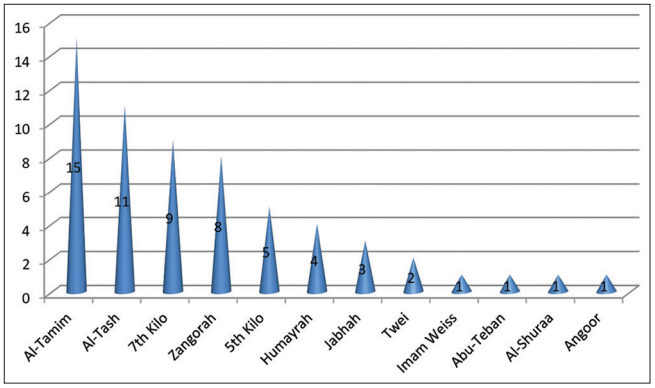

Figure 4: Distribution of cutaneous leishmaniasis in region B of Al-Ramadi during the two-year period. Chi-squared = 21.7 **, ** sig. at 0.01, * sig at 0.05. Highly significant in Al-Tamim (p value < 0.01).

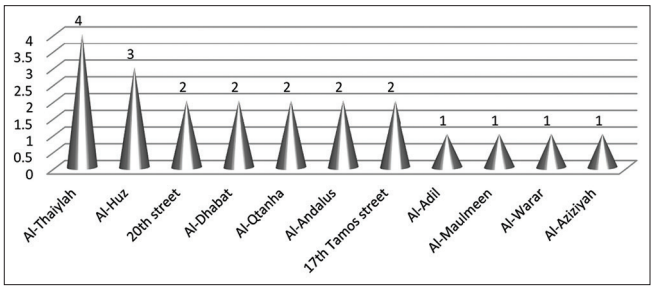

Figure 5: Distribution of cutaneous leishmaniasis in region C of Al-Ramadi during the two-year period. Chi-squared = 8.1 *. ** sig. at 0.01, * sig at 0.05. Significant involvement in Al Al-Thaiylah (p value < 0.05).

with some variation in the number of cases. There are numerous factors that play a role in the outcome of the infection, such as availability of the vector and reservoirs for the parasite and health services planning for eradication and control of the vectors, in addition to the cultural behavior of the population that resides in these particular regions.

There was a difference in rate of infection during the years 2020 (53.7%) and 2021 (46.3%). This variation

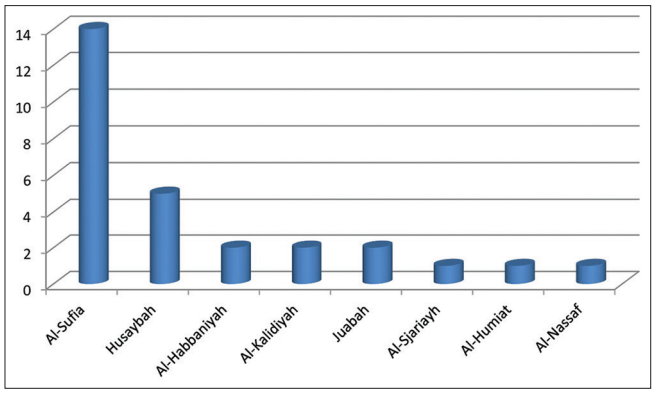

Figure 6: Distribution of cutaneous leishmaniasis in region D of Al-Ramadi during the two-year period. Chi-squared = 41.5 **. ** sig. at 0.01, * sig at 0.05. Significantly high in Al-Sufia (*p* value < 0.01).

may be explained by two factors. The first one may be related to an improvement in the public health services. These services will control the source of the infections and provide a perfect management for the patients. The second reason behind this variation may be due to the disease itself. CL is characterized by an instability in its behavior, sometimes presenting with high and unsuspected epidemics and with a low rate in others [19].

Due to presence of the Euphrates River, there are widespread areas of agricultural farms, particularly on the right side (region A). These areas resemble a rural district, where most people engage in a farming work as a main source of their income. This farming job by itself increases the risk of CL, as described by Alzahrani et al. [20] and Yadon et al. [21].

In rural areas, most people are used to build their houses inside or nearby their farms. This will expose them more to the insect bites [18]. Animal breeding is distributed through the regions. The presence of animals close to the houses will increase the risk of infection, as mentioned by Votýpka et al. [22]. These animals will represent a reservoir for the parasites [23,24].

The risk of infection will increase especially when these animals are put in a clay-made building with multiple fissures in their walls especially, during rainfall [22]. This will create a hot and humid weather that resemble an ideal environment for the spread of the sand fly [25].

The recorded cases within the city center (Region C), in comparison with other regions, were the lowest rate (16.88%). This is because the living conditions in region C resemble an urban district. The presence of regular house construction and arrangement will decrease the risk of infection, as described by Rojas et al. [26]. The availability of nearby health services with good housing and domestic sanitary conditions will limit the disease spread [25].

The outbreak of CL occurs when many non-immune people migrate to regions where transmission is high [17].This occurred when the city was prone to a terrorist attack. This forced people to leave their houses and migrate to different parts of the country. Also, most of them had difficult living conditions and bad health services within camps.

Numerous factors determine the risk of infection with CL, such as poverty, malnutrition, and population migration [19,27]. Environment and climate changes may affect the disease activity as described by Hakkour et al. [25]. When these factors are applied to the main parts of the city, a difference in the rate of infection from region A to region C will be noticed. Also, these variations will determine the risk of infection in different parts of the same region. Accordingly, we find that Albu-Ali Jassim area is the most involved within region A and the same may apply to other regions.

CONCLUSION

Numerous factors determine the endemicity of cutaneous leishmaniasis in a particular area. Therefore, determination of the focus and sources of the infection through geographical study of the area is the first step in order to control outbreaks and epidemics of the disease and to provide protection for the community.

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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. Mancy A, Awad KA, Abd-AL-Majeed T, Jameel NF. The epidemiology of cutaneous leishmaniasis in Al-Ramdai, Iraq. Our Dermatol Online J. 2022;13:402-7.
2. Sharquie KE, Noaimi AA, Saleh BA. Cutaneous leishmaniasis as imitator of skin diseases and a diagnostic challenge. J Cosm Dermatol Scien Applicat. 2018;8:158-77.
3. AL-Aubaidi I, Al Bayati N, Al Haidari S, Al-Azzawi M. Some histopathological features of cutaneous leishmaniasis-in Iraqi patients. Int J Pharm Tech Res. 2016;9:640-5.
4. Reithinger R, Dujardin JC, Louzir H, Pirmez C, Alexander B, Brooker S. Cutaneous leishmaniasis. Lancet Infect Dis. 2007;7:581-96.
5. Barkati S, Ndao M, Lib M. Cutaneous leishmaniasis in the 21st century: From the laboratory to the bed. Curr Opin Infect Dis. 2019;32:419-25.
6. El-Deen LD, Abul-Hab J, Abdulah SA. Clinico-epidemiological study of cutaneous leishmaniasis in a sample of Iraqi Armed Forces. Iraqi J Comm Med April. 2006;19:98-103.
7. Abdulla QB, Shabila NP, Al-Hadithi TS. An outbreak of cutaneous leishmaniasis in Erbil Governorate of Iraqi Kurdistan Region in 2015. J Infec Dev Ctries. 2018;12:600-7.
8. Bailey MS, Lockwood DNJ. Cutaneous leishmaniasis. Clin Dermatol. 2007;25:203-11.
9. Masmoudi A, Hariz W, Marrekchi S, Amouri M, Turki H. Old World cutaneous leishmaniasis: Diagnosis and treatment. J Dermatol Case Rep. 2013;7:31.
10. Al-Warid HS, Al-Saqur IM, Al-Tuwaijari SB, Zadawi KAMAL. The distribution of cutaneous leishmaniasis in Iraq: Demographic and climate aspects. Asian Biomedicine. 2017;11:255-60.
11. Aytekin S, Ertem M, Yağdıran O, Aytekin N. Clinico-epidemiologic study of cutaneous leishmaniasis in Diyarbakir Turkey. Dermatol Online J. 2006;12:14.
12. Al-Obaidi M, Yassen M, Al-Saqur IM. Survey study on the prevalence of cutaneous leishmaniasis in Iraq. Iraqi J Scien. 2016;57:2181-7.
13. Khan SJ, Muneeb S. Cutaneous leishmaniasis in Pakistan. Dermatol Online J. 2005;11:4.
14. James WB, Berger TG, Elastone DM. Parasitic infestations, bites and stings: In Andrews diseases of the skin, clinical dermatology. 13th ed. Vol. 1. Philadelphia: WB Saunders company; 2020. 491-526 p.
15. Thakur S, Joshi J, Kaur S. Leishmaniasis diagnosis: An update on the use of parasitological, immunological and molecular methods. J Parasit Dis. 2020;44:253-72.
16. Singh S. New developments in diagnosis of leishmaniasis. Indian J Med Res. 2006;123:311.
17. Al-Bajalan MMM, Al-Jaf SMA, Niranji SS, Abdulkareem DR, Al-Kayali KK, Kato H. An outbreak of Leishmania major from an endemic to a non-endemic region posed a public health threat in Iraq from 2014-2017: Epidemiological, molecular and phylogenetic studies. PLoS Negl Trop Dis. 2018;12:e0006255.
18. Al-Hayali HL. Overview on epidemiology of leishmaniasis in Iraq. Rafidian J Scien. 2021;30:28-37.
19. AlSamarai AM, AlObaidi HS. Cutaneous leishmaniasis in Iraq. J Inf Develop Coun. 2009;3:123-9.
20. Alzahrani MJ, Elfaki N, Abdalla YHA, Alkhadher MA, Ali MHM, Ahmed WAM. Cutaneous leishmaniasis: Associated risk factors and prevention in Hubuna, Najran, Saudi Arabia. Int J Gen Med. 2023;16:723-31.
21. Yadon ZE, Rodrigues LC, Davies CR, Quigley MA. Indoor and peridomestic transmission of American cutaneous leishmaniasis in northwestern Argentina: A retrospective case-control study. Am J Trop Med Hyg. 2003;68:519-26.
22. Votýpka J, Kasap OE, Volf P, Kodym P, Alten B. Risk factors for cutaneous leishmaniasis in Cukurova region, Turkey. Trans R Soc Trop Med Hyg. 2012;106:186-90.
23. De Araujo AR, Portela NC, Feitosa APS, da Silva OA, Ximenes RAA, Alves LC, et al. Risk factors associated with American cutaneous leishmaniasis in an endemic area of Brazil. Rev Inst Med Trop. 2016;58:86.
24. Alsamarai AM, Alobaidi AH, Aljumaili ZKM, Jasim MM, Qatal S. Cutaneous leishmaniasis in Iraq: A continuing endemic disease. J Drug Des Res. 2016;3:1204.
25. Hakkour M, Hmamouch A, Mahmoud El Alem M, Bouyahya A, Balahbib A, El Khazraji A, et al. Risk factors associated with leishmaniasis in the most affected provinces by leishmania infantum in Morocco. Interdiscip Perspect Infect Dis. 2020;2020: 6948650.
26. Rojas CA. An ecosystem approach to human health and the prevention of cutaneous leishmaniasis in Tumaco, Colombia. Cad Saude Publica. 2001;17:S193-200.
27. Ngere I, Boru WG, Isack A, Muiruri J, Obonyo M, Matendechero S, et al. Burden and risk factors of cutaneous leishmaniasis in a peri-urban settlement in Kenya, 2016. PLoS One. 2020;15:e0227697.

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Our Dermatology Online

Original Article

Epidemiological, clinical, and etiological aspects and management of chronic ulcers at the University Hospital Center of Dermatology in Bamako, Mali

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ABSTRACT

Background: Chronic ulcers of the lower limb (CULL) are characterized by non-healing skin loss, often associated with vascular, neurological, infectious, traumatic, or tumoral factors. These ulcers are prevalent, recurrent, severe, and have significant socio-economic implications. While Western data show a higher prevalence among women and the elderly, with varying rates (0.10% to 0.80%), developing countries, especially in sub-Saharan Africa, report a higher prevalence among young men due to infectious causes. Despite their impact, CULL often lacks attention from health authorities, resulting in delays in medical consultation. This study aims to share experiences in understanding the epidemioclinical aspects and management of CULL. **Objective:** The objective was to offer a comprehensive overview of the epidemiological and clinical characteristics and treatment strategies for chronic lower limb ulcers observed at the University Hospital Center of Dermatology in Bamako. **Patients and Methods:** Conducted at the Dermatology and Venereology Department of the University Hospital Center of Dermatology in Bamako, this cross-sectional study spanned a period from January to December 2021. It included 520 patients, with 22.1% having chronic ulcers of the lower limbs. Males (52.2%) were predominant, with an average age of 42.4 years. Trauma triggered 73.0% of the cases, and more than half waited over a year before seeking medical help. Bacteriological examinations revealed microbial infections in 67.8% of the cases. **Results:** There was a 22.1% prevalence of chronic lower limb ulcers among the 520 patients. Males represented 52.2%, with a median age of 42.4 years. Trauma was the primary trigger in 73.0% of the cases. Bacteriological examinations identified various infections, with 67.8% being infectious in origin. There were diverse characteristics in size, shape, and edge conditions of the ulcers. Trauma was the leading factor in 73.0% of the cases. Bacteriological examinations identified Gram-negative bacilli, *Staphylococcus aureus*, *Streptococcus*, with 67.8% of the ulcers being infectious in origin. There was outpatient treatment in 64.3% of the cases. Therapies included postural drainage, venotonics, vasculoprotectors, analgesics, compression stockings, and surgical interventions. Antibiotic therapy based on antibiograms for infectious ulcers. There was maintenance treatment with delayed penicillin in recurrent cases; successful skin grafting in 80.9% of cases, with 40.8% achieving complete healing in less than three months.

Key words: Chronic ulcers, Epidemiological, Clinical, Etiological, Management

INTRODUCTION

The chronic ulcer of the lower limb (CULL) is defined as a loss of skin substance without a spontaneous tendency to heal. It is generally located in the dependent part of the lower limbs (LL), associated with a pathological process of various etiologies: vascular, neurological, infectious, traumatic, or tumoral [1]. Chronic ulcers

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of the lower limbs are common, recurrent, severe, and have a negative socio-economic impact [2]. Reading epidemiological data from Western series clearly shows that the patients are mostly women and elderly individuals (40–80 years) [3-5]. The analysis conducted by Begaud [2] based on thirteen epidemiological studies published between 1983 and 1997 showed a high prevalence within the general European population. According to this study, the rate fluctuated between 0.10% and 0.80%. In France, this represented at least 60,000 to 180,000 individuals among a population of 60 million. In the U.S., 500,000 to 600,000 individuals are treated for CULL each year [6]. In contrast, in developing countries, especially in sub-Saharan Africa, chronic ulcers of the lower limbs affect young men (25 to 35 years old), with a male-to-female ratio ranging between 1:5. In Africa, the predominant etiology is infectious and is exacerbated by malnutrition and precarious living conditions [7-10]. The studies conducted in Africa do not allow for the determination of a continental prevalence of the chronic ulcer of the lower limb [7-11]. A study conducted in Mali in 2004 reported that, out of 105 cases of chronic ulcers of the lower limbs, 53.3% were of infectious origin, and men represented 60% of the cases [12]. Despite these initial compelling results and the devastating nature of these ulcers, often leading to dramatic complications such as the risk of tetanus, septicemia, hemorrhages, and malignant degeneration, as well as their major socio-economic impact, chronic ulcers of the lower limbs do not receive sufficient attention from health authorities. Added to this is the delay in seeking medical consultation and resorting to traditional practitioners, resulting in serious complications. The aim of this work was to share our experience in understanding the epidemioclinical aspects and management of chronic ulcers of the lower limbs.

Objective

The objective was to present in detail the epidemiological and clinical aspects and therapeutic approaches adopted for chronic ulcers of the lower limbs identified at the University Hospital Center of Dermatology in Bamako.

PATIENTS AND METHODS

Our study was conducted at the Dermatology and Venereology Department of the University Hospital Center of Dermatology in Bamako. The University Hospital Center of Dermatology in Bamako is a specialized center for research on leprosy and endemic-epidemic diseases. It is located in the IV district of the Bamako District, specifically, in the Djicoroni-Para neighborhood. In addition to leprosy, its scope of activities includes dermatology, STIs/HIV-AIDS, and vaccine research. Several units are distinguished within the center: Leprology, Dermatology, Biology, Surgery-Rehabilitation, and the Vaccine Development Center (CVD).

We conducted a cross-sectional, descriptive study with prospective data collection on patients hospitalized and receiving outpatient care for chronic ulcers of the lower limbs at the Dermatology and Venereology Department of the University Hospital Center of Dermatology in Bamako for one year (from January to December 2021). It included all patients diagnosed with ulcers persisting for more than three months and followed at the Dermatology Department of the University Hospital Center of Dermatology in Bamako during the study period. Patients lost to follow-up or those who refused to participate in the study were excluded. A survey form allowed us to gather the following data.

Sociodemographic and epidemiological data (age, sex, ethnicity, occupation, marital status, and place of origin), medical history (HIV, diabetes, sickle cell anemia, etc.), surgical history, and lifestyle factors (tobacco, alcohol, substance abuse, herbal remedies).

Clinical and etiological data based on circumstances of occurrence; characteristics of the ulcer (location, size, shape, edges, base, periwound skin); general examination.

Paraclinical data: complete blood count (CBC)/ erythrocyte sedimentation rate (ESR), fasting blood glucose, HIV serology, pus and/or serosity sampling for bacteriological examination and antibiogram, hemoglobin electrophoresis/Emmel test, V.D.R.L./ T.P.H.A, X-ray of the affected lower limb, and lesion biopsy for anatomopathological examination. Additional tests may be requested depending on the clinical orientation; therapeutic data (management according to etiology); treatment outcomes. The epidemiological, clinical, and paraclinical data collected through a questionnaire was entered and analyzed using SPSS 16.0 software and document writing was performed using MS Office Word 2016. The free and informed consent of all patients was obtained before their inclusion.

RESULTS

Epidemiological Aspects

From January to December 2021, 520 patients were hospitalized and followed at the Dermatology and Venereology Department of the University Hospital Center of Dermatology in Bamako, including 115 cases of chronic ulcers of the lower limbs (Fig. 1), representing a hospital prevalence of 22.1%.

The male sex represented 52.2% (60 cases). The average age was 42.4 years, with extremes ranging from 10 to 75 years. The most represented age group was between 30 and 39 years, accounting for 26.1%. Among the identified professions, artisans and workers were the majority, accounting for 33.9%. Professions involving prolonged standing were present in 49.6% of the cases, mainly composed of traders and workers. The patients came from all regions of Mali, with a significant representation from Bamako (34.8%). A history of chronic smoking was reported in 23.5%, and a combination of antibiotics + NSAIDs + traditional therapy was found in 66.1% of our patients.

Clinical Aspects

Trauma was the most common triggering factor, accounting for 73.0% of the cases. More than half of the patients waited over a year before their first consultation (61 cases), representing 53.0%. The size, shape, and condition of the edges varied (rounded, polycyclic, geographic contour) (Fig. 2).

Bacteriological examinations conducted on our patients found Gram-negative bacilli in four cases, accounting for 21.1% (*Pseudomonas aeruginosa*, *Escherichia coli*), *Staphylococcus aureus* in six cases, accounting for 31.6%, *Streptococcus* (*Streptococcus spp.*, *Enterococcus spp.*) in seven cases, accounting for 36.8%, and plurimicrobial infections in two cases (Fig. 3), accounting for 10.5%. Infectious origin ulcers comprised 67.8% of our series, including 60.9% of bacterial origin, 5.2% of fungal origin (Fig. 4), and 1.7% of parasitic origin (cutaneous leishmaniasis).

Therapeutic Aspects

Patients were treated on an outpatient basis in 64.3% of the cases.

Several therapies were used for venous ulcers, including postural drainage by elevating the limbs associated with strict rest, venotonics (Veinosmine*, Cyclo 3 fort*), vasculoprotectors (Ginkor fort*), analgesics (Paracetamol 500 mg), elastic compression

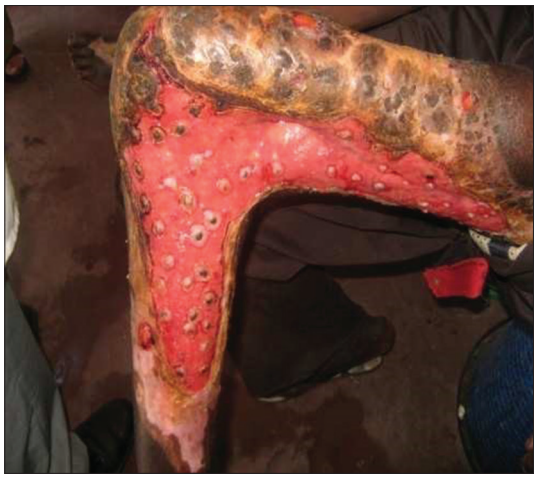

Figure 2: Necrotizing ulcer with a rupture of the Achilles tendon.

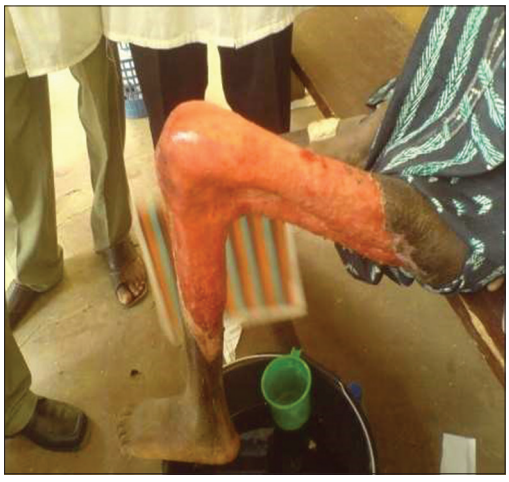

Figure 1: Large ulceration affecting one-third of the thigh.

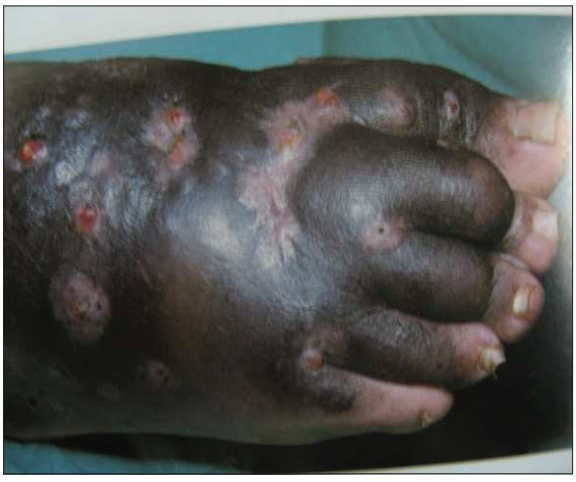

Figure 3: White grain mycetoma.

Figure 4: Budding ulcer, immunosuppressed condition.

stockings and bands, and drainage kinesiotherapy for lymphedema. For arterial ulcers, the patients were given vasculoprotectors (Ginkor fort*), analgesics (Paracetamol 500 mg), and antiplatelet agents (low-dose aspirin, heparin). Then, the patients were referred to surgery for further management. Regarding infectious ulcers, depending on the etiology, patients received antibiotic therapy based on the antibiogram or, alternatively, broad-spectrum antibiotic therapy (Amoxi + Clavulanic Acid: 50–100 mg/kg/day, 1 to 3 doses). Analgesics (Paracetamol: 40 mg/kg/day in 2 to 3 doses/day), intramuscular or peri-lesional Glucantime, thermotherapy on lesions, antifungal treatment (Fluconazole: 200 mg per day) were also administered. In the case of malignant degeneration confirmed by histology, surgical intervention with lymph node dissection or leg amputation was performed in orthopedic surgery. Potassium permanganate bath followed by dermal Betadine was the most commonly used, representing 83.5% of the cases, followed by mechanical and/or chemical debridement (Cutimed Gel*), performed in almost all cases (90.4%) as local care. Iron supplementation and multivitamin therapy were administered in all cases of clinical and/or biological anemia, with tetanus vaccination performed in all cases.

Therapeutic Evolution

Maintenance treatment with delayed penicillin for 3 to 4 months after healing was given in recurrent ulcer cases and in cases of lymphedema. Skin grafting was successfully performed in 80.9% (93 cases). In our study, 47 patients (40.8%) achieved complete healing in less than three months of treatment.

COMMENTS AND DISCUSSION

Methodology

Out of a total of 520 patients hospitalized and followed in the service for one year, we included 115 cases of chronic ulcers of the lower limbs. The reduced sample size of 115 was due to the lack of means for some patients to undergo additional examinations and to fulfill prescriptions, as well as the loss of follow-up for certain patients.

Epidemiology

In our sample, men were the most affected, with a sex ratio of 1.1. The age group of 30–40 years was the most represented and particularly active (26.1%). This epidemiological data was comparable to those by Cissé [11] in Mali, who found a sex ratio of 3.1 in favor of men, with an average age of 38.45 years +/- 12.3. A study by Alzouma [12] in 2004 found a predominance of young men with an average age of 41.59 years +/- 18.4 and a sex ratio of 1.5. In general, our studies were not comparable to those conducted in Western countries, in which the maximum incidence was observed in the elderly, preferably in females, with a peak around 70–80 years [1]. This difference is explained by the frequency of trauma, the main triggering factor for chronic ulcers of the lower limbs in young individuals, constituting the most active layer of our population. We found 57 cases of professions with prolonged standing, representing 49.57%, which explains the frequency of varicose ulcers in our sample. The problem is that we cannot withdraw them from their activities or change their profession. There is also the issue of insufficient infrastructure or rather qualified healthcare personnel in certain regions, given that many of our patients resided in rural areas.

Clinical Aspects

Trauma to the lower limb (MI) was the most commonly reported triggering factor, accounting for 73% of the cases. This frequency is higher than that found by Cissé [11] in Mali, which was 54%, and by Alzouma [12] in Mali, which was 65.7%. Once again, our study confirmed the damage caused by neglected traumas to the lower limbs in our region. The characteristics of the ulcer, such as the number, location, size, shape, condition of the edges, base, and peri-ulcer skin, varied widely and often assisted us in determining the etiology. These elements allowed us to assess the severity and chronicity of the ulcerations. Thus, 61.7% of our cases had lesions

on the right leg, and 16.5% had bilateral involvement. Bilateral involvement is an indicative factor for certain etiologies (vascular, hematological). Necrotic, purulent, and fibrinous lesions accounted for 88.7% of the cases, indicating the severity of infection. The condition of the edges and the base of the ulceration helped evaluate chronicity, direct toward a specific etiology (tumoral, mycobacteria), and predict prognosis or healing duration. In our study, the edges were elevated in 54.8% and jagged in 1.7% of the cases. The base was necrotic in 88.7% of the cases, with granulation observed in 15.7% of the cases. Varicose lesions suggested a vascular etiology of the ulceration; in our series, varices were observed in 4.3% of the patients. Clinical anemia was found in 33.9% of the cases, and a general state alteration was present in 2.6% of our patients. This may be explained by malnutrition and wound exudates. The presence of pain was reported in 67% of the cases. This presence of pain allowed us to consider malignant transformation, especially when associated with an ulceration that budded and bled at the slightest touch, and to think of an inflammatory process of infectious origin. Meanwhile, in the literature [1], the presence of pain was mainly assessed initially to classify vascular UCMI into two etiologies: venous or arterial.

Paraclinical Aspects

Paraclinical examinations were conducted on our patients. HIV serology was positive in 3.5% (4 out of 43 performed), hemoglobin abnormalities in 6.1% of the cases (7 out of 19 performed, including 4 SS trait cases and 3 AS trait cases), hyperglycemia in 5.2% of the cases (6 out of 74 performed), and biological anemia found in 3.5% of the cases (4 out of 63 performed). In our series, there was nothing to suggest that anemia was caused by the ulcer, and vice versa, yet it may be affirmed that it contributes to delayed healing. Most patients showed clinical improvement early in the anti-anemia treatment. SS sickle cell patients seem to be more affected by leg ulcers than those with AS traits, which is easily understandable: tissue damage is more significant in the former. Pus samples from the ulcer were obtained in 30 cases out of 115 patients. Bacteriological examinations revealed Gram-negative bacilli (*Pseudomonas aeruginosa*, *Escherichia coli*) in 4 cases, *Staphylococcus aureus* in 6 cases, *Streptococcus* (*Streptococcus spp.*, *Enterococcus spp.*) in 5 cases, and cases of polymicrobial infections in 4 cases. Taking into account the number of cases where the base of the ulcer is purulent (102 cases), the number of bacteriological examinations performed was insufficient; 85 cases, or 73.9%, should have undergone pus sampling for bacteriological examination. In our series, only 41 patients underwent a leg X-ray: normal in 31 cases, bone involvement in 10 cases. This complication is formidable because germs lodged in bone structures are less accessible to antibiotic therapy. Management often requires surgical intervention; 2 cases were amputated in our series, representing 1.7%. Histological examinations were conducted in 32 out of 115 cases: no signs of malignancy were observed in 26 cases, or 22.6%, while signs of malignancy were present in 6 cases, or 5.2% (verrucous squamous cell carcinoma in 2 cases, differentiated keratinizing and infiltrating squamous cell carcinoma in 4 cases). Ulcers resistant to treatment, evolving over many years, have a risk of cancerization. However, they remain a rare yet not exceptional complication. Regarding vascular ulcers, Doppler ultrasound of the lower limbs was performed in 17 cases. Unlike in developed countries, Doppler ultrasound of the lower limb veins is not routinely performed in our regions due to its cost, which is not always accessible to all patients.

Therapeutic Aspects

All patients in our study received various types of local care. A potassium permanganate (KMnO4) bath of the affected limb before dressing was administered to disinfect the wound and facilitate healing. Skin grafting with success was performed in 80.9% of the cases to accelerate healing, strengthen the scar, and alleviate pain. We referred two cases to orthopedic surgery for amputation due to total necrosis of the affected limb. For treating infections, a combination of amoxicillin and clavulanic acid was used in 85% of the cases at the beginning of treatment, later replaced by another antibiotic sensitive according to the results of the antibiogram. In cases of clinical and/or biological anemia, iron supplementation was systematic. Tetanus vaccination was administered to all patients upon admission. Analgesics, multivitamins, antiparasitics, and anxiolytics were used as needed. The healing of leg ulcers often requires strict rest, which may only be achieved in a hospital setting. 32.5% of our patients were treated for a period equal to or longer than three months. However, any treatment exceeding three months further increases the already high cost of ulcer treatment.

Evolution

In our series, we observed 104 cases of favorable evolution (Figs. 5a – 5c), including 78 cases of complete healing, 11 cases of unfavorable evolution, including

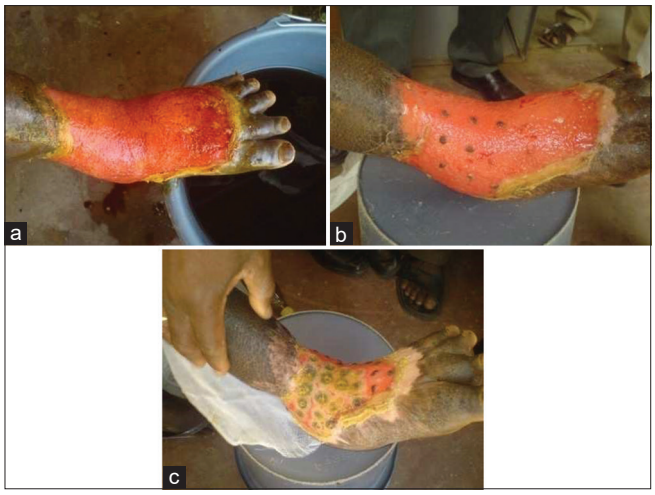

Figure 5: (a) Beginning of grafting after ulcer budding. (b) Ulcer with patch grafting. (c) Several weeks after grafting.

2 cases of recurrence, 7 cases of complications, and 2 cases of stationary evolution. Thus, the therapeutic success was evaluated at 67.8% (complete healing). However, more than 1/4 of the patients (34 cases, 29.57%) were not reviewed after discharge.

CONCLUSION

At the end of our case study, it was clear that patient neglect or ignorance and the inadequacy of healthcare services were factors that had led the initial lesions to evolve into chronicity. Any ulceration of the lower limbs should be taken seriously by patients, healthcare professionals, and health authorities. Furthermore, chronic leg ulcers should receive early intervention to prevent dramatic complications.

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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. Amblard P, Leccia MT. Leg ulcer. Encycl Méd Chir. 2001:16.
2. Begaud B. Epidemiology of leg ulcers. Ann Dermatol Venereol. 2002;129:1225-6.
3. Morrell CJ, Walters SJ, Dixon S, Collins KA, Brereton LM, Peters J, et al. Cost effectiveness of community leg ulcer clinics: Randomised controlled trial. BMJ. 1998;316:1487-91.
4. Franks PJ, Bosanquet N, Connolly M, Oldroyd MI, Moffatt CJ, Greenhalgh RM, et al. Venous ulcer healing: Effect of socioeconomic factors in London. J Epidemiol Community Health. 1995;49:385-8.
5. Nelzen O, Bergqvist D, Lindhagen A. Venous and non-venous leg ulcers: Clinical history and appearance in population study. Br J Surg. 1994;81:82-7.
6. Tanla JP. Leg ulcers. J Am Acad Dermatol. 1991:965-87.
7. Pierard GE, Franchimont C, Vardar M, Zaghloul A. Tropical ulcers. In: Pierard GE, Caumus E, Franchimont C, Arrese Estrada J. Tropical Dermatology. Brussels: Editions de L'Universite de Bruxelles/AUPELF. 1993:579-83.
8. Gheerert P, Song M. Clinical aspects of lower limb ulcers. Rev Med Brux. 1997;8:238-40.
9. Mazer A, Sankale M. Chronic ulcers of the lower limbs. Guide de Med. In Africa and the Indian Ocean, 1988;156:148-52.
10. Mahe A. Dermatology on dark skin. Pract Dermatol. 2001;159.
[11 Cissé F. Chronic ulcers of the lower limbs: Diagnostic and therapeutic possibilities. Med Thesis Bamako. 1990;74.
12. Kadri A. Chronic ulcers of the lower limbs: Epidemiological, clinical, etiological, and therapeutic aspects. Med Thesis Bamako. 2004;46-57.

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Our Dermatology Online

Original Article

DRESS syndrome and liver involvement: A study of 72 patients

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ABSTRACT

Background: DRESS syndrome (*drug reaction with eosinophilia and systemic symptoms syndrome*) is a severe drug-induced skin reaction that may be life-threatening, particularly due to its visceral involvement. The liver is the primary organ responsible for the metabolism of most medications. Several reviews and articles have highlighted the liver as the most affected organ in DRESS syndrome, making it intriguing to study this aspect in more detail. **Materials and Methods**: This was a retrospective, descriptive, and analytical study conducted at the dermatology department in Fez, Morocco, from 2014 to 2023, including all cases presenting with DRESS syndrome diagnosed based on clinical, biological, histological, and chronological arguments, with a RegiSCAR score classified as probable or definite. Hepatic involvement was assessed based on the classification of drug-induced hepatitis using alkaline phosphatase (ALP) levels, alanine aminotransferase (ALT) levels, and the ALT/ALP ratio (R), thus defining three clinical forms: cytolytic (ALT > 2 or R > 5), cholestatic (ALP > 2 or R < 2), and mixed (2 < R < 5). **Results**: 72 patients were included, with 47.2% experiencing hepatic involvement, including 48.5% with cytolytic, 36.4% with cholestatic, and 15% with mixed forms. Among these, 55.9% had associated renal involvement, 29.9% presented with erythroderma, 55.9% with a maculopapular rash, 8.8% with a morbilliform rash, 5.9% with an erythema multiforme-like eruption, and 79.9% had eosinophilia. Allopurinol was the most implicated drug (50%), followed by neuroleptics (17.6%), Salazopyrin (14.7%), and antibiotics (8.8%). The association between Salazopyrin and hepatic involvement was significant ($p < 0.05$), while the statistical analysis of other parameters did not reveal such an association. Management involved local care, with 50% of the patients placed on corticosteroid therapy. 8.8% of the patients died, while the others showed normalized liver function tests in 74.19% of cases, with the rest lost to follow-up. **Conclusion:** Hepatic involvement is common in DRESS syndrome, predominantly manifesting as cytolytic or cholestatic patterns. Maculopapular rash and erythroderma are the most commonly observed cutaneous phenotypes. These patients are more likely to have associated renal involvement and eosinophilia. Allopurinol, neuroleptics, and Salazopyrin are the most frequently implicated drugs.

Key words: DRESS syndrome, Liver, Hepatic, Allopurinol, Drug

INTRODUCTION

DRESS syndrome is a severe drug reaction defined by a clinical and biological presentation that includes high fever, facial edema, skin rash, polyadenopathy, mononucleosis-like syndrome, eosinophilia, and visceral involvement [1]. Its pathophysiology has become clearer with the identification of viral reactivations, including human herpesvirus 6 (HHV-6), human herpesvirus 7 (HHV-7), cytomegalovirus (CMV), and Epstein–Barr virus (EBV) [2]. Its severity is associated with systemic manifestations that may progress to

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multi-organ failure, jeopardizing the prognosis [3]. Hepatic involvement is well-documented in DRESS syndrome, ranging from a simple transient abnormality in liver function tests to severe hepatic failure, known as drug-induced liver injury (DLI), an idiosyncratic drug-related liver injury [4,5]. Drug-induced hepatotoxicity remains challenging to ascertain due to the absence of diagnostic criteria and specific biomarkers. However, in cases of suspected drug involvement and the absence of viral or autoimmune causes, the likelihood of drug-induced hepatotoxicity remains highly probable [5].

MATERIALS AND METHODS

Study Design

We conducted a retrospective, descriptive, and analytical study within the dermatology department of Hassan II University Hospital in Fes, Morocco, over a period of nine years. We included all patients hospitalized for DRESS syndrome. The diagnosis was based on clinical criteria (skin rash), biological criteria (eosinophilia, lymphopenia, or leukocytosis, alteration of renal or hepatic function), histological criteria through a skin biopsy, chronological criteria (time between drug intake and symptomatology), with reporting to our institution's pharmacovigilance center. The RegiSCAR score was calculated for all our patients and categorized as probable or definite. Other cases of severe drug reactions were excluded.

Hepatic involvement was either incidentally discovered based on biochemical abnormalities or during clinical signs such as jaundice or asthenia. Causality assessment relied primarily on chronological and clinical criteria, eliminating other potential causes and demonstrating the suspected drug's role [6]. The classification of the type of hepatitis was defined based on alkaline phosphatase (ALP), alanine aminotransferase (ALT) levels, as well as the ALT(N)/ALP(N) ratio; N = upper limit: cytolytic injury (ALT > 2N or ratio > 5), cholestatic injury (ALP > 2N or ratio < 2), and mixed injury (2 < ratio < 5) [6].

We studied the incidence of hepatic involvement and the principal clinical, biological, and evolutionary characteristics in patients with this dysfunction: type of skin rash, eosinophilia, renal failure, implicated drugs, and vital prognosis.

Analytical Study

Our data was analyzed with SPSS software, version 26, and descriptive results were reported as valid percentages (%). The chi-squared test and Fisher's test were employed to explore significant correlations between hepatic involvement and the various parameters studied. The result was considered significant if the p value was less than 0.05. The p value could not be calculated in certain cases and we designated these results as *(-)*.

RESULTS

Epidemiological Data

We collected data from 72 patients diagnosed with DRESS syndrome. The average age was 56 years, and the sex ratio (M/F) was 0.6. Hepatic involvement was observed in 34 patients (47.2%), primarily detected through laboratory tests. Additionally, 3 patients (4%) presented with cutaneous-mucosal jaundice associated with asthenia. Drug-induced hepatitis manifested as cytolytic in 17 cases (50%), cholestatic in 12 (35.3%), and mixed in 5 (14.7%) (Fig. 1). Patients with hepatic involvement had an average age of 53 years, with a female predominance of 61.8%, and a history of diabetes (17.6%), renal insufficiency (2.9%), and cardiovascular abnormalities (41.2%). No significant differences were found in age, sex, or medical history between patients with and without hepatic involvement.

Clinical and Systemic Manifestations and Drugs Involved

Among patients with hepatic involvement, 19 (55.9%) had a maculopapular rash (Fig. 2a), 10 (29.4%) had erythroderma (Fig. 2b), 3 (8.8%) had morbilliform rash, and 2 (5.9%) had polymorphic erythema described

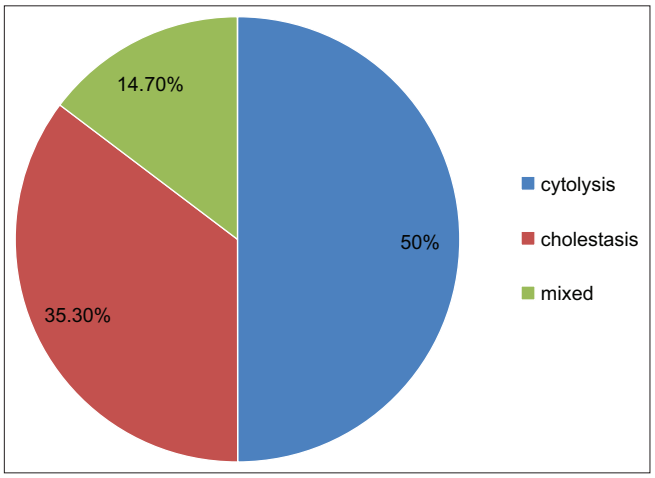

Figure 1: Different forms of acute drug hepatitis.

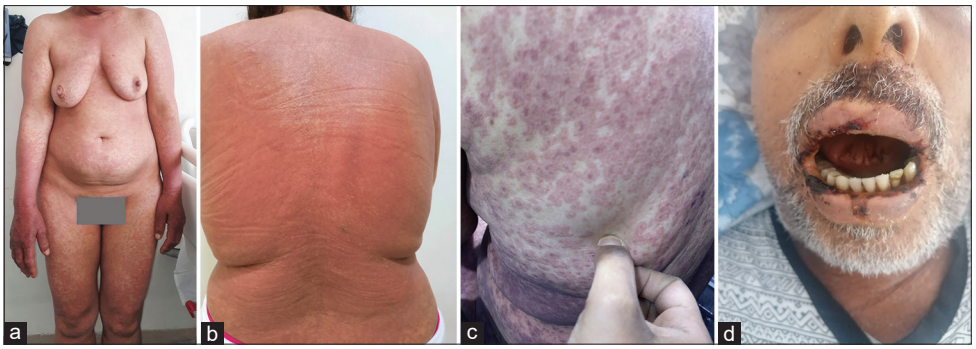

Figure 2: Clinical photos of different skin patterns: a) maculopapular rash, b) erythroderma, c) erythema multiforme-like, d) mucosal involvement.

as a diffuse rash associated with target lesions and/or pseudo-target lesions (Fig. 2c). Notably, 19 patients (55.9%) had mucosal involvement (Fig. 2d). There was no significant association between the type of skin eruption and hepatic involvement. Clinical characteristics of patients with hepatic impairment are summarized in Table 1.

Regarding systemic manifestations in patients with hepatic involvement, 27 cases (79.4%) had eosinophilia, 19 (55.9%) had renal insufficiency, and 1 (2.9%) had respiratory involvement. No significant association was found between systemic involvement and hepatic impairment. Systemic manifestations are summarized in Table 2. The most implicated drugs, in order of frequency, were allopurinol (50%), followed by neuroleptics (17.6%), sulfasalazine (14.7%), and antibiotics (8.8%). The association between sulfasalazine and hepatic involvement was significant ($p < 0.05$), while the association between other therapeutic classes and hepatic impairment did not show a significant correlation. Incriminated drugs in patients with and without hepatic impairment are summarized in Table 3.

Treatment and Prognosis

Therapeutic management locally was consistent regardless of hepatic abnormality, primarily involving local care, initiation of topical corticosteroids compounded or in a 30 g protocol. Among all patients with DRESS syndrome, 22 cases (30.6%) were treated with injectable corticosteroids in mini-boluses of 0.5 mg/kg of methylprednisolone, followed by oral administration. Notably, 17 patients (77.2%) with corticosteroid therapy experienced hepatic involvement. Concerning prognosis, 3 patients (8.8%) with hepatic abnormalities died. Among these three deceased patients, two had cytolytic patterns, and one exhibited cholestasis.

Table 1: Clinical characteristics of patients with and without hepatic impairment

	Liver damage+ *n*=34	Liver damage – *n*=38	*p* value
Age/years (average)	53.82	59.34	Not significant
Sex			Not significant
Female	21 (61.8%)	24 (63.2%)	
Male	13 (38.2%)	14 (36.8%)	
Medical history			
Diabetes	6 (17.6%)	9 (23.7%)	Not significant
Renal insufficiency	1 (2.9%)	5 (13.2%)	
Cardiovascular disorder	14 (41.2%)	13 (34.2%)	
Clinical phenotype			
Rash maculopapular	19 (55.9%)	16 (43.2%)	-
Morbilliform exanthema	3 (8.8%)	6 (16.2%)	-
Erythroderma	10 (29.4%)	9 (24.3%)	-
Erythema polymorphe-like	2 (5.9%)	6 (16.2%)	-
Mucosal involvement	19 (55.9%)	19 (50%)	Not significant

Table 2: Systemic manifestations in patients with and without hepatic impairment

	Liver damage+ *n*=34	Liver damage – *n*=38	*p* value
Hypereosinophilia	27 (79.4%)	31 (81.6%)	-
Renal insufficiency	19 (55.9%)	19 (50%)	Not significant
Respiratory involvement	1 (2.9%)	5 (13.2%)	Not significant

Table 3: Incriminated drugs in patients with and without hepatic impairment

	Liver damage+ *n*=34	Liver damage – *n*=38	*p* value
Allopurinol	17 (50%)	20 (52.6%)	Not significant
Neuroleptics	6 (17.6%)	7 (18.4%)	Not significant
Antibiotics	3 (8.8%)	4 (10.5%)	-
Sulfasalazine	5 (14.7%)	0	*p*=0.02 (significant)
Anti-inflammatory drugs	1 (2.9%)	2 (5.3%)	-

The causes of death were sepsis, end-stage renal failure, and multiorgan failure in a patient with a history of severe cardiovascular disease. The remaining patients showed normalization of hepatic parameters in 74.19%, while the rest were lost to follow-up.

DISCUSSION

DRESS syndrome is a delayed drug hypersensitivity reaction occurring 2 to 6 weeks after taking the medication. It is a severe drug eruption that may have life-threatening consequences. Its clinical and biological characteristics are now well-known, enabling its identification. The diagnosis relies on a triad, including a skin rash, hematological abnormalities such as eosinophilia or atypical lymphocytosis, and visceral involvement, notably affecting the liver and kidneys. The liver is the most commonly affected organ in DRESS syndrome [4,7-9]. This involvement, or what we may call drug-induced liver injury (DLI), may range from a simple biological disturbance to hepatic failure [7]. Indeed, the liver is the organ where the metabolism of several drugs takes place. The diagnosis of drug-induced hepatitis remains a challenge for hepatologists due to the lack of standardized diagnostic criteria and reliable biological markers [5]. Various definitions and upper limits for AST, ALT, alkaline phosphatase, or bilirubin levels exist. Considering hepatic tolerance that may occur, some authors suggest diagnosing drug-induced hepatitis if transaminase levels exceed five times the normal without clinical signs, or if alkaline phosphatase levels are more than two times the normal, or if bilirubin is more than two times the normal [10]. We based our definition on the initial one, which was also adopted by I-Chun Lin et al. in their retrospective study involving 72 patients [8]. This definition, chosen by hepatologists at our university hospital, guided our approach [6].

Moreover, our results showed that the liver is frequently affected (47.2%), which was in line with the findings by Lee et al. (45%) [9]. It is noteworthy that a literature review on liver involvement in DRESS syndrome conducted by Sylvia A Martinez-Cabriale et al. asserts that the liver is the most affected organ in DRESS syndrome, with frequencies varying among authors from 51% to 87% [7]. The pathophysiology seems to be explained by the viral reactivation of HHV6 that occurs during DRESS syndrome and may lead to hepatitis. Another hypothesis is related to the infiltration of eosinophils secondary to excessive inflammatory reaction and the influx of IL-5 during DRESS syndrome [7].

The most noted form of drug-induced liver injury (DLI) in our series was the cytolytic form (50%), followed by the cholestatic form (35.3%) and the mixed form (14.7%). Indeed, according to Sylvia A Martinez-Cabriales et al., acute hepatitis is often either cytolytic or cholestatic depending on the age of the patient and the implicated drugs [7,8]. It seems that cytolytic involvement is more common in younger subjects under antibiotics and carbamazepine, whereas older subjects under allopurinol or phenytoin tend to present the cholestatic form [8]. This aligns with our results, as our patients with liver involvement had an average age of 53 years, relatively young, which explains the predominant cytolytic involvement in our series. On the other hand, allopurinol was the most incriminated drug in our study, which may be explained by the fact that the majority of our patients had comorbidities such as cardiovascular history, diabetes, or renal insufficiency, making allopurinol a commonly prescribed medication by general practitioners, cardiologists, or nephrologists. Furthermore, our results showed a significant association between the use of sulfasalazine and liver involvement. The involvement of sulfasalazine in DRESS syndrome has been reported in the literature in several case reports [11-13]. Its association with drug-induced hepatic injury has also been documented [14], both in DRESS syndrome and in acute generalized exanthematous pustulosis [14,15]. A study reported that beta-lactam antibiotics, allopurinol, non-steroidal anti-inflammatory drugs, and sulfamides were the major contributors to DRESS syndrome with liver involvement [9]. Another study reported that sulfamides (92.9%), followed by antiepileptics (86.3%) and allopurinol (78%), presented the highest risk of inducing liver damage in DRESS syndrome [8].

Regarding associated clinical features, our series showed that the maculopapular rash was the most observed (55.9%) in patients with liver involvement, followed by erythroderma (29.4%), morbilliform exanthem (8.8%), and erythema polymorphe-like (5.9%), defined by the presence of a rash and lesions in a target or pseudo-target pattern. Walash et al., in their series of 27 patients with DRESS syndrome, demonstrated that erythema polymorphe-like and the presence of purpura were associated with more severe liver involvement when compared to other types of eruptions [16]. However, defining a cutaneous phenotype as a prognostic marker for visceral involvement remains a subject of controversy, and a study by Kettani et al. did not show a significant association in this regard [17].

Regarding systemic manifestations, Lee et al. reported that renal dysfunction was more frequent in patients with hepatic dysfunction (39% vs. 1%, $p = 0.001$), and patients with hepatic dysfunction were more

likely to have renal dysfunction (96% vs. 34%, $p = 0.001$) [18]. This aligned with our results, in which renal insufficiency was more common in patients with liver involvement (55.9%) when compared to those without involvement (50%).

Therapeutic management is not well standardized, and the utility of systemic corticosteroid treatment is a subject of debate. A study by Lee et al. demonstrated that, in patients with DRESS syndrome and hepatic involvement, the use of systemic corticosteroids did not provide additional benefits in terms of disease duration and improvement in liver function [9]. Furthermore, a favorable outcome was reported in a study by Decloux et al., in which fulminant hepatitis was treated with methylprednisolone 1 g/day for three days, followed by a prolonged course of prednisone (3750 mg over thirty days) [19]. It is interesting to note that some authors observed relapses after tapering corticosteroids and had to resume oral corticotherapy at higher doses, highlighting once again that DRESS syndrome is a chronic inflammatory syndrome with an unpredictable long-term course [4].

The mortality rate in DRESS syndrome ranges from 5% to 10%, which is primarily attributed to severe involvement of the internal organs such as the liver, heart, lungs, and kidneys. Severe forms, such as hepatic encephalopathy or fulminant hepatitis requiring urgent liver transplantation, have a poor prognosis and significant morbidity and mortality [20]. In our series, the vast majority of the patients presented with an asymptomatic form of drug-induced liver injury (DLI), explaining the reduced mortality and subsequent normalization of their biological parameters. In their case series, Ichai et al. found that 43% (7/16) of patients with hepatic involvement during DRESS syndrome either underwent transplantation ($n = 5$) or died ($n = 2$) [20]. DILI stands as a crucial contributor to acute liver failure, carrying substantial morbidity and mortality implications. Each medication exhibits a distinctive pattern of liver injury, and the prognosis varies accordingly. In addition to considering the specific drug type, factors such as age, bilirubin levels, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and prothrombin time (PT) are assessed as indicators of mortality. Despite this, the precise thresholds for bilirubin, PT, or other factors that reliably predict the severity or mortality risk in patients with drug-induced liver injury (DILI) remain undefined. In their study, Sunil Kumar et al. found that patients with DRESS syndrome exhibited less severe liver impairment when compared to those without DRESS syndrome [21]. However, prompt management involving the immediate cessation of the causative drug and the identification of systemic involvement, especially in the liver, could lead to a better prognosis for the patient. The benefit of high-dose systemic corticosteroid treatment remains a subject of controversy.

Study Limitations

Our study had several limitations. Despite relying on the meticulous registry of the adverse drug reactions database from a single medical center, our university hospital, in close collaboration with the pharmacovigilance center, the number of cases was limited. This limitation hindered our ability to draw didactic comparisons and obtain statistically significant results. All our findings demonstrated a non-significant association, except for the association between sulfasalazine and hepatic involvement. Finally, a comprehensive interpretation of our results would require a better understanding of the underlying pathological mechanisms of liver lesions. A large prospective study would be essential to address these questions, particularly regarding the various clinical and biological characteristics and the management of patients with hepatic involvement in DRESS syndrome.

CONCLUSION

The liver is the most affected organ in DRESS syndrome, often presenting as asymptomatic drug-induced liver injury (DLI) and rarely as severe fulminant hepatitis. The clinical form of hepatitis varies with age and the implicated drug, and the associated clinical and biological characteristics remain a subject of ongoing research. Our series demonstrated a predominance of cytolytic hepatitis in a relatively young population, primarily associated with allopurinol. We found a significant association between Salazopyrin and hepatic dysfunction. The correlation between cutaneous phenotype and hepatic involvement is variable, with patients having hepatic dysfunction being more prone to developing renal insufficiency. High-dose corticosteroids appear to be beneficial for some, yet for others, there is no observed benefit in terms of the severity of hepatic involvement.

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.

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

REFERENCES

1. Descamps V, Mardivirin L, Janela B, Musette P, Ranger-Rogez S. Le syndrome d'hypersensibilité (DRESS) n'est qu'une maladie virale. Rev Fr Allergol. 2010;50:171-3.
2. Descamps V, Ranger-Rogez S, Musette P, Barbaud A. Le DRESS (drug reaction with eosinophilia and systemic symptoms): une synergie médicaments-virus qui peut conduire en réanimation. Réanimation. 2011;20:223-7.
3. Chebbi W, Souissi J, Chelli J, Larbi F, Zantour B, Habib Sfar M. DRESS syndrome: Report of three cases. Pan Afr Med J. 2014;19:166.
4. Lens S, Crespo G, Carrión JA, Miquel R, Navasa M. Severe acute hepatitis in the DRESS syndrome: Report of two cases. Ann Hepatol. 2010;9:198-201.
5. Devarbhavi H. An Update on Drug-induced liver injury. J Clin Exp Hepatol. 2012;2:247-59.
6. Abid H, Lahmidani N, El yousfi M, Benajah D, El abkari M, Aqodad N. Le point sur l'hépatite médicamenteuse. RMG. 2019;10:100-6.
7. Martinez-Cabriales SA, Shear NH, Gonzalez-Moreno EI. Liver involvement in the drug reaction, eosinophilia, and systemic symptoms syndrome. World J Clin Cases. 2019;7:705-16.
8. Lin IC, Yang HC, Strong C, Yang CW, Cho YT, Chen KL. Liver injury in patients with DRESS: A clinical study of 72 cases. J Am Acad Dermatol. 2015;72:984-91.
9. Lee T, Lee YS, Yoon SY, Kim S, Bae YJ, Kwon HS. Characteristics of liver injury in drug-induced systemic hypersensitivity reactions. J Am Acad Dermatol. 2013;69:407-15.
10. Fontana RJ, Seeff LB, Andrade RJ, Björnsson E, Day CP, Serrano J, et al. Standardization of nomenclature and causality assessment in drug-induced liver injury: Summary of a clinical research workshop. Hepatology. 2010;52:730-42.
11. Kanabaj K, Jenerowicz D, Jankowska L, Żaba Z. DRESS syndrome: A dermatological emergency: Sulfasalazine-related acute drug reaction case report. Heliyon. 2023;9:e20021.
12. Michel F, Navellou JC, Ferraud D, Toussirot E, Wendling D. DRESS syndrome in a patient on sulfasalazine for rheumatoid arthritis. Joint Bone Spine. 2005;72:82-5.
13. Girelli F, Bernardi S, Gardelli L, Bassi B, Parente G, Dubini A et al. A new case of DRESS syndrome induced by sulfasalazine and triggered by amoxicillin. Case Rep Rheumatol. 2013;2013:409152.
14. Jennings PE, Blandford RL, Rosenthal FD. Acute sulphasalazine hepatotoxicity. Postgrad Med J. 1986;62:305-6.
15. Białynicki-Birula R, Cisoń W, Krefft-Trzciniecka H, Cisoń H. Acute generalized exanthematous pustulosis caused by sulfasalazine. Our Dermatol Online. 2024;15:71-74.
16. Walsh S, Diaz-Cano S, Higgins E, Morris-Jones R, Bashir S, Bernal W. Drug reaction with eosinophilia and systemic symptoms: Is cutaneous phenotype a prognostic marker for outcome? A review of clinicopathological features of 27 cases. Br J Dermatol. 2013;168:391-401.
17. Kettani F, Hali F, Baline K, Chiheb F. Dress syndrome : phénotype cutané et atteinte viscérale (étude rétrospective de 62 cas). Rev Fr Allergol. 2020;60:69-74.
18. Lee WM, Squires RH Jr, Nyberg SL, Doo E, Hoofnagle JH. Acute liver failure: Summary of a workshop. Hepatology. 2008;47:1401-15.
19. Descloux E, Argaud L, Dumortier J, Scoazec JY, Boillot O, Robert D. Favourable issue of a fulminant hepatitis associated with sulfasalazine DRESS syndrome without liver transplantation. Intensive Care Med. 2005;31:1727-8.
20. Ichai P, Laurent-Bellue A, Saliba F, Moreau D, Besch C, Francoz C. Acute liver failure/injury related to drug reaction with eosinophilia and systemic symptoms: Outcomes and prognostic factors. Transplantation. 2017;101:1830-7.
21. Sunil Kumar N, Remalayam B, Thomas V, Ramachandran TM, Sunil Kumar K. Outcomes and predictors of mortality in patients with drug-induced liver injury at a tertiary hospital in south India: A Single-Centre Experience. J Clin Exp Hepatol. 2021;11:163-70.

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Our Dermatology Online

Original Article

Serum lipid profile pattern in lichen planus: A cross-sectional study in northeast India

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ABSTRACT

Background: Lichen planus (LP) is a chronic idiopathic T cell-mediated papulosquamous disorder clinically characterized by firm, shiny, polygonal, pruritic, 1–3 mm, flat-topped, erythematous to violaceous papules and plaques. Oral LP has a characteristic whitish streak in a reticular pattern (Wickham striae). Recent scientific literature has emphasized the strong association between chronic inflammation in LP and cardiovascular disease. This study was undertaken to study if dyslipidemia is associated with LP. **Materials and Methods:** After informed consent, thirty-eight willing patients aged between 10 and 80 years of age with clinical presentations suggestive of lichen planus who had attended the Dermatology OPD of RIMS in Manipur, India, were included in the study. Histopathology was done to confirm doubtful cases. Detailed history, examination, and investigations were conducted for all patients. Dermoscopic examination was done to aid in clinical diagnosis. **Results:** Females outnumbered males (m/f: 1:1.7). A majority of the patients (84.2%) had a duration of disease above six months. Dyslipidemia was found in 50% of the patients (n = 19). The mean levels of HDL, TC, LDL, TG, and VLDL were 47 ± 8.89 mg%, 166.11 ± 34.93 mg%, 107.95 ± 26.17 mg%, 152.95 ± 63.46 mg%, and 19.55 ± 5.94 mg%, respectively. The single most common lipid abnormality found was deranged HDL (13.2%), followed by abnormal TC (10.5%), TG (7.9%), and deranged VLDL (2.6%). 15.8% of the patients had multiple lipid abnormalities. The 40–49 year (31.5%) group was the most commonly associated with dyslipidemia, which was statistically significant. Dyslipidemia was the most commonly seen in the reticular type (42.1%) of LP, although not statistically significant. No statistically significant correlation was found between dyslipidemia and clinical types nor with the symptoms of LP. **Conclusions:** Dyslipidemia was present in half of the patients, and the most common single abnormality was low HDL. A majority had multiple lipid abnormalities. A statistically significant portion of the patients in their 40s had dyslipidemia. Statistically significant abnormal TG and LDL were observed in age groups 40–49 years and 60–79 years, respectively. Hence, all patients with LP should undergo lipid profile testing for early detection and primary prevention of metabolic syndrome and cardiovascular complications.

Key words: Lichen planus, Inflammation, Dyslipidemia, Cardiovascular morbidity

INTRODUCTION

LP represents a $CD8^+$ T cell-mediated autoimmune disease in which CD8+ T cells are recruited into the skin leading to interface dermatitis [1]. The activated lymphocytes release mediators such as IL-2, IL-4, IL-10, IFN –γ, TNF- α, and TGF-β and trigger apoptosis [2]. Clinically, it is characterized by pruritic, purplish, plane-topped papules and plaques with white streaks and koebnerization (Figs. 1a – 1c). On histopathology, epidermal changes such as hyperkeratosis, focal hypergranulosis, elongated rete ridges, basal cell degeneration, and focal dermoepidermal separation with band-like dense lymphocytic infiltrate in the papillary dermis are seen [1] (Fig. 2).

There is growing evidence of the association between LP and cardiovascular risk factors such as dyslipidemia.

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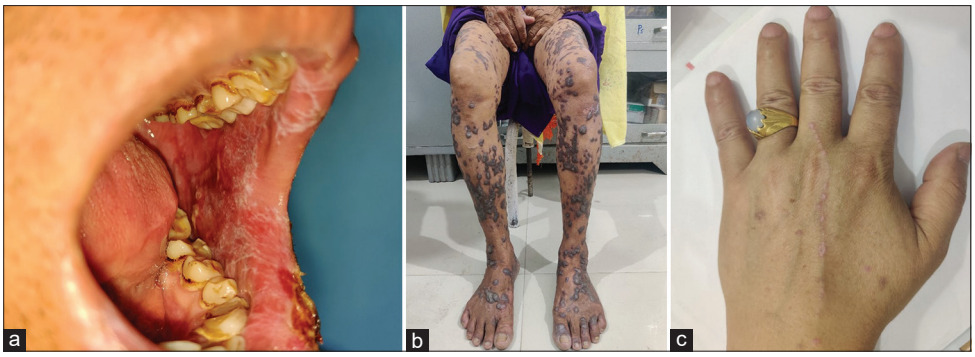

Figure 1: (a) Pruritic, purplish, plane-topped papules and plaques on the bilateral lower limbs. (b) Whitish, thread-like streaks (Wickham's striae) in a patient with the reticular type of oral lichen planus. (c) Koebnerization in a patient with the plaque type of cutaneous lichen planus.

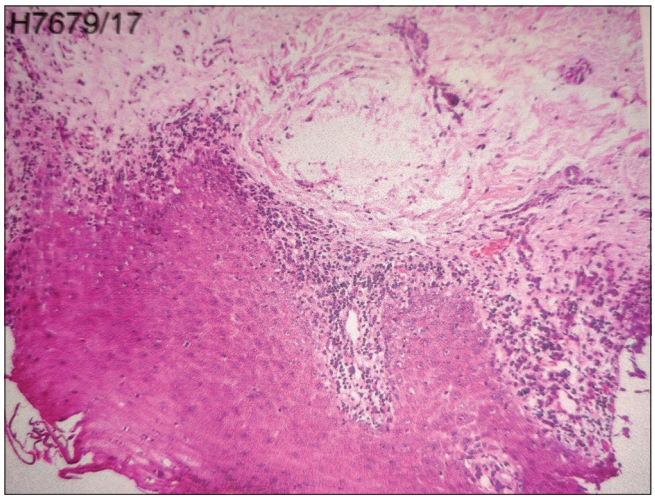

Figure 2: Band-like lymphocytic infiltration in the upper dermis with exocytosis of lymphocytes and focal basal cell vacuolization in the epidermis.

LP, being a chronic inflammatory condition, may explain this observation. High plasma IL-6 levels in oral LP were found to be associated with high total cholesterol (TC) and triglyceride (TG) and low high-density lipoprotein levels (HDL) [3,4].

Few studies have been done in this regard. If the association between LP and dyslipidemia is established, lipid level screening in patients with LP may be useful to detect individuals at risk and begin preventive treatment against cardiovascular disease.

This study, therefore, was undertaken to study if dyslipidemia is associated with LP.

MATERIALS AND METHODS

This was a cross-sectional, observational study conducted over a period of two years at the Dermatology OPD of RIMS in Imphal. Willing patients of both sexes and aged 10–80 years with lichen planus were included in the study after informed consent. Patient confidentiality was ensured.

Pregnant or lactating women and patients on treatment for LP in the past six months were excluded.

Consecutive sampling was employed. Both cases and controls were subjected to proper history taking, clinical examination, and laboratory tests. Dermoscopic examination was performed in doubtful cases. Fasting serum lipid profile was measured by enzymatic endpoint method.

Dyslipidemia was diagnosed based on the NCEP ATP III guidelines:

a. Serum total cholesterol (TC) > 200 mg/dL.
b. Serum triglycerides (TG) > 150 mg/dL.
c. Serum low-density lipoprotein cholesterol (LDL-C) > 130 mg/dL.
d. Serum high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL for males and < 50 mg/dL for females.
e. If the patient was already receiving treatment for dyslipidemia.

Data was analyzed with SPSS, version 21.0. For inferential statistics, chi-squared/Fisher exact test was employed. A p value < 0.05 was considered statistically significant. Student t-test was employed to compare means.

Ethics Statement

Ethical approval was obtained from the institute ethics committee.

RESULTS

The age of the study population ranged from 11 to 72 years, with a majority in the age group of 60–69 years

(21.1%) (Fig. 4). The mean and median age were 44.87 ± 17.51 years and 46.5 years, respectively. The age range for males and females were 11–72 years and 17–65 years, respectively.

Females outnumbered males with a M: F ratio of 1:1.7 (Fig. 5). A majority had a duration of disease > 6 months (84.2%) (Fig. 6). The mean disease duration was 21.05 ± 28.81 months. The mean and median BMI were 24.23 ± 2.81 and 24.35, respectively.

Dyslipidemia was found in 50% of the cases (n = 19).

Table 1 shows the mean values and standard deviations of lipid profile parameters among the cases.

The mean levels of HDL, TC, LDL, TG, and VLDL were 47 mg/mL, 166.11 mg/mL, 107.95 mg/mL, 152.95 mg/mL, and 19.55 mg/mL, respectively.

The most common single lipid abnormality was deranged HDL (13.2%), followed by abnormal TC (10.5%), TG (7.9%), and VLDL (2.6%). Multiple deranged lipid parameters were seen in 15.8, among which deranged TC with TG and deranged HDL with TG (5.3% each) was most commonly seen (Table 2).

The most common age group associated with dyslipidemia was 40–49 years (31.5%) followed by 20–29 years (21.1%) (Table 3). This finding was statistically significant (p = 0.046).

Dyslipidemia was most commonly seen in the reticular variant (42.1%), followed by the plaque (15.8%), hypertrophic (10.5%), and erosive (10.5%) types (Table 4). However, this finding was statistically insignificant.

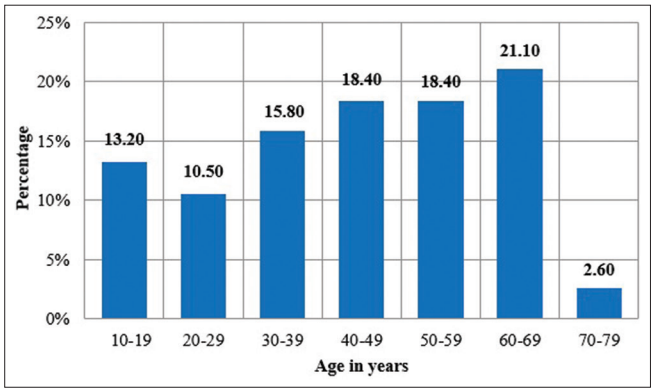

Figure 4: Age distribution of the patients (n = 38).

Among symptomatic patients, abnormal TG, TC, HDL, LDL, and VLDL were seen in 21.6%, 18.9%, 18.9%, 5.4%, and 5.4% of the patients, respectively (Table 5). However, this finding was statistically insignificant.

Out of 18.4% of the patients with abnormal HDL, 5.3% had reticular LP, followed by 2.6% each for the plaque, hypertrophic, erosive, follicular, and reactive variants.

LDL was found to be raised in the reticular (2.6%) and mixed (2.6%) types whereas VLDL was found to be high in the hypertrophic (2.6%) and reticular types (2.6%).

Among patients with high TC, 10.5% had the reticular type, followed by 5.3% with the plaque type and 2.6% with the erosive type.

High TG was found in 7.9% with the reticular variant and 2.6% each with the plaque, hypertrophic, erosive, LPP, and mixed types.

However, the correlation between the clinical types of LP and dyslipidemia was found to be statistically insignificant (Table 4).

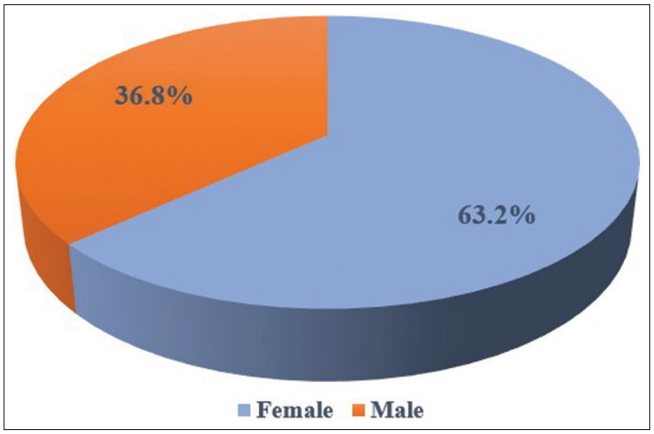

Figure 5: Sex distribution.

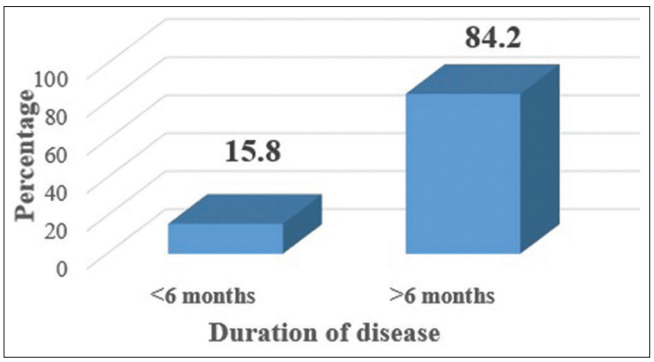

Figure 6: Duration of disease.

Table 1: Mean and standard deviation of lipid profile in patients with lichen planus

Parameter (mg/dL)	HDL	TC	LDL	TG	VLDL
Mean	47.00	166.11	107.95	152.95	19.55
SD	8.89	34.93	26.17	63.46	5.94

Table 2: Lipid profile abnormalities in patients with lichen planus

Parameter	Frequency *n* (%)
Nil	19 (50%)
Others	6 (15.8%)
HDL	5 (13.2%)
TC	4 (10.5%)
TG	3 (7.9%)
VLDL	1 (2.6%)

Table 3: Association between dyslipidemia and age group

Age Group	Dyslipidemia *n* (%)		*p* Value
	Yes	No	
10–19	1 (5.3)	4 (21.05)	0.046
20–29	4 (21.1)	0 (0)	
30–39	2 (10.5)	4 (21.05)	
40–49	6 (31.5)	1 (5.3)	
50–59	2 (10.5)	5 (26.3)	
60–69	3 (15.8)	5 (26.3)	
70–79	1 (5.3)	0 (0)	
Total	19 (100)	19 (100)	

Table 4: Association between clinical types and dyslipidemia

Clinical Type	Dyslipidemia Present n (%)	Dyslipidemia Absent n (%)	*p* Value
Reticular	8 (42.1)	7 (36.8)	0.997
Plaque	3 (15.8)	4 (21.1)	
Hypertrophic	2 (10.5)	2 (10.5)	
Erosive/ulcerative	2 (10.5)	1 (5.3)	
Follicular	1 (5.3)	1 (5.3)	
Lichen Planus pigmentosus	1 (5.3)	1 (5.3)	
Mixed	1 (5.3)	2 (10.5)	
Reactive	1 (5.3)	1 (5.3)	
Total	19 (100)	19 (100)	

Table 5: Distribution of symptoms and serum lipid profile

Serum Lipid	Value	Symptoms		Total
		Present	Absent	
HDL				
Normal	Frequency	30	1	31
	Percentage	81.6	100	81.6
Low	Frequency	7	0	7
	Percentage	18.4	0	18.4
p value	0.795			
LDL				
Normal	Frequency	35	1	36
	Percentage	94.7	100	94.7
Low	Frequency	2	0	2
	Percentage	5.3	0	5.3
p value	0.095			
VLDL				
Normal	Frequency	35	1	36
	Percentage	94.7	100	94.7
Low	Frequency	2	0	2
	Percentage	5.3	0	5.3
p value	0.662			
TC				
Normal	Frequency	30	1	31
	Percentage	81.1	100	81.6
Low	Frequency	7	0	7
	Percentage	18.9	0	18.4
p value	0.795			
TG				
Normal	Frequency	29	1	30
	Percentage	78.4	100	78.9
Low	Frequency	8	0	8
	Percentage	21.6	0	21.1
p value	0.708			

DISCUSSION

In this study, the age of the patients ranged from 11–72 years, with a majority of the patients in the age group of 60–69 years (21.1%). The mean and median age were 44.87 ± 17.51 years and 46.5 years, respectively, comparable to findings by Chalkoo et al. [5], Kar et al. [6], Arias Santiago et al. [7], Aniyan et al. [8], and Manasa et al. [9].

Females (63.2%) were more commonly affected than males (36.8%), similarly to other studies [10-13]. The male-to-female ratio was 1:1.7, similarly to findings by Chalkoo et al. [5] with a M: F ratio of 1:1.85. The mean and median BMI among the patients were 24.23 ± 2.81 and 24.35, respectively, comparably to findings by Hammam et al. [14] yet lower than in those by Manasa et al. [9] and Khan et al. [15].

The duration of the disease ranged from 1 month to 11 years. A majority of the patients had symptoms for more than six months (82.4%), similarly to other studies [7,12]. The mean age of disease duration was 21.05 ± 28.81 months, similarly to studies by Hashba et al. [12] (20.5 ± 26.1 months) and Arias Santiago et al. [7] (1.8 years in females, 1.6 years in males) yet longer than in studies by Ozkur et al. [16] (8.4 ± 8.3 months), which may be due to the neglect of symptoms by patients in our region.

Dyslipidemia was observed in 50% (n = 19) of the patients. This prevalence was higher than in findings by Agarwala et al. [17] with 35.9% of the patients having dyslipidemia, yet lower than in those by Azeez et al. [18] with 63.8% of the patients having dyslipidemia.

The mean for HDL was comparable to studies by Azeez et al. [18] and others [8,13,14]. It was higher

Table 6: Distribution of clinical types and serum lipid profile

Serum Lipid	Value	Clinical Type									Total
		Plaque	Hypertrophic	Erosive	Reticular	Follicular	LPP	Reactive	Mixed	*p* value	
HDL											
Normal	Freq.	6	3	2	13	1	2	1	3	0.699	31
	%	15.8	7.9	5.3	34.2	2.6	5.3	2.6	7.9		81.6
Low	Freq.	1	1	1	2	1	0	1	0		7
	%	2.6	2.6	2.6	5.3	2.6	0	2.6	0		18.4
LDL											
Normal	Freq.	7	4	3	14	2	2	2	2	0.550	36
	%	18.4	10.5	7.9	36.8	5.3	5.3	5.3	5.3		94.7
Low	Freq.	0	0	0	1	0	0	0	1		2
	%	0	0	0	2.6	0	0	0	2.6		5.3
VLDL											
Normal	Freq.	7	3	3	14	2	2	2	3	0.752	36
	%	18.4	7.9	7.9	36.8	5.3	5.3	5.3	5.3		94.7
Low	Freq.	0	1	0	1	0	0	0	0		2
	%	0	2.6	0	2.6	0	0	0	0		5.3
TC											
Normal	Freq.	5	4	2	11	2	2	2	3	0.716	31
	%	13.1	10.5	5.3	28.9	5.3	5.3	5.3	7.9		81.6
Low	Freq.	2	0	1	4	0	0	0	0		7
	%	5.3	0	2.6	10.5	0	0	0	0		18.4
TG											
Normal	Freq.	6	3	2	12	2	1	2	2	0.898	30
	%	15.8	7.9	5.3	31.6	5.3	2.6	5.3	5.3		78.9
Low	Freq.	1	1	1	3	0	1	0	1		8
	%	2.6	2.6	2.6	7.9	0	2.6	0	2.6		21.1

than in studies by Kar et al. [6] and others [8,9], yet lower than in studies by Arias-Santiago et al. [7] and Özkur et al. [16].

The mean for TC was comparable to findings by Aniyan et al. [8] yet lower than those by Kar et al. [6].

The mean for LDL was comparable to findings by Aniyan et al. [8]. It was higher than findings by Manasa et al. [9] yet lower than those by Kar et al. [6] and others [7,10,11,16].

The mean for TG was comparable to findings by Aniyan et al. [8]. It was higher than findings by Arias-Santiago et al. [7] and others [11,13], yet lower than those by Chalkoo et al. [5].

Deranged HDL (13.2%) was the most common single lipid abnormality, followed by abnormal TC (10.5%), TG (7.9%), deranged VLDL (2.6%). 15.8% of the patients had multiple deranged lipid parameters. This finding differed from that by Aniyan et al. [8] in which deranged VLDL was the most commonly seen, followed by abnormal TG, HDL, and LDL, in that order.

Dyslipidemia was most commonly observed in the 40–49 year-old (31.5%) age group, followed by the 20–29 (21.1%) year-old age group. This was found statistically significant ($p = 0.046$). Although dyslipidemia is generally more common in the older age group, in this study it was found to be more common in the age group of 40–49 years. This observation agreed with the fact that LP is a disease of the middle-aged population.

Abnormal LDL profile was most common in the 60–79 year-old age group. This finding was statistically significant ($p = 0.002$). This differed from findings by Aniyan et al. [8] in which the 46–60 year-old age group most commonly had high LDL.

TG abnormality was the highest in the 40–49 year-old age group. This was statistically significant ($p = 0.042$). Again, this finding differed from that by Aniyan et al. [8] in which the 31–45 year-old age group was most commonly affected.

Although insignificant statistically, the 40–49 year-old age group most commonly had low HDL ($p = 0.186$). TC abnormality was most common in the 30–59 year-old age group.

There were 37 symptomatic patients, among which HDL was found to be low in 18.4% and abnormal TG,

TC, LDL, and VLDL were found in 21.1%, 18.9%, 5.3%, and 5.3% of the patients, respectively. However, none of these findings were statistically significant.

Among the 18.4% of the patients with abnormal HDL, 5.3% had reticular LP, followed by 2.6% each with the plaque, hypertrophic, erosive, follicular, and reactive variants. LDL was found to be high in the reticular and mixed types (2.6% each). VLDL was found to be high in the hypertrophic and reticular types (2.6% each).

Among the 18.9% of the patients with high TC, 10.5%, 5.3%, and 2.6% had the reticular, plaque and erosive types, respectively. 21.1% of the patients had high TG, among whom 7.9% had the reticular variant and 2.6% each had the plaque, hypertrophic, erosive, LPP, and mixed types.

However, the correlation between the clinical types of LP and dyslipidemia was found to be statistically insignificant (Table 6).

CONCLUSION

Dyslipidemia was present in half of the patients with low HDL, being the single most common abnormality. A statistically significant portion of the patients in their 40s had dyslipidemia despite the fact that dyslipidemia is generally more common among the elderly, which may suggest that LP is a disease of the middle age. Statistically significant abnormal TG and LDL were observed in the 40–49 and 60–79 year age groups, respectively. Hence, all patients with LP should be screened for lipid profile abnormalities as a screening procedure for early detection and primary prevention of metabolic syndrome and cardiovascular complications.

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. Boch K, Langan EA, Kridin K, Zillikens D, Ludwig RJ, Bieber K. Lichen planus. Front Med. 2021;8:737813.
2. Meller S, Gilliet M, Homey B. Chemokines in the pathogenesis of lichenoid tissue reactions. JID. 2009;129:315-9.
3. Toader MP, Taranu T, Constantin MM, Olinici D, Mocanu M, Costan VV, et al. High serum level of interleukin-6 is linked with dyslipidemia in oral lichen planus. Exp Ther Med. 2021;22:1-8.
4. Shenoy C, Shenoy MM, Rao GK. Dyslipidemia in dermatological disorders. North Am J Med Sci. 2015;7:421-8.
5. Chalkoo AH, Peerzada GY, Ahmad MB. Lipid levels in patients with oral lichen planus: A case-control study. IJHSR. 2016;6:180-4.
6. Kar BR, Panda M, Patro N. Metabolic derangements in lichen planus: A case control study. JCDR. 2016;10:WC01-3.
7. Arias-Santiago S, Buendía-Eisman A, Aneiros-Fernández J, Girón-Prieto MS, Gutiérrez-Salmerón MT, Mellado VG, et al. Cardiovascular risk factors in patients with lichen planus. Am J Med. 2011;124:543-8.
8. Aniyan KY, Guledgud MV, Patil K. Alterations of serum lipid profile patterns in oral lichen planus patients: A case–control study. Contemp Clin Dent. 2018;9:S112-21.
9. Manasa D R, Chandru M C, Ravi M Rathod, Vidya Kuntoji. Association of dyslipidemia in lichen planus patients at KIMS, Hubli: A case control study. Med Int J of Biochemistry. 2018;8:1.
10. Kumar SA, Raju PK, Gopal KV, Rao TN. Comorbidities in lichen planus: A case–control study in Indian patients. IDOJ. 2019;10:34-7.
11. López-Jornet P, Camacho-Alonso F, Rodríguez-Martínes MA. Alterations in serum lipid profile patterns in oral lichen planus. Am J Clin Dermatol. 2012;13:399-404.
12. Hashba H, Joy Bifi AT, Sridharan R, Sreenivasan A, Mathew P. Prevalence of metabolic syndrome in patients with lichen planus: A cross-sectional study from a tertiary care center. IDOJ. 2018;9:304-8.
13. Kurian G, Krishnan S, Shakthi P. A prospective case control study on metabolic syndrome in lichen planus in a tertiary care centre. Int J Res Dermatol. 2017;3:427-32.
14. Hammam MA, Bakry OA, Soliman SE, Abd El Hamid EM, Khateeb E. Lipid profile in cases of lichen planus. Menoufia Med J. 2020;33:1050.
15. Khan S, Pirzado MS, Kalhoro HB, Rajper N, Memon SM, Memon FH. Frequency of dyslipidemia in patients with lichen planus: A comparative cross-sectional study. J Liaquat Uni Med Health Sci. 2021;1:1-10.
16. Özkur E, Uğurer E, Altunay İK. Dyslipidemia in lichen planus: A case-control study. Med Bull Sisli Etfal Hosp. 2020;54:62-6.
17. Agarwala MK, Peter D, Thomas N, Paul T, Asha HS, Thomas M, et al. Is lichen planus a marker for dyslipidemia and metabolic syndrome? J Am Acad Dermatol. 2016;74:AB257.
18. Azeez N, Asokan N. Association of lichen planus with dyslipidemia: A comparative, cross-sectional study. Clin Dermatol Rev. 2019;3:68-71.

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Our Dermatology Online

Original Article

Dermoscopy of vulvar pigmented lesions: A series of 59 cases

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ABSTRACT

Background: Due to the lack of a large series of benign and malignant vulvar lesions, the features of dermoscopy are not well established. **Objective:** The aim of our study was to describe the epidemiological profile and the clinical and dermoscopic characteristics that may indicate malignancy or benignity in vulvar hyperpigmentation. **Materials and Methods:** From June 2020 to June 2023, we conducted a retrospective, prospective study involving 42 patients with 59 pigmented lesions. **Results:** The parallel, homogeneous, and globular patterns were observed in benign lesions (nevi, lentigo, melanosis). The cerebriform pattern was observed in seborrheic keratosis and Bowen's disease (BD). In cases of BD, we also observed white, structureless areas, glomerular vessels, a homogeneous brownish-gray area, and brown dots. **Conclusion:** Good clinico-dermoscopic correlation should guide the diagnosis and management of pigmented vulvar lesions. Dermoscopy may be helpful in distinguishing between a benign lesion and a malignant lesion, yet in cases of doubt, a biopsy may be necessary.

Key words: Dermoscopy, Vulvar, Pattern, Pigmented

INTRODUCTION

Pigmented vulvar lesions include a wide range of conditions that may be either of melanocytic origin by hyperplasia (nevus, melanoma) or epithelial hyperpigmentation without significant melanocytic hyperplasia (post-inflammatory pigmentation, vulval melanosis, and lentigo), or of non-melanocytic origin (seborrheic keratosis, vulval intraepithelial neoplasia (VIN), condyloma, angiokeratoma). Vulvar melanoma is a rare gynecological disease that accounts for 5% of all neoplasms of the vulva [1] and 3–7% of all women's melanomas [2]. Early melanoma may share some clinical and dermoscopic features with benign lesions and may, therefore, be a source of anxiety for both the patient and the dermatologist [3]. Diagnosing melanoma based on clinical criteria alone is often unreliable, and histological examination is considered necessary. However, dermoscopy is a non-invasive tool that helps doctors differentiate melanoma from other pigmented and non-pigmented skin lesions. It provides numerous clues about the structure of the skin in the epidermis, the dermoepidermal junction, and the dermis. For the detection of lesion borders, numerous methods have been developed [4]. To our knowledge, there have been few studies on the dermoscopic features of pigmented vulvar lesions. The aim of our study was to describe the epidemiological profile and the clinical and dermatoscopic characteristics of vulvar hyperpigmentation.

MATERIALS AND METHODS

This retrospective, prospective study evaluated the clinical and dermoscopic assessment of pigmented vulvar lesions. However, histological examination was performed in cases of suspected malignancy. The sample of patients was collected on consultation at the Dermatology Department of the HASSAN II University Hospital of Fez in Morrocco during the

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period from June 2020 to June 2023. The pictures analyzed were taken using a digital dermoscopy system (Dermatoscope DermLite DL4). The latter was packaged in disposable food packaging to avoid microbiological contamination. The dermoscopic images were taken by the same dermatologist to avoid diversification during the procedure, and the dermoscopic images were evaluated by two different dermatologists. The selection of dermoscopic patterns was based on the results of the literature [4,5].

RESULTS

A total of two hundred women were examined, among whom 42 presented with 59 pigmented lesions. The age range was 4–79 years (median: 42). Histological examination was performed in twelve patients, with four cases of suspected melanoma, four cases of Bowen's disease (BD), and four cases of diagnostic uncertainty between condyloma and seborrheic keratosis (SK). We collected 16 cases of melanosis, 13 of seborrheic keratosis, 10 of condylomas, 9 of nevi, 7 of lentigo, and 4 of Bowen's disease.

The clinical appearance of the lesion (Table 1) was raised in 38 cases and the macular in 21 cases (Figs. 1a and 1b). It was multifocal in 35 cases, unifocal in 24 cases, and melanosis was in most cases multifocal, contrary to lentigo and nevi. Lesions were preferentially located on the labia majora (37 cases vs. 16 cases on the labia minora, 4 cases on the posterior fourchette, and 2 cases on the clitoris). 35 lesions were larger than 6 mm, and 24 lesions were smaller than 6 mm.

Dermoscopic analysis of our pigmented lesion series was performed.

For melanosis, the parallel pattern was observed in 12 cases, and the homogeneous pattern in 4 cases. As for lentigo, the parallel pattern was observed in 5 cases (Fig. 2a), and the homogeneous pattern in 1 case. For nevi, the globular pattern was observed in 3 cases (Fig. 2b), the homogenous, brown pattern in 3 cases (Fig.2c), and the bicomponent pattern with a peripheral reticular pattern and central homogeneous pattern in 1 case (Fig. 2d).

Meanwhile, we suspected melanoma in 4 cases. The first patient presented a recent appearance of a pigmented clitoral macule with a hyphal pattern and irregular dots on dermoscopy (Fig. 2e). Histology was suggestive of lentigo. The second patient had a history of acral melanoma and presented a pigmented vulvar macule. Dermoscopy revealed a multicomponent pattern, irregular dots and globules, and a bluish-white veil (Fig. 2f). Histology confirmed the diagnosis of melanosis. The third patient had an uncertain date of onset of a small, blue, vulvar papule with a homogeneous blue pattern on dermoscopy, which was histologically confirmed as a blue nevus. The last patient, a teenager, presented with an increase in the size and thickness of her congenital vulvar lesion. Dermoscopy revealed a blackish-blue background,

Table 1: Clinical and dermoscopic features of the 59 lesions included

Patient age (yrs.)	4–79 yrs. (median: 42)
Clinical appearance (n (%))	
Multifocal	35 (60%)
Unifocal	24 (40%)
Size (n (%))	
> 6 mm	35 (59.3%)
< 6 mm	24 (40.7%)
Elementary lesions (n (%))	
Raised	38 (64.4%)
Macular	21 (35.6%)
Localization (n (%))	
Labia majora	37 (62.7%)
Labia minora	16 (27.1%)
Clitoris	2 (3.42%)
Posterior fourchette	4 (6.78%)
Dermoscopic patterns (n (%))	
Melanosis	
Parallel	12 (75%)
Homogeneous	3 (18.75%)
Multicomponent	1 (6.25%)
Lentigo	
Homogeneous	1 (14.29%)
Parallel	5 (71.43%)
Multicomponent	1 (14.29%)
Nevus	
Globular	3 (33.33%)
Brown homogenous	3 (33.33%)
Blue homogeneous	1 (11.11%)
Bi-component	1 (11.11%)
Multicomponent	1 (11.11%)
SK	
Papillomatous	8 (61.54%)
Fingerprint-like parallel structures	2 (15.38%)
Vascular pattern	2 (15.38%)
Comedo-like opening	7 (53.84%)
Milia-like cysts	1 (7.69%)
Condyloma	
Papillomatous	9 (90%)
Finger-like	1 (10%)
Combined	1 (10%)
Vascular pattern	9 (90%)
Knoblike pattern	7 (70%)
Bowen's disease	
Brown homogeneous areas	4 (100%)
White homogeneous areas	3 (75%)
Cerebriform	2 (50%)
Glomerular vessels	3 (75%)
Polymorphous vessels	1 (25%)
Brown globules	1 (25%)

a bluish-white veil, and chrysalises, confirming the diagnosis of a deep-penetrating blue nevus by histology. As for the dermoscopy of seborrheic keratosis, we noted well-defined lesions with a papillomatous pattern in 8 cases, comedo-like openings in 7 cases (Fig. 2g), fingerprint-like structures in 2 cases, a vascular pattern in 2 cases, and milia-like cysts in 1 case. (Fig. 2h) In seborrheic keratosis-like condylomas, we observed a papillomatous pattern in 9 cases, a finger-like pattern in 1 case, a mixed pattern in 1 case (Fig. 2i), a vascular pattern in 9 cases, and a knob-like pattern in 7 cases (Fig. 2j). For patients with Bowen's disease, the cerebriform pattern was observed in 2 cases, white, structureless areas in 3 cases, erosions in 2 cases, glomerular vessels in 3 cases, polymorphic vessels in 1 case, a homogeneous, brownish-gray area in 4 cases, and brown dots in 1 case. (Figs. 2k and 2l) (Table 1).

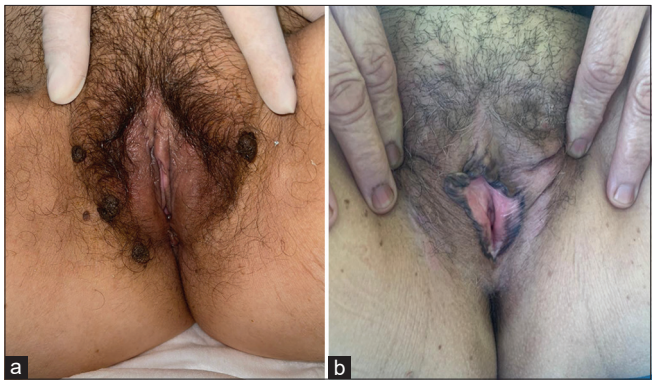

Figure 1: a) Raised pigmented lesions. b) Pigmented macular lesions.

DISCUSSION

Dermoscopy, as a non-invasive technique, has become a fundamental element in the assessment of skin and mucosal lesions, whether pigmented or not, while improving diagnostic accuracy. However, the examination and assessment of mucosal lesions may

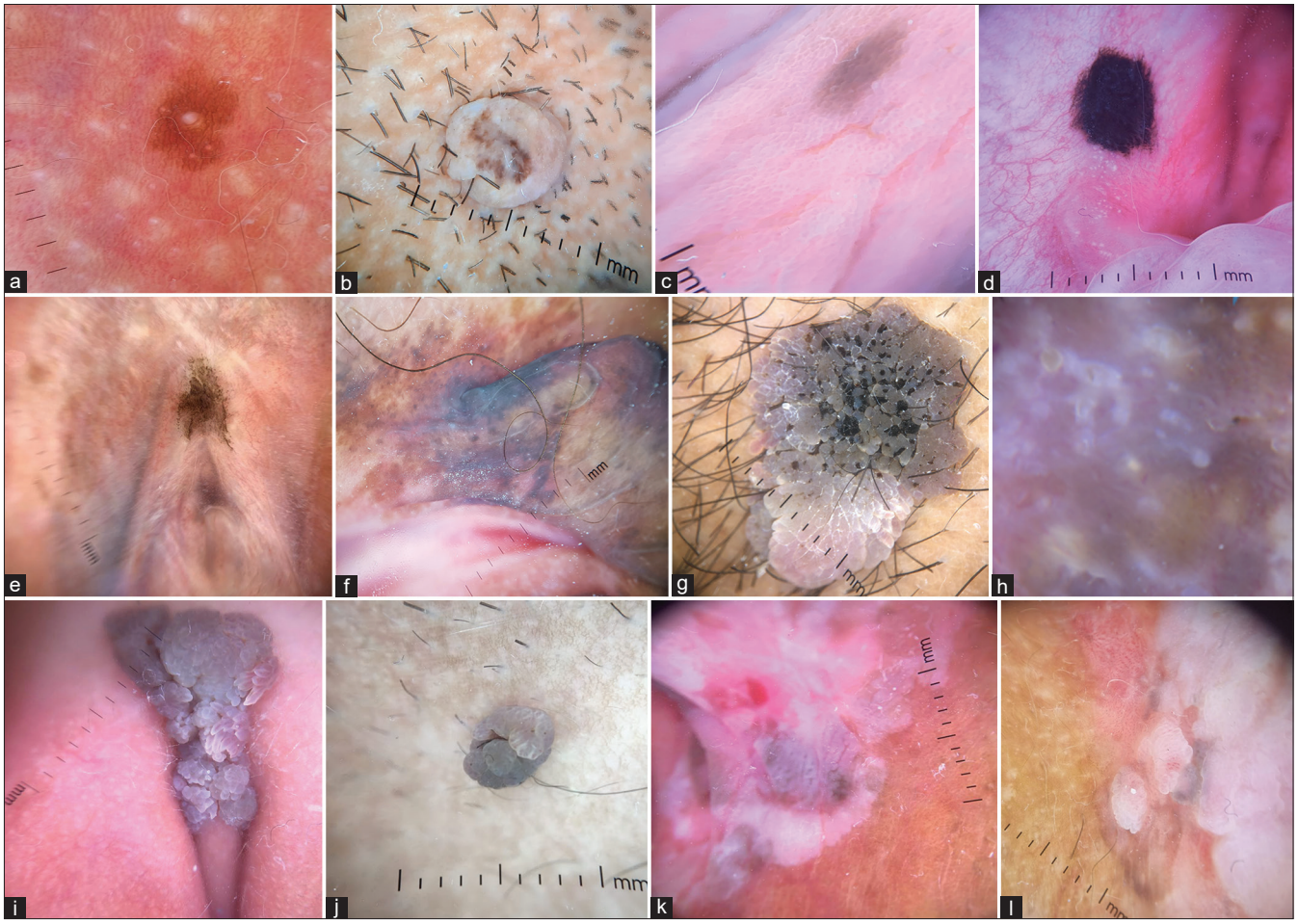

Figure 2: a) Parallel pattern (lentigo). b) Globular pattern (nevi). c) Homogenous brown pattern (nevi). d) Bi-component pattern: peripheral reticular pattern, homogeneous central pattern (nevi). e) Bi-component pattern: hyphal pattern, irregular dots (lentigo). f) Multicomponent pattern (melanosis). g) Papillomatous pattern, comedo-like openings (SK). h) Milia-like cysts, tortuous linear vessels (SK). i) Papillomatous pattern, finger-like pattern, filiform vessels (condyloma acuminata). j) Knob-like pattern (condyloma acuminata). k) Cerebriform pattern, erosion, white structureless areas, glomerular vessels. l) White structureless areas, glomerular vessels, brown dots (pigmented Bowen's disease).

be difficult to perform. First of all, especially in female patients, the lesion may be in a place that is difficult to examine and the patient may feel embarrassed. Secondly, the stretching of the mucosa during the examination could affect the dermoscopic findings. Thirdly, the contact probes should be protected in order to avoid the risk of infection [6,7].

Pigmented lesions represent a wide range of conditions, from benign to malignant, infectious to post-inflammatory [8]. Dermoscopically, they show various patterns with somewhat confusing terminology, including the homogeneous or structureless pattern, the globular pattern, the parallel pattern with its variants, the ring-like pattern with its variants, and the fish scales, and hyphal patterns, which are probably due to external technical issues related to lesion examination with a dermoscope or photographing techniques [9]. It is also possible to identify specific dermoscopic features of other etiologies, such as comedo-like openings and milia-like cysts.

Melanosis, also known as vulvar lentiginosis and melanotic macule, the most common pigmented vulvar lesion in reproductive women [10], typically presents as pigmented macules, often multifocal, and is more common in individuals with darker skin phototypes [11]. Vulvar melanosis is more commonly reported in perimenopausal women [12]. Histologically, melanosis is due to an increase in pigmentation restricted to the basal keratinocytes and melanocytes [13,14]. Dermoscopically, vulvar melanosis presents with either a homogeneous or heterogeneous pattern of brown or black shades without red, gray or blue colors and generally without the typical melanocytic dermoscopic structures [12]. Various patterns have been described, including the structureless, parallel, reticular-like, cobblestone-like, ring-like, and globular patterns. Our results are consistent with the literature and show a predominance of the parallel and homogeneous patterns [5,12].

Vulvar nevi, on the other hand, represent 2.3% of melanocytic nevi cases [15]. They often appear in childhood with dermoscopic patterns similar to their cutaneous counterparts [11]. The most common patterns are the globular and homogeneous [5,11]. Common nevi generally have a single or bicomponent pattern, rarely a multicomponent pattern, in contrast to atypical melanocytic nevi of the genital type, which may be observed in reproductive age and which have a multicomponent pattern and may mimic malignant melanoma. The whitish-blue veil and irregular dots may also be seen [4]. Our results are consistent with the literature, with a predominance of globular and homogeneous patterns [4,11,12].

Meanwhile, in the presence of a multicomponent pattern, melanoma should be considered, especially if associated with heterochromia, white, gray, blue, or red colors, asymmetrically distributed irregular dots and globules, irregular and atypical vessels have also been described [16,17]. Fortunately, we have not found any cases of melanoma of the vulva in our series.

Bowen's disease presents dermoscopically with bluish-grey dots and globules in a linear arrangement and glomerular or dotted vessels. The cerebriform pattern and hypo- or hyperpigmented structureless areas have also been described [18,19]. Our results are also consistent with case reports in the literature, with a predominance of homogeneous brown areas and glomerular vascularization, although the cerebriform pattern was more common in our cases [18].

Seborrheic keratoses, unusual benign lesions of the genitalia, present with a papillomatous pattern on dermoscopy, which may overlap with Bowen's disease and pigmented vulvar intraepithelial neoplasia, yet there are milia-like cysts and comedo-like openings [5,20], which is consistent with the literature regarding the predominance of the papillomatous pattern and the presence of comedo-like opening [4].

Condylomas acuminata present with different patterns, including the cerebriform, depending on the age of the lesions, yet with less pigmented than seborrheic keratosis. They generally lack milia-like cysts and comedo-like openings and have prominent vascular patterns and vessels surrounded by a white halo [20]. Thus, the cerebriform pattern may be seen in benign lesions such as SK, yet we have milia-like cysts, rarely comedo-like openings as a result of maceration [20]. It may also be seen in malignant lesions such as Bowen's disease and vulvar intraepithelial neoplasia, yet we have bluish-gray dots in a linear arrangement and glomerular vascularization. [18,20].

CONCLUSION

Despite the predominance of benign pathologies, we must always be wary of atypical cases, such as those of our patients, who presented with a compound pattern and whose biopsy excluded melanoma. We should also

be wary of any cerebriform pattern and fear Bowen's disease and VIN in the absence of milia-like cells and comedo-like openings in the presence of glomerular vessels, peripheral brown dots and globules in a linear arrangement, and white or brown structureless areas.

REFERENCES

1. Falcicchio G, Vinci L, Cicinelli E, Loizzi V, Arezzo F, Silvestris E, et al. Vulvar malignant melanoma: A narrative review. Cancers (Basel). 2022;1421:5217.
2. Dunton CJ, Berd D. Vulvar melanoma, biologically different from other cutaneous melanomas. Lancet. 1999;3549195:2013-4.
3. Lenane P, Keane CO, Connell BO, Loughlin SO, Powell FC. Genital melanotic macules: clinical, histologic, immunohistochemical, and ultrastructural features. J Am Acad Dermatol. 2000;424:640-4.
4. Cengiz FP, Emiroglu N, Wellenhof RH. Dermoscopic and clinical features of pigmented skin lesions of the genital area. An Bras Dermatol. 2015;902:178-83.
5. Ronger-Savle S, Julien V, Duru G, Raudrant D, Dalle S, Thomas L. Features of pigmented vulval lesions on dermoscopy. Br J Dermatol. 2011;1641:54-61.
6. Hofmann-Wellenhof R. Special criteria for special locations 2: Scalp, mucosal, and milk line. Dermatol Clin. 2013;314:625-ix.
7. Cinotti E, Campoli M, Pataia G, Ouerdane Y, Thuret G, Gain P, et al. How transparent film applied on dermatologic imaging devices in order to prevent infections affects image quality? Skin Res Technol. 2019;252:229-33.
8. Edwards L. Pigmented vulvar lesions. Dermatol Ther. 2010;235:449-57.
9. Lin J, Koga H, Takata M, Saida T. Dermoscopy of pigmented lesions on mucocutaneous junction and mucous membrane. Br J Dermatol. 2009;1616:1255-61.
10. Rock B, Hood AF, Rock JA. Prospective study of vulvar nevi. J Am Acad Dermatol. 1990;221:104-6.
11. Kamat D, Vinay K. Dermatoscopy of nonvenereal genital dermatoses: A brief review. Indian J Sex Transm Dis AIDS. 2019;401:13-9.
12. De Giorgi V, Gori A, Salvati L, Scarfì F, Maida P, Trane L,et al. Clinical and dermoscopic features of vulvar melanosis over the last 20 years. JAMA Dermatol. 2020;15611:1185-91.
13. Venkatesan A. Pigmented lesions of the vulva. Dermatol Clin. 2010;284:795-805.
14. Heller DS. Pigmented vulvar lesions: A pathology review of lesions that are not melanoma. J Low Genit Tract Dis. 2013;173:320-5.
15. Mannone F, De Giorgi V, Cattaneo A, Massi D, De Magnis A, Carli P. Dermoscopic features of mucosal melanosis. Dermatol Surg. 2004;308:1118-23.
16. De Pascalis A, Perrot JL, Tognetti L, Rubegni P, Cinotti E. Review of dermoscopy and reflectance confocal microscopy features of the mucosal melanoma. Diagnostics (Basel). 2021;111:91.
17. Vaccari S, Barisani A, Salvini C, Pirola S, Preti EP, Pennacchioli E, et al. Thin vulvar melanoma: A challenging diagnosis. Dermoscopic features of a case series. Clin Exp Dermatol. 2020;452:187-93.
18. Narahira A, Yanagi T, Kitamura S, Hata H, Shimizu H. Dermoscopic features of genital pigmented Bowen's disease: Report of a case and review of the published work. J Dermatol. 2019;4610:e390-1.
19. Maatouk I, Apalla Z, Errichetti E, Lallas A. Dermoscopy for venereologists: An update on patterns of tumors, inflammatory and infectious diseases of the genitalia, and tips for differential diagnosis. Int J Dermatol. 2021;6010:1211-8.
20. Seong SH, Jung JH, Kwon DI, Lee KH, Park JB, Baek JW, et al. Dermoscopic findings of genital keratotic lesions: Bowenoid papulosis, seborrheic keratosis, and condyloma acuminatum. Photodiagnosis Photodyn Ther. 2021;36:102448.

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Our Dermatology Online

Brief Report

Dermatologists and burnout: Myth or reality?

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ABSTRACT

Background: Although dermatologists are known to have a good level of job satisfaction, they no longer rank among the happiest healthcare professionals. Our study aimed to estimate the prevalence of burnout among dermatologists and define its risk factors and methods of prevention. **Materials and Methods:** This was a multicenter, cross-sectional study conducted in Morocco over five months from February to June 2022. **Results:** A total of 313 responded to the survey, among which 70.95% suffered from burnout. The risk factors associated with burnout were the female sex ($p < 0.001$), being married ($p = 0.025$), having children ($p = 0.001$), full-time work ($p = 0.05$), lack of time for research ($p < 0.001$), excessive documentation ($p < 0.001$), confrontation with aggressive patients ($p < 0.001$) as well as insufficient remuneration at work ($p < 0.001$). **Conclusion:** Burnout among dermatologists is pervasive and costly for professional life. Institutions need to provide stress management interventions, and dermatologists must balance patient care with other interests such as research and teaching.

Key words: Burnout, Psychology, Dermatology, Risk factors, Prevention and control

INTRODUCTION

Burnout is a state of emotional exhaustion, depersonalization, and low personal accomplishment leading to low productivity [1]. It is a major problem among healthcare professionals, affecting not only the quality of life of doctors yet also the quality of care provided [2].

Burnout among dermatologists has received particular attention in the last decade [3]. Although known to have a good job satisfaction level, dermatologists no longer rank among the happiest health professionals [4]. A limited number of publications have treated burnout among dermatologists and no studies have been conducted in the Maghreb before.

Our study aimed to estimate the prevalence of burnout among dermatologists in Morocco and to define its risk factors and methods of prevention.

MATERIALS AND METHODS

This was a multicenter, cross-sectional study conducted in Morocco over five months from February to June 2022. Participants were dermatologists in training (interns and residents) and specialists practicing in public and private sectors. We excluded dermatologists not practicing or retired.

Data collection was conducted using an online survey distributed on social media platforms. It consisted of three sections: sociodemographic data, work-related data, and the original version of the Maslach Burnout Inventory (MBI) [5]. The MBI consists of twenty-two items that explore three dimensions: emotional exhaustion (nine items), dehumanization (five items), and personal fulfillment at work (eight items). Each scale gave a score, and the three of them allowed us to situate the state of burnout. We considered the burnout mild when only one dimension was affected, moderate if two dimensions were affected, and severe when all dimensions were affected.

Statistical analyses were performed using IBM SPSS Statistics 26.0. Univariate analysis was performed using the chi-squared test. The multivariate analysis was performed using logistic regression (stepwise descending method). The significance level was at 0.05.

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Ethics Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The data collected was anonymous and confidential and informed consent was obtained from all the participants included in the study.

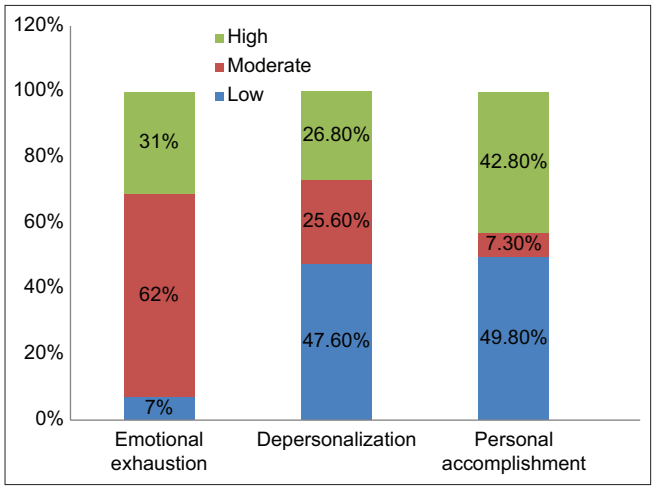

Figure 1: The distribution of the levels of the subdimensions of burnout among the dermatologists.

RESULTS

A total of 313 dermatologists responded to the survey. Regarding the socio-demographic characteristics, there was a predominance of females and the 25–35 age group. 71.2% were married and 89.6% had children. 19.5% had a personal psychiatric history of anxiety or depression and 81% were on psychotropic medication. 46.3% were psychologically affected by the COVID-19 pandemic and 2.6% had addictive behaviors, such as smoking and/or drinking alcohol.

Regarding work-related characteristics, 57.2% were specialists and 66.5% had been practicing for less than five years. All participants practiced in an urban environment (55.9%). 53.7% practiced in a university hospital and 46.3% in the office. 81.2% worked full time, 70.6% worked less than eight hours a day, and 58.1% more than five days a week. Most doctors lacked time to do research, 59.1% found documentation excessive, and a third brought unfinished work home or had a

Table 1: Sociodemographic factors associated with burnout among dermatologists

Sociodemographic factor	Burnout + Population (%)	Burnout – Population (%)	*p* Value	OR	IC 95%	
					Lower Bound	Upper Bound
Age						
25–35 years	171 (77)	35 (38.5)	< 0.001	0.57	0.46	0.70
> 35 years	51 (23)	56 (61.9)				
Sex						
Female	220 (99.1)	65 (71.4)	< 0.001	10.80	2.83	41.14
Male	2 (0.9)	26 (28.6)				
Marital status						
Single	72 (32.4)	18 (19.8)	0.025	1.18	1.03	1.36
Married	150 (67.6)	73 (80.2)				
Children						
Yes	129 (58.1)	71 (78)	0.001	1.27	1.11	1.45
No	93 (41.9)	20 (22)				
Regular sports activity						
Yes	137 (61.7)	63 (69.2)	0.208	1.09	0.95	1.26
No	85 (38.3)	28 (30.8)				
Religious practice						
Yes	209 (94.1)	86 (94.5)	0.901	1.01	0.75	1.37
No	13 (5.9)	5 (5.5)				
Personal psychiatric history						
Yes	59 (26.6)	2 (2.2)	< 0.001	0.66	0.60	0.74
No	163 (73.4)	89 (97.8)				
Suicidal ideation						
Yes	8 (3.6)	0 (0)	0.110	0.70	0.65	0.75
No	214 (96.4)	91 (100)				
Psychological impairment by the COVID-19 pandemic						
Yes	130 (58.6)	15 (16.5)	< 0.001	4.37	2.63	7.26
No	92 (41.4)	76 (83.5)				
Addictive behaviors (tobacco and/or alcohol)						
Yes	6 (2.7)	2 (2.2)	1.000	0.94	0.62	1.41
No	216 (97.3)	89 (97.8)				

Table 2: Work-related factors associated with burnout among dermatologists

Work-related factor	Burnout + Population (%)	Burnout – Population (%)	*p* Value	OR	IC 95%	
					Lower Bound	Upper Bound
Institution						
University hospital	104 (46.8)	30 (33)	0.024	0.84	0.73	0.97
Practice	118 (53.2)	61 (67)				
Duration of practice						
0–5 years	173 (77.9)	25 (27.5)	< 0.001	0.56	0.45	0.69
> 5 years	49 (22.1)	75 (72.5)				
Work						
Full time	174 (78.4)	80 (87.9)	0.05	1.18	1.02	1.37
Part-time	48 (21.6)	11 (12.1)				
Working hours per day						
< 8 hrs.	149 (67.1)	72 (79.1)	0.034	0.85	0.74	0.97
8–12 hrs.	73 (32.9)	19 (20.9)				
Number of working days per week						
Between 3 and 5 days	85 (38.3)	46 (50.5)	0.046	1.16	0.99	1.34
> More than 5 days	137 (61.7)	45 (49.5)				
Lack of time for research						
Yes	206 (92.8)	58 (63.7)	< 0.001	3.06	2.27	4.13
No	16 (7.2)	33 (36.3)				
Excessive documentation						
Yes	161 (72.5)	24 (26.4)	< 0.001	4.03	2.68	6.06
No	61 (27.5)	67 (73.6)				
Administrative and clerical tasks						
Yes	91 (41)	13 (14.3)	< 0.001	0.71	0.63	0.81
No	131 (59)	78 (85.6)				
Unfinished work at home						
Yes	70 (31.5)	31 (34.1)	0.663	1.03	0.88	1.20
No	152 (68.5)	60 (65.9)				
Online consultation requests						
Yes	215 (96.8)	88 (96.7)	1.000	0.98	0.65	1.49
No	7 (3.2)	3 (3.3)				
Stressful event at work in the last 12 months						
Yes	149 (67.1)	60 (65.9)	0.840	0.98	0.84	1.14
No	73 (32.9)	31 (34.1)				
Confrontation with demanding, aggressive or rude patients						
Yes	147 (66.2)	88 (96.7)	< 0.001	1.53	1.37	1.71
No	75 (33.8)	3 (3.3)				
Work						
Alone	120 (54.1)	59 (64.8)	0.080	1.13	0.98	1.30
In a team	102 (45.9)	32 (35.2)				
Problem of communication with teachers						
Yes	55 (24.8)	6 (6.6)	< 0.001	0.73	0.65	0.82
No	167 (75.2)	85 (93.4)				
Communication problems with colleagues						
Yes	74 (33.3)	8 (8.8)	< 0.001	0.71	0.63	0.80
No	148 (66.7)	83 (91.2)				
Adequate remuneration for work						
Yes	71 (32)	58 (63.7)	< 0.001	1.49	1.25	1.76
No	151 (68)	33 (36.3)				

lot of administrative and office tasks. 78.9% received online consultation requests through social networks and mobile phones and 75.1% were confronted with aggressive patients, 42.8% worked in a team, among which 91.04% followed the hierarchical model and only 41.2% felt sufficiently remunerated for their work.

Overall, two hundred and twenty-two dermatologists (70.95%) suffered from burnout in at least one of the subscales of the MBI. Reduced personal accomplishment was found in 42.8% of the participants, emotional exhaustion in 31%, and depersonalization, loss of empathy, and dehumanization in 26.8%. Burnout was classified as mild in 57.2%, moderate in 33.7%, and severe in 9.1% of the participants (Fig. 1).

After statistical analysis, the sociodemographic risk factors significantly associated with burnout among dermatologists were the female sex, being married, having children, and psychological affection by the COVID-19 pandemic. Age between 25 and 35 years and the absence of a personal psychiatric history were

considered as protective factors (Table 1). Regarding work-related factors, full-time work, lack of time for research, excessive documentation, confrontation with demanding, aggressive, or rude patients, and insufficient remuneration at work were considered risk factors for burnout. Working in the office for less than eight hours a day, less than five years in practice, in the absence of administrative tasks, or having communication problems with colleagues and teachers were considered protective factors (Table 2).

DISCUSSION

Our study revealed that dermatologists commonly suffer from burnout, with a predominance of the mild form (57.2%). The Medscape National Physician Burnout and Suicide Report published in 2022 reported a lower burnout rate (33%) among dermatologists [6].

In our series, the MBI score revealed that almost 50% of the dermatologists had a low rate of personal accomplishment, while a high rate of emotional exhaustion and depersonalization were found in 31% and 26.8%, respectively. According to Shoimer's study, the results were similar, with a higher rate of emotional exhaustion [7], which may be explained by the inclusion of residents only in this study.

In our study, the sociodemographic risk factors of burnout among dermatologists were the female sex, being married, having children, and psychological affection by the COVID-19 pandemic. The female sex has long been considered a risk factor due to the burden of childcare responsibilities in their households [6]. The challenges posed by the COVID-19 pandemic also exacerbate existing burnout. In an American study, the most common COVID-19 related burnout factors among dermatologists were uncertainty about the future, teledermatology, fear of exposing loved ones to COVID-19, and reduced remuneration [8]. Age between 25 and 35 years was considered a protective factor in our study. While in another study, women aged between 20–35 and 55 years and over were particularly vulnerable to burnout [9]. In fact, age or work experience may not be the real cause of burnout, yet rather the accumulation of stress problems in modern work life [2].

Regarding work-related factors, full-time work, lack of time for research, excessive documentation, confrontation with aggressive or rude patients, and insufficient remuneration at work were considered risk factors of burnout. These results are consistent with the literature [10,11]. In our series, working in a practice, for less than eight hours per day and less than five years, without administrative and office tasks were considered protective factors. This could be explained by the increased rate of burnout in hospitals due to the high workload. The assessment of burnout among Canadian dermatology residents revealed that they are more prone to burnout and that examinations were the main factor contributing to their burnout (61%). In addition, demanding workloads within the hospital was also a risk factor [7]. The absence of communication problems with colleagues and teachers was also considered as a protective factor. According to Darban et al., the mean burnout score decreased significantly during the follow-up phase after training in communication skills [12].

CONCLUSIONS

Burnout among dermatologists is pervasive, pernicious, and costly for professional and human life. The risk factors are intraindividual, interindividual, and organizational, hence the interest in implementing a prevention program in these different levels.

Institutions should make efforts and provide stress management interventions and training in communication techniques and also involve dermatologists, especially residents, in decision-making and implement better management of administrative tasks. Dermatologists should also seek a balance between patient care and other interests such as research and teaching, learn to work in a team, and adopt a healthier lifestyle.

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. De Hert S. Burnout in healthcare workers: Prevalence, impact and preventative strategies. Local Reg Anesth. 2020;13:171-83.
2. Lindblom KM, Linton SJ, Fedeli C, Bryngelsson IL. Burnout in the

working population: Relations to psychosocial work factors. Int J Behav Med. 2006;13:51-9.
3. Elsaie ML, Hussein SM, Zaky MS, Hanafy NS, Jafferany M. Therapeutic implications of prevalence and predictor risk factors for burn out syndrome in Egyptian dermatologists: A cross-sectional study. Dermatol Ther. 2020;33:e14327.
4. Shanafelt TD, West CP, Sinsky C, Trockel M, Tutty M, Satele DV, et al. Changes in burnout and satisfaction with work-life integration in physicians and the general US working population between 2011 and 2017. Mayo Clin Proc. 2019;94:1681-94.
5. Maslach C, Jackson SE, Leiter MP. Maslach Burnout Inventory: Third edition. 1997.
6. Physician Burnout and Depression Report 2022: Stress, Anxiety, and Anger [Internet]. Medscape. Available in: https://www.medscape.com/slideshow/2022-lifestyle-burnout-6014664. Accessed 16 June 2022.
7. Shoimer I, Patten S, Mydlarski PR. Burnout in dermatology residents: A Canadian perspective. Br J Dermatol. 2018;178:270-1.
8. Shah P, Dorrell DN, Feldman SR, Huang WW. The impact of the coronavirus disease 2019 pandemic on dermatologist burnout: A survey study. Dermatol Online J. 2021;27:1.
9. Marchand A, Blanc ME, Beauregard N. Do age and gender contribute to workers' burnout symptoms? Occup Med Oxf Engl. 2018;68:405-11.
10. Colon A, Gillihan R, Motaparthi K. Factors contributing to burnout in dermatologists. Clin Dermatol. 2020;38:321-7.
11. Nagler AR, Shinkai K, Kimball AB. Burnout among all groups of physicians: Mitigation strategies for dermatologists. JAMA Dermatol. 2020;156:1049-50.
12. Darban F, Balouchi A, Narouipour A, Safarzaei E, Shahdadi H. Effect of communication skills training on the burnout of nurses: A cross-sectional study. J Clin Diagn Res JCDR. 2016;10:IC01-4.

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Our Dermatology Online

Case Report

Cutaneous leishmaniasis in Senegal: When the practitioner is disarmed

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ABSTRACT

Cutaneous leishmaniasis causes a problem of management in Senegal. Herein, we report a case illustrating this problem. A 55-year-old patient from Dahra Djoloff (260 km north of Dakar) developed diffuse cutaneous leishmaniasis due to *Leishmania major*. The management was hampered by the unavailability of Glucantime in the country. Despite the endemicity of leishmaniasis and the existence of NTD control programs, Glucantime remains inaccessible in Senegal. Leishmaniasis control policies should focus on the problems of the patient, particularly the accessibility of glucantime.

Key words: Cutaneous leishmaniasis, Senegal, Therapeutic difficulties

INTRODUCTION

Cutaneous leishmaniasis, a neglected tropical disease (NTD), is endemic in Senegal. While there is an expansion of its geographical area and the emergence of the visceral form, therapeutic means of medicine are difficult to access [1,2]. Through this observation, we return to this problem of care.

CASE REPORT

Mr. AK, 55-years-old, was from Dahra Djoloff, a dry and arid area located an average of 260 km north of Dakar. He did not report a notion of traveling seven months before the onset of the illness. He was referred by his attending physician for the management of disseminated skin lesions located on the arms and trunk. An examination revealed a diffuse, painless, crusty ulcer with a fleshy base with raised and infiltrated margins (Figs. 1a and 1b). The PCR study of a biopsy core isolated *Leishmania major*. Complete blood counts, transaminases, kidney function, and electrocardiogram were normal. Retroviral serology was negative. The diagnosis of diffuse cutaneous leishmaniasis was retained. The management was hampered by the unavailability of *N*-Methyl-D-glucamine (Glucantime*) in the country. The first phase of processing was incomplete because only two boxes ordered from France had arrived.

DISCUSSION

This observation is being reported in order to share two points. The first concerns the origin of the patient, which is remarkable because it is not known as a Leishmaniasis endemic area. According to our practice and studies on the disease, cases from this geographical area have never been reported [1,2]. This was the first case of cutaneous leishmaniasis in a patient from Dahra Djoloff, which predicts a beginning of modification in the distribution of leishmaniasis in Senegal in a context where the WHO reports since the COVID pandemic, epidemic outbreaks in certain regions of the world [3]. Indeed, although there is an endemicity of leishmaniasis in Senegal, it is rampant in the region of Thiès (50 km north of Dakar) and in that of the Senegal

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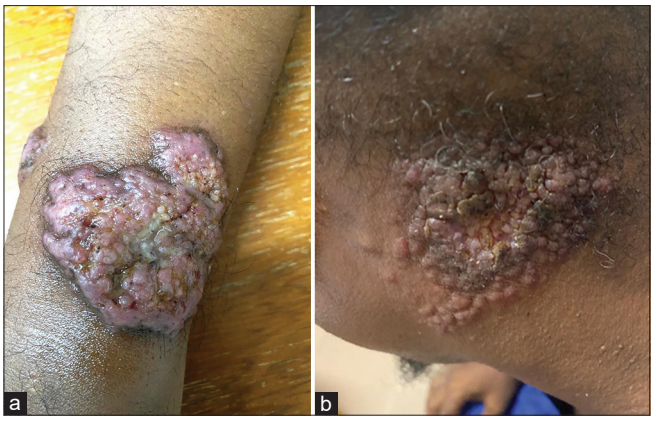

Figure 1: (a) Cutaneous leishmaniasis with a diffuse, crusty ulcer on the arms. (b) Crusty ulcer on the neck due to leishmaniasis.

River located in the extreme north of the country in eastern Senegal. An expansion of the geographical area with indigenous cases from the capital (Dakar) has been reported [1]. Climate change facilitating the development of the vector could explain the emergence of cases in the capital. Entomological studies aimed at isolating the sandfly would make it possible to certify the actual expansion of its mapping.

This expansion would have a significant impact on patients because the Senegalese dermatologist is entirely helpless in the management of leishmaniasis. No molecule among the recognized anti-infectives is available in the country at a time when there is a ministerial program against NTDs. Amphotericin B, pentamidine, and N-Methyl-D-glucamin antimoniate (Glucantime*) are inaccessible. The latter, the main therapeutic weapon that we had, is nowadays nowhere to be found. Sporadically, it is obtained from some, if not a pharmacy as a result of an individual order of inaccessible cost. The price of a box of five ampoules, which was 35,000 FCA (52 euros) six years ago, is currently 65,000 FCF (99 euros). Thus, the amount of 792 euros (six times the minimum wage) is required for the two-cycle cure of ten days each. This significant budget is beyond the financial capacity of most of our patients without health insurance. This is a neglected and persistent obstacle in the treatment of the disease. These therapeutic difficulties are recurrent despite the expression of needs regularly renewed [2]. Yet, NTD seminars are increasingly organized, while Glucantime* remains untraceable and health workers are poorly trained in diagnosing and managing the disease.

The strategy to combat leishmaniasis should be more patient-centered by facilitating the accessibility of Glucantime* through a policy of availability in hospital pharmacies and by subsidizing or even free treatment. On the other hand, the training of health personnel in the recognition of different clinical forms as varied as multiple is a cornerstone in the fight against NTDs, especially leishmaniasis.

CONCLUSION

Leishmaniasis control policies should focus on the problems of the patient, particularly the accessibility of Glucantime.

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. Diop A, Diallo K, Ndiaye M, Diousse P, Diatta BA, Valiollah A, et al. Origine géographique et aspects cliniques de 87 cas de leishmaniose cutanée suivis dans un hôpital de Dakar. Med Afr Noire. 2016;63:308-13.
2. Ndiaye M, Cisse DF, Djigal A, Sow A, Lelo S, Ly F, et al. A case of visceral leishmaniasis in a 4-year-old child living in nonendemic area located in suburbs of Dakar, Senegal. Case Rep Infect Dis. 2023;2023:2354935.
3. Leishmaniasis fact sheet. Geneva: World Health Organization; 2022 (https://www.who.int/news-room/fact-sheets/detail/leishmaniasis, accessed October 2022)

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Our Dermatology Online

Case Report

A peculiar in situ case of cutaneous leukocytoclastic vasculitis induced by urinary infection

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ABSTRACT

Cutaneous leukocytoclastic vasculitis (LCV) is a disease thought to be related to the presence of immune complex deposition within small blood vessel walls. A 58-year-old female presented with purpuric papules on both legs, occurring concurrent with urinary symptoms. Histologically, an intraepidermal blister with luminal fragmented neutrophils was present. A dermal infiltrate was observed surrounding blood vessels; mild perivascular leukocytoclastic debris favored a diagnosis of LCV. Both direct immunofluorescence and immunohistochemistry staining also favored a diagnosis of LCV. Reactivity of the involved vessels was observed to multiple antibodies and complement, with overexpression of von Willebrand factor, CD15, and CD45. The ribosomal protein Phospho-S6 was also detected within the involved vessels, and on the blister roof and floor. The clinical triggering factor was a urinary infection that had progressed to urosepsis; the symptoms were effectively treated. We present an unusual case, where multiple immune reactions correlate with clinical and histologic changes characteristic of LCV.

Key words: Cutaneous leukocytoclastic vasculitis, Sialyl Lewis, CD45, Von willebrand factor

Abbreviations

Cutaneous leukocytoclastic vasculitis (CLCV), leukocytoclastic vasculitis (LCV), small vessel vasculitis (SVV), von Willebrand factor (VWF), Sialyl Lewis (sLeX), anti-neutrophil cytoplasmic antibody (ANCA), neutrophil extracellular traps (NETs), direct immunofluorescence (DIF), basement membrane zone (BMZ).

INTRODUCTION

Cutaneous leukocytoclastic vasculitis (LCV) is a small vessel vasculitis illustrated histopathologically by the presence of immune complex-mediated vasculitis of the dermal capillaries and venules on the skin [1]. The majority of cases are idiopathic; however, infections and medications are the most frequent triggers. Systemic diseases could also be the cause of LCV [1].

CASE REPORT

A 58-year-old female presented with acute onset of a skin rash that was present for one week; she also reported urinary symptoms, but no abdominal pain or headache. The skin rash began as a sudden eruption of pruritic, erythematous-to-violaceous, non-blanchable macules and papules involving the lower extremities (Fig. 1a). Fever was also present. There was no history of recent drug intake; her kidney function testing was normal. Hepatitis B and C, as well as HIV titers were negative. Leukocytosis was present. Her hemoglobin, extractable nuclear antibodies panel, anti-Complement C1Q antibodies, cryoglobulins, and Complement C3 and C4 levels were normal. There were no red blood cell fragments or hemolysis detected. Serum levels of IgG, IgA, and IgM were all within normal limits. Her C reactive protein was elevated, and urinalysis was abnormal, showing cloudy urine. Urinary culture and blood cultures were obtained, and

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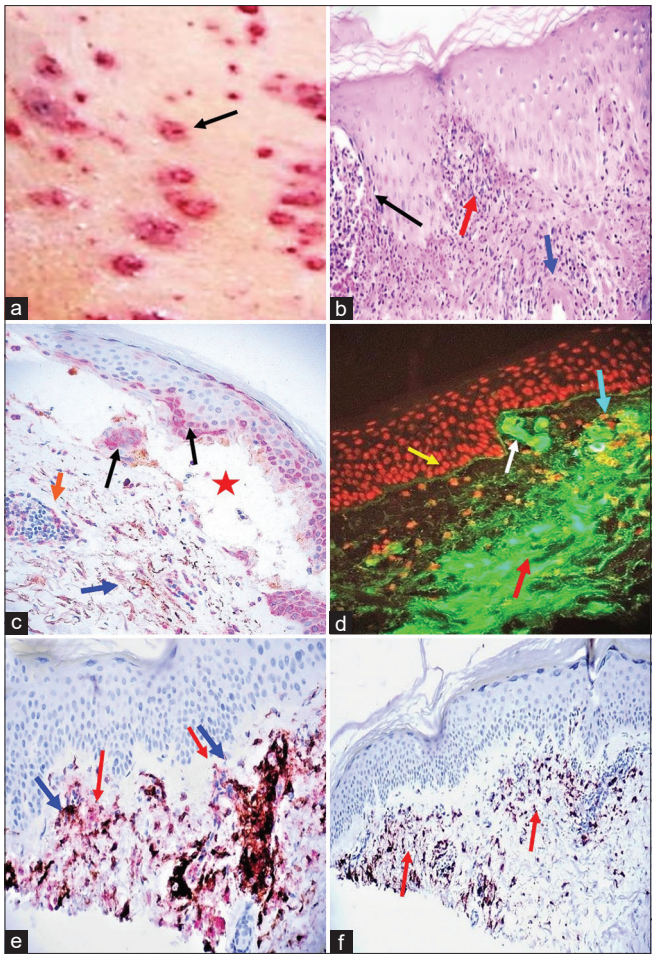

Figure 1: In (a) we show the clinical lesions (black arrow). In (b) a representative H&E stain shows the dermal LCV (blue arrow), a vesicle in the epidermis (black arrow), and the inflammatory infiltrate in a dermal papilla (red arrow) (100X). In (c) double IHC staining shows a subepidermal blister (red star), and pink staining around the blister demonstrates the presence of Ribosomal Protein Phospho-S6 (Ser240, Ser244) in the top of the blister as well as on the blister floor (black arrows). Similar positivity with this antibody was found within blood vessel walls (orange arrow). Brown staining in the dermis represents antibodies directed against Complement 4 (C4; blue arrow) (200X). In (d) the DIF stain is positive for FITC conjugated antibodies directed against human fibrinogen, showing positive green staining in the area of a dermal papilla (white arrow). Additionally, there was also weak basement membrane zone staining for fibrinogen (yellow arrow). The light blue arrow points to four positive dermal vessel walls (round structures), and a strong positive area in the dermis (red arrow). The nuclei of the cells were highlighted with TO-PRO-3 stain, a red nuclear and chromosome counterstain (200X). (e) Double IHC staining using an antibody to von Willebrand Factor (brown staining; blue arrows), colocalizing with positive staining for CD45 antibody (pink staining; red arrows) in the dermal vessels (200X). (f) IHC stain showing positive staining with CD51 stain around upper dermal vessels (brown staining) colocalizing with an antibody directed against CD15 (pink staining). The red arrows point toward the combined positivity (200X).

both were positive for gram-negative rods. A diagnosis of sepsis secondary to urinary tract infection (UTI) (urosepsis) was established by isolating *Proteus spp*, and accordingly intravenous administration of Ceftriaxone was initiated.

The skin biopsy microscopic examination demonstrated a focal intraepidermal vesicle formation with neutrophils and other fragmented cellular debris in the vesicle lumina. An inflammatory infiltrate was present in and around the dermal blood vessels, including those within dermal papillae (Fig. 1b). Overall, there was a florid inflammatory process involving capillaries and small blood vessels within the superficial dermis. Fibrin deposition and fibrinoid necrosis were observed within blood vessel walls; neutrophil infiltration was present within the vessel walls, accompanied by fragmented neutrophil nuclei, extravasated erythrocytes, and some perivascular lymphocytes (Fig. 1c). A diagnosis of cutaneous leukocytoclastic vasculitis (LCV) was rendered. After five days of antibiotics and low dose corticosteroids, there was clinical improvement of the skin lesions.

Further testing was performed using direct immunofluorescence (DIF), as well as immunohistochemical (IHC) studies. Please see Table 1 for the used antibodies. Our results are shown in Figure 1. In Figure 1b, we demonstrate the leukocytoclastic vasculitis (LCV). In Figure 1c, double IHC staining shows a subepidermal blister with staining around the blister demonstrates the presence of Ribosomal Protein Phospho-S6 in the top of the blister as well as on the blister floor and blood vessel walls. IHC also shows staining in the dermis using antibodies against Complement 4. In Figure 1d, the DIF stain is positive for FITC conjugated antibodies directed against human fibrinogen, were positive in the area of a dermal papilla, some weak basement membrane zone, and dermal vessels. Figure 1e shows double IHC staining using an antibody to von Willebrand Factor colocalizing with positive staining for CD45 antibody (Fig. 1f). IHC stain showing positive staining with CD51 stain around upper dermal vessels colocalizing with an antibody directed against CD15.

DISCUSSION

Leukocytoclastic vasculitis (LCV) and cutaneous leukocytoclastic vasculitis (CLCV) (limited to the skin) are sometimes associated with other immune reactions, and/or medications, collagen-vascular diseases, infections, paraproteinemias, vaccines, biologic treatments, and neoplasias. About 50% of cases remain idiopathic [2]. LCV is a histopathologic manifestation of a common form of small vessel vasculitis (SVV) that can involve the skin and internal organs [2,3]. LCV can

Table 1: Antibodies used for DI, IIF and confocal microscopy, dilutions, catalog numbers and sources.

Catalogue	Antibody	Findings
F0202-2.	Polyclonal rabbit anti-human IgG FITC, 1:20, 1:20 dil, Agilent Dako	Epidermis NETS (+++). BMZ linear (+). Vessels superficial and deep vessels (+++). Cytoid bodies under BMZ. C ANCAS (++).
F0203-2	Polyclonal rabbit anti-human IgM FITC, 1:20 dil, Agilent Dako	Cytoid bodies under BMZ(+).
F0204-2	Polyclonal rabbit anti-human IgA FITC, 1:20 dil, Agilent Dako	BMZ granular (+). Superficial granular stain on the vessels of the dermis (++). Cytoid bodies in the papillary dermis (++).
F020102-2	Polyclonal rabbit anti-human C3 FITC, 1:20 dil, Agilent Dako	BMZ granular deposits (++). Superficial, communicating, and deep vessels (++). Cytoid bodies in papillary dermis (++).
F0111-02	Polyclonal rabbit anti-human Fibrinogen FITC, 1:40 dil, Agilent Dako	Linear BMZ (++). Mid-dermis strong band deposits that are mostly present at the cell's junctions (++++). Superficial, communicating, and deep dermal vessels (++++)
F0117-2	Polyclonal rabbit anti-human Albumin-FITC 1:40 dil, Agilent Dako	BMZ Linear (+). Vessels stain in both superficial vessels (+).
F0254-2	Polyclonal rabbit anti-human C1-q FITC, 1:20 dil, Agilent Dako	Negative
X0929-1	Negative Control Reagent, Rabbit F(ab')2/FITC, Control, FITC. Solid phase absorbed F(ab')2, 1 mL, dil 1:20, Agilent Dako	Negative
T3605	TO-PRO-3. Thermo Fisher Scientific.	Works perfect
Immunohistochemistry		
Clone F8/86	Von Willebrand Factor, Agilent DAKO, ready to use	Positive stain around all the small vessels mainly in the upper dermis
IR52761-2	Monoclonal Mouse Anti-Human CD45, Leucocyte Common Antigen	Positive around all the small vessels in upper dermis (++++).
GA06261-2	CD15, Clone Carb-3, FLEX RTU. Agilent Dako	Positive around all the small vessels in upper dermis (++++).
F0169,	Complement C4 from Dako FLEX.	Positive in the corneal cells above the blister, inside both upper and lower borders of the blisters, as well as in the small upper dermal vessels (+++). Some positive cells junctions like between the medium dermis were also seen (++).
701845	Phospho-S6 (Ser240, Ser244) recombinant rabbit monoclonal antibody (11H14L20) from Thermo Fischer Scientific.	Positive in the corneal cells above the blister, inside both upper and lower borders of the blisters, as well as in the small upper dermal vessels (+++).

present as part of a systemic disease, most frequently involving ANCA-associated vasculitides, connective tissue diseases, cryoglobulinemia's, IgA vasculitis (formerly known as Henoch-Schönlein purpura) and hypocomplementemic urticarial vasculitis [4]. When LCV is suspected, an extensive work-up is usually necessary to determine whether the process is skin-limited, or a manifestation of systemic vasculitis or disease.

We present a case of leukocytoclastic vasculitis, manifested initially by cutaneous lesions. The case was linked to a urinary infection that became systemic; this phenomenon has been previously described [5].

In addition to the histological features clearly showing an LCV, the complementary DIF and IIF studies demonstrated immune complexes in the dermal blood vessels; we observed complement, fibrinogen, and immunoglobulin IgA positivity. Additional and unusual findings in our case included strong positivity for von Willebrand Factor (VWF), CD15, CD45, complement C4 and Phospho-S6 Ribosomal Protein (Ser240/244).

In our case, Ribosomal Protein Phospho-S6 (Ser240, Ser244) implicates an immune process that may represent an intermediate stage between the cutaneous and the systemic form of LCV. Notably, the deposition of complement and immunoglobulins, as well as fibrinogen at the dermal epidermal junction has been reported by others [6]. Multiple studies focusing on the DIF findings of LCV have not reported the complex local immune responses in skin biopsies that we present here [7,8].

The presence of VWF has not been studied properly in LCV. In our case, the anti-VWF antibody was strongly positive and colocalized with CD45 and CD15 and with Ribosomal Protein Phospho-S6 (Ser240/244). Recent studies highlight the involvement of VWF and its regulator, ADAMTS13, in mechanisms that underline a possible bridge between vascular inflammation and immunothrombosis [9]. VWF and ADAMTS13 seem to play roles in leukocyte rolling, adhesion, extravasation, vascular permeability, ischemia/reperfusion injury, complement activation, and NETosis [8].

In our case, we used antibodies directed against CD15 [Sialyl Lewis^{X}(sLeX), a stage-specific embryonic antigen] what has been shown to be important in leukocyte tethering and rolling [10]. In our case, it appears that CD15 possibly contributed to leukocyte tethering to the vascular endothelium. The tethering role may explain how CD15 was expressed in a co-localized manner with the observed CD45 positivity [10].

CONCLUSION

Leukocytoclastic vasculitis is a process that can be triggered by many factors, and the characteristics of the biopsy-correlating immune and inflammatory response must thus be studied accordingly.

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. Baigrie D, Goyal A, Crane JS. Leukocytoclastic Vasculitis. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 29489227.
2. Fraticelli P, Benfaremo D, Gabrielli A. Diagnosis and management of leukocytoclastic vasculitis. Intern Emerg Med. 2021;16:831-41.
3. Chango Azanza JJ, Calle Sarmiento PM, Lopetegui Lia N, Alexander SA, Modi V. Leukocytoclastic vasculitis: an early skin biopsy makes a difference. Cureus. 2020;12:e7912.
4. Bhesania S, Raol K, Medina C, Ilyas S, Bhesania J, Barmanwalla A. Leukocytoclastic vasculitis: depiction of the diagnostic dilemma. Cureus. 2021;13:e17462.
5. Abdelnabi M, Cavazos A, mitral N, tarbox M. Leucocytoclastic vasculitis secondary to urinary tract infection caused by extended-spectrum β-lactamase producing Klebsiella pneumonia. BMJ Case Rep. 2023;16:e2555395.
6. Magro CM, Mo JH, Kerns MJ. Leukocytoclastic vasculitis in association with linear epidermal basement membrane zone immunoglobulin deposition: Linear vasculitis. Clin Dermatol. 2022;40:639-50.
7. Lath K, Chatterjee D, Saikia UN, Saikia B, Minz R, De D, et al. Role of direct immunofluorescence in cutaneous small-vessel vasculitis: experience from a tertiary center. Am J Dermatopathol. 2018;40:661-6.
8. Takatu CM, Heringer APR, Aoki V, Valente NYS, de Faria Sanchez PC, de Carvalho JF, et al. Clinicopathologic correlation of 282 leukocytoclastic vasculitis cases in a tertiary hospital: a focus on direct immunofluorescence findings at the blood vessel wall. Immunol Res. 2017;65:395-401.
9. Gragnano F, Sperlongano S, Golia E, Natale F, Bianchi R, Crisci M, et al. The role of von willebrand factor in vascular inflammation: from pathogenesis to targeted therapy. Mediators Inflamm. 2017;2017:5620314.
10. Zhang Y, Ohkuri T, Wakita D, Narita Y, Chamoto K, Kitamura H, et al. Sialyl lewisx antigen-expressing human CD4+ T and CD8+ T cells as initial immune responders in memory phenotype subsets. J Leukoc Biol. 2008;84:730-5.

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Our Dermatology Online

Case Report

Usefulness of ultrasonography in the assessment of skin lesions of cutaneous t-cell lymphoma

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ABSTRACT

Cutaneous T-cell lymphoma (CTCL) poses a challenge in terms of diagnosis and assessment of disease progression. High-frequency ultrasound (HFUS) is a non-invasive imaging modality used for evaluating dermal changes, including the assessment of infiltrative intensity in CTCL. HFUS encompasses the assessment of infiltrative intensity, visualization of tumor characteristics, and monitoring of disease progression and treatment response. By providing detailed and precise information regarding the affected skin layers, HFUS contributes to the diagnostic process and aids in the management of this complex disease. Herein, we present the case of a 79-year-old male diagnosed with mycosis fungoides (MF), whose disease was confirmed by HFUS examination during PUVA therapy.

Key words: Ultrasonography, Diagnostic imaging, CTCL, Mycosis fungoides, MF, Skin diseases

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) accounts for approx. 4% of all non-Hodgkin lymphomas and represents 75–80% of all primary cutaneous lymphomas [1]. It exhibits a male predominance, with a male-to-female ratio of 2:1 [2,3].

The incidence of CTCL rises with advancing age, with an average age at diagnosis ranging from 50 to 60 years old [3]. The etiopathogenesis of CTCL remains unclear. Several theories have been proposed, including viral infections such as Epstein–Barr virus (EBV) and human T-cell lymphotropic virus type 1 (HTLV-1), which may lead to a chronically dysregulated immune state. Genetic factors, such as specific human leukocyte antigen (HLA) types precisely the upregulation of HLA-G, in conjunction with the expression of interleukin-10 (IL-10) [4], as well as exposure to certain chemicals and medications, have also been implicated [5]. The cutaneous manifestations of CTCL may be patches papules, plaques, nodules, and/or tumors, which have the potential to ulcerate and undergo necrosis, leading to the formation of varioliform scars upon healing [6]. Approx. 10% of individuals with CTCL experience extracutaneous spread, indicating the involvement of organs or tissues beyond the skin.

High-frequency ultrasound (HFUS) is a non-invasive imaging technique employed for the evaluation of dermal alterations. Its utilization encompasses the assessment of infiltrative intensity in CTCL.

Skin sonographic examinations were conducted at the Department of Dermatology in Wroclaw using a taberna pro medicum (tpm) GmbH device manufactured in Lüneburg, Germany. The device operates at a frequency of 22.5 MHz. The transducer allows for tissue penetration up to a depth of 8 mm, offering a vertical (axial) resolution of 80 μm and a horizontal (lateral) resolution of 200 μm. For data acquisition and storage, the DUBmicro®tpm software was employed. This software facilitates the recording and storage of ultrasound data obtained during the examinations. Echogenicity measurements of

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structures were evaluated using both the A mode and B mode.

CASE REPORT

A 79-year-old male presented for the first time at the Department of Dermatology in Wrocław in 2018. At that time, he exhibited scattered, well-demarcated erythematous and scaling lesions on the skin of the upper and lower extremities, as well as the trunk. It was accompanied by pruritus (4/10 on the NRS scale). Treatment with PUVA (psoralen and UVA) (27 sessions) and clobetasol propionate ointment 0.5 mg/mL b.i.d led to partial improvement of the skin lesions. Laboratory tests revealed elevated levels of beta-2-microglobulin (2.62 mg/I, normal: 2.5 mg/l) and total IgE (3210 IU/mL, normal: 100 IU/mL).

During hospitalization in 2020, the treatment plan included the addition of subcutaneous methotrexate (20 mg/p.w.).

During hospitalization in January 2021, immunophenotyping of peripheral blood revealed CD4+/CD7-: 8%, CD4+/CD27-: 23.0%, and CD4+/CD8+: 1:4:1. Furthermore, the histopathological result of the temporal tumor biopsy obtained during the previous hospitalization indicated diffuse infiltration of lymphocytes, plasma cells, histiocytic cells, some neutrophils, eosinophils, and occasional multinucleated giant cells in the dermis. Elastolysis was observed. The lymphocyte population mainly consisted of CD3+ T cells, with very few CD20+ B cells. A relatively small number of cells expressed CD5 and CD7 (partial loss of expression), while scattered and small clusters of cells showed CD30 expression. CD68 expression was observed in numerous cells (macrophages), and MUM-1 expression was detected in several cells (Fig. 1). The histological findings in conjunction with the clinical presentation supported the diagnosis of MF. The diagnosis was once again confirmed by an immunohistochemical examination, which detected CD30+ cells in the epidermis as well as a Ki67 expression of 10%. Additionally, features of epidermotropism were observed, which may correspond to the progressive phase of MF. In January 2022, new erythematous and infiltrated lesions appeared. Peripheral lymph node ultrasonography did not reveal any abnormalities. The patient underwent treatment with bexarotene initiated in May 2022. Since then, the patient has been under the care of the dermatology clinic for completion of the mSWAT (modified Severity Weighted Assessment Tool) questionnaire, which is a requirement in the bexarotene program. In April 2023, the patient returned to the Department of Dermatology in Wrocław. Upon physical examination, diffuse erythematous and infiltrated lesions were observed on the cervical region, hairy scalp, trunk, and extremities (Figs. 2 and 3). These cutaneous manifestations were accompanied by prominent epidermal desquamation and xerosis. Notably, the affected areas on the hairy scalp exhibited follicular miniaturization.

Following the patient's admission, a successive evaluation utilizing the mSWAT was undertaken. The score was 61. Subsequently, an HFUS examination was conducted.

The HFUS depiction of healthy skin showcased a conventional profile in accordance with the attributes

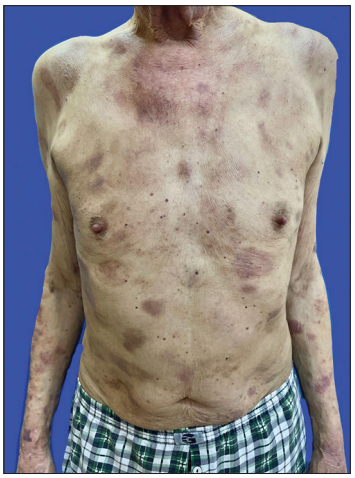

Figure 1: Acanthosis, epidermotropism, and massive infiltration in the dermis (typical features of CTCL).

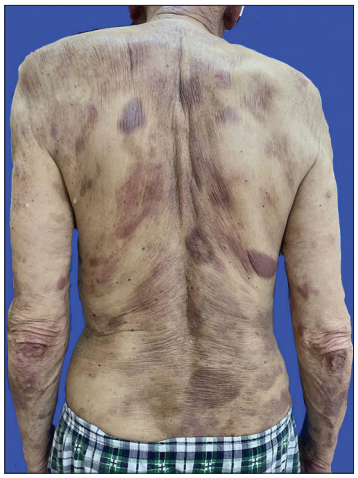

Figure 2: Diffuse erythematous and infiltrated lesions on the trunk and extremities (front).

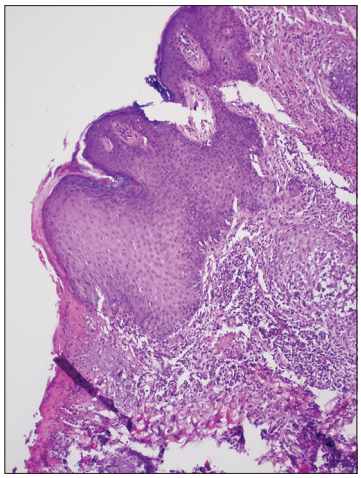

Figure 3: Diffuse erythematous and infiltrated lesions on the trunk and extremities (back).

commonly observed in a 79-year-old individual (Fig. 4).

The assessment of the patient's cutaneous condition unveiled the presence of massive dermal infiltrates, accompanied by a notable augmentation in dermal thickness (Fig. 5).

Hematological consultation confirmed the compatibility of PUVA phototherapy with concurrent bexarotene chemotherapy. The total dose of phototherapy was 20.9 mJ/m^2 during eighteen sessions resulting in favorable clinical outcomes.

DISCUSSION

HFUS represents a non-invasive and cost-effective diagnostic modality that finds application in the evaluation of dermatological treatments. Furthermore, HFUS exhibits potential in the monitoring of disease progression in specific dermatoses. This imaging technique offers valuable insights into the efficacy of interventions and aids in the assessment of tissue characteristics, facilitating a comprehensive understanding of the underlying pathophysiology and treatment response [7]. There are still only several reports in the literature on the investigation of CTCL's patients with HFUS [7-11].

Yukun Wang et al. [8] conducted a study involving 26 patients, consisting of 2 individuals diagnosed with Sézary syndrome, 2 with folliculotropic mycosis fungoides (fMF), and 22 with the classical variant of mycosis fungoides (cMF). Among the cohort, a subgroup of 16 individuals presented with early-stage

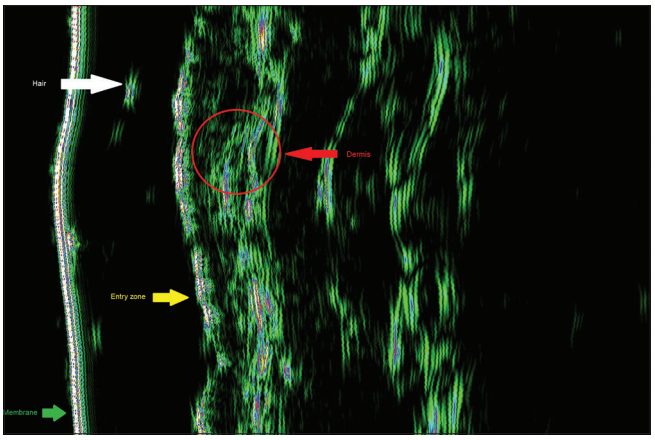

Figure 4: HFUS typical for a 79-year-old man.

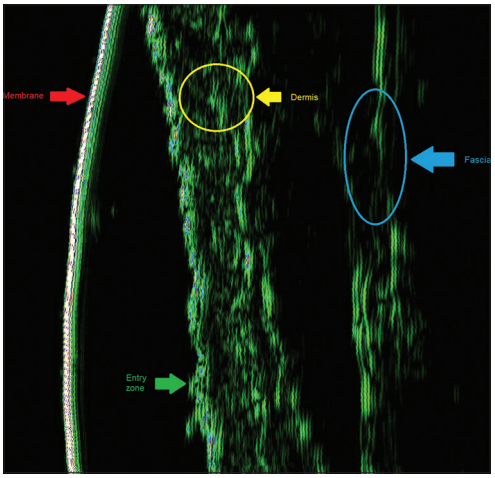

Figure 5: Massive infiltration in the dermis.

manifestations characterized by the presence of patches or plaques. Ultrasonographic examination revealed a subepidermal, hypoechoic band in these cases, with only three lesions at the plaque stage exhibiting partial extension into the superficial dermal layer. Conversely, in the advanced-stage group of seven patients with tumor formations, infiltrative changes involving the deep dermis or subcutaneous tissue were observed. Furthermore, notable observations were made in two instances of fMF lesions and one case of Sézary syndrome. These particular lesions exhibited distinctive features, including well-defined, subepidermal, hypoechoic bands accompanied by heterogeneous hypoechoic regions surrounding hair follicles in the dermal layer. Anita Mandawa et al. [9] conducted a retrospective multicenter study utilizing data from centers in Spain, Italy, India, and Chile to assess the ultrasonographic characteristics in patients with both B-cell and T-cell cutaneous lymphomas. HFUS was utilized for the evaluation of primary cutaneous lesions, consistently demonstrating dermal thickening

across the entire cohort. The lesions exhibited a hypoechoic echotexture characterized by the absence of calcifications or central necrosis. Classification based on ultrasonographic features identified focal infiltrative, nodular, pseudonodular, and diffuse infiltrative patterns. Notably, T-cell lymphomas exhibited a higher propensity for diffuse infiltrative changes relative to the other discerned patterns.

Polanska et al. [10], used a 20 MHz HFUS probe to study MF patients and found SLEB thickness decreased with phototherapy, suggesting it could monitor treatment response.

According to research by Iris Wohlmuth-Wieser et al. [11], HFUS measured thicker skin in CTCL and psoriasis compared to AD patients.

CONCLUSIONS

In summary, HFUS is a valuable and non-invasive diagnostic tool for assessing skin conditions and dermatological treatments. It may also help monitor disease progression and treatment effectiveness in cutaneous lymphomas such as mycosis fungoides and T-cell lymphomas. HFUS is known for its ability to provide precise diagnostic information and track treatment responses in different stages and types of the lymphomas.

REFERENCES

1. Keto J, Hahtola S, Linna M, Väkevä L. Mycosis fungoides and Sézary syndrome: A population-wide study on prevalence and health care use in Finland in 1998-2016. BMC Health Serv Res. 2021;21:166.
2. Korgavkar K, Xiong M, Weinstock M. Changing incidence trends of cutaneous T-cell lymphoma. JAMA Dermatol. 2013;149:1295-9.
3. Rodd A, Ververis K, Karagiannis T. Current and emerging therapeutics for cutaneous t-cell lymphoma: Histone deacetylase inhibitors. Lymphoma. 2012;2012:290685.
4. Urosevic M, Willers J, Mueller B, Kempf W, Burg G, Dummer R. HLA-G protein up-regulation in primary cutaneous lymphomas is associated with interleukin-10 expression in large cell T-cell lymphomas and indolent B-cell lymphomas. Blood. 2002;99:609-17.
5. Mirvish JJ, Pomerantz RG, Falo LD Jr, Geskin LJ. Role of infectious agents in cutaneous T-cell lymphoma: Facts and controversies. Clin Dermatol. 2013;31:423-31.
6. Bagherani N, Smoller BR. An overview of cutaneous T cell lymphomas. F1000Res. 2016;5:F1000 Faculty Rev-1882.
7. Levy J, Barrett DL, Harris N, Jeong JJ, Yang X, Chen SC. High-frequency ultrasound in clinical dermatology: A review. Ultrasound J. 2021;13:24.
8. Wang Y, Niu Z, Liu J, Zhu Q, Liu Z, Liu Y, et al. Value of high-frequency ultrasound in accurate staging of mycosis fungoides/Sézary syndrome. J Ultrasound Med. 2020;39:1927-37.
9. Mandava A, Koppula V, Wortsman X, Catalano O, Alfageme F. The clinical value of imaging in primary cutaneous lymphomas: Role of high resolution ultrasound and PET-CT. Br J Radiol. 2019;92:20180904.
10. Polańska A, Dańczak-Pazdrowska A, Olek-Hrab K, Osmola-Mańkowska A, Bowszyc-Dmochowska M, Żaba R, et al. High-frequency ultrasonography: New non-invasive method in assessment of skin lymphomas. Skin Res Technol. 2018;24:517-21.
11. Wohlmuth-Wieser I, Ramjist JM, Shear N, Alhusayen R. Morphologic features of cutaneous t-cell lymphomas using dermoscopy and high frequency ultrasound. J Clin Med. 2020;10:17.

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Our Dermatology Online

Case Report

Recurrent panniculitis in a patient with myelodysplastic neoplasms: A case of neutrophilic lobular panniculitis

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ABSTRACT

Neutrophilic dermatoses (ND) encompass a diverse group of inflammatory skin disorders characterized by sterile, predominantly neutrophilic infiltrates. Herein, we present the case of a 38-year-old male with very high-risk hypocellular myelodysplastic neoplasms (MDS) exhibiting recurrent neutrophilic panniculitis (NP) involving the lower extremities. The patient underwent hematopoietic progenitor cell transplantation (HPCT) resulting in lesion remission. This case emphasizes the importance of considering NP in ND diagnoses, especially in the context of hematological disorders. Diffusion of such cases is essential for healthcare professionals to enhance their ability to recognize and effectively address this rare condition.

Key words: Neutrophilic dermatoses, Myelodysplastic neoplasms, Neutrophilic panniculitis

INTRODUCTION

Neutrophilic dermatoses (ND) are a group of inflammatory skin disorders characterized by a sterile, predominantly neutrophilic infiltrate on histopathology. The neutrophilic infiltrate may extend from the epidermis to subcutaneous tissue, leading to uncommon clinical-pathological entities and complex overlapping conditions [1,2]. ND manifests as deep, erythematous, tender, and painful nodules or plaques that typically affect the arms, legs, and trunk [1,3,4]. The lesions typically persist for approx. two weeks and usually result in post-inflammatory hyperpigmentation. Myelodysplastic neoplasms (MDS) have been associated with these groups of dermatoses. First-line treatment involves oral corticosteroids. Some dermatoses may resolve spontaneously, although recurrence is common [2,3,5-7].

CASE REPORT

A 38-year-old male from Mexico City, diagnosed with very high-risk hypocellular MDS (IPSS-R score of 6.5 points) and without any known comorbidities, was evaluated two years after his MDS diagnosis by our dermatology department. He had been actively receiving medical treatment with darbepoetin alfa, filgrastim, and eltrombopag. The patient presented an intermittently and slightly painful nodule with a localized increase in temperature in the right lower extremity in the previous 48 hours, which was not associated with fever or other systemic symptoms. He improved after treatment with indomethacin, and the nodule resolved within several weeks. Two months later, he developed a blistering plaque without fever or additional symptoms. A skin biopsy was performed, and the results revealed superficial and deep neutrophilic dermatosis with microabscesses of neutrophils and neutrophilic lobular panniculitis (Fig. 1). At this point, he received therapy with amoxicillin/clavulanate, which resulted in the involution of the lesion, leading to residual post-inflammatory hyperpigmentation (Fig. 2a). Three months later, a nodule with overlying erythema and increased local temperature reappeared, resolving within 72 hours without any treatment.

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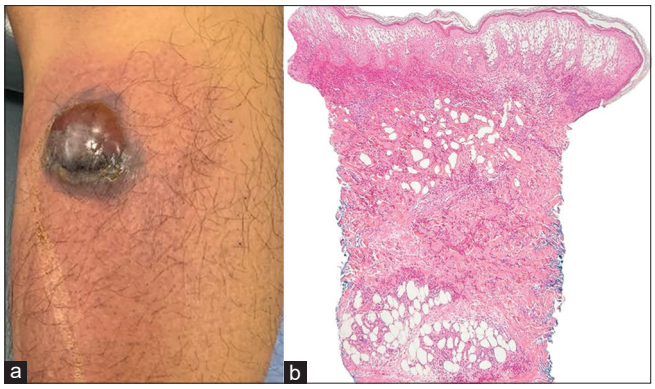

Figure 1: a) Dermatosis localized to the right lower extremity characterized by a 2 cm erythematous-violaceous, cup-shaped neoformation presenting a smooth, shiny surface with well-defined regular borders on erythematous skin and increased volume. b) Superficial and deep neutrophilic dermatoses with microabscesses of neutrophils and neutrophilic lobular panniculitis.

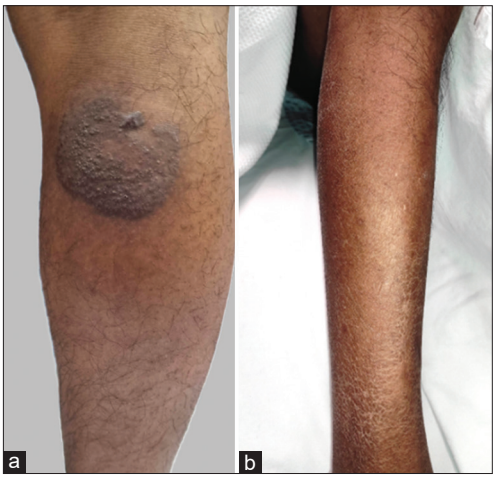

Figure 2: (a) Post-inflammatory hyperpigmentation. (b) Follow-up with the resolution of the lesion after hematopoietic progenitor cell transplantation.

Another biopsy indicated septal and lobular panniculitis without vasculitis, and stains and cultures for bacteria and fungi were negative. Laboratory studies showed the interferon-gamma release assay to be negative multiple times throughout the evaluation, no leukocytosis, neutrophils fewer than 5,000 and below 50%. The patient was scheduled for hematopoietic progenitor cell transplantation (HPSCT). After the transplant, he was evaluated by the dermatology team, presenting only grade II mucositis, which was managed with analgesia. There was no relapse of the lesions after the HPSCT during follow-up (Fig. 2b).

DISCUSSION

This was a patient with recurrent bilateral lower extremity panniculitis. In his approach, it was crucial to exclude the possibility of an infectious source to exclude cellulitis; all cultures and stains were negative. Two biopsies indicated an abundant neutrophilic infiltrate, which led to the presumption of classic Sweet's syndrome; however, the patient did not meet the necessary criteria for diagnosis. Classic Sweet's syndrome is typically defined by the presence of two major criteria and two minor criteria [8]. Our patient did meet the two major criteria, which were the abrupt onset of tender nodules and a dense neutrophilic infiltrate in the biopsy. However, out of the four minor criteria, our patient only met one, which was the association with a hematologic disease. After excluding other potential diagnoses, we reached the conclusion of neutrophilic (lobular) panniculitis (NP). As mentioned earlier, NP has been associated with MDS. A study by Sutra-Loubet et al. demonstrated a strong association between NP and MDS. Out of the eight reported cases of NP, MDS was identified in six, that is, in 75% of the patients [2]. The mechanisms by which HPSCT induced remission of the lesions remain unknown. Nevertheless, we propose that the treatment of the underlying disease (in this case, MDS) may act as a protective factor against recidivism.

CONCLUSION

NP is a rare condition within the ND group, named *lobular* because the inflammation predominates in the fat lobules. Hematological malignancies should be investigated in patients in whom NP is found [9]. NP is a diagnosis of exclusion, and it must be known that overlapping is a frequent feature within the ND spectrum, making diagnoses even more difficult. The differentiation of NP from other NDs is relevant since there is no standardized protocol for its diagnosis or approach. Healthcare professionals may only consider the suspicion of this condition if they are familiar with it, which is why we believe the diffusion of these cases is so important.

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.

REFERENCES

1. Delaleu J, Lepelletier C, Calugareanu A, De Masson A, Charvet E, Petit A, et al. Neutrophilic dermatoses. Rev Med Interne. 2022;43:727-38.

2. Sutra-Loubet C, Carlotti A, Guillemette J, Wallach D. Neutrophilic panniculitis. J Am Acad Dermatol. 2004;50:280-5.
3. Ichiki T, Sugita K, Goto H, Shindo M, Yamamoto O. Localized pegfilgrastim-induced neutrophilic dermatosis with tissue G-CSF expression: A mimicker of Sweet's syndrome. Acta Derm Venereol. 2019;99:685-6.
4. Becherer K, Golda N, Feldman M, Diaz-Arias A, Caldwell C. Neutrophilic panniculitis associated with myelodysplastic syndrome with abnormal nuclear forms. J Cutan Pathol. 2009;36:1024-6.
5. Qian L, Shen J, Cen J, Yin W, Ma Y. Myelodysplastic syndrome with neutrophilic panniculitis: A report of two cases and a literature review. Oncol Lett. 2015;9:1954-6.
6. Kim H, Youn H, Shin H, Yahng A, Lee E, Kwon C. Neutrophilic panniculitis following azacitidine treatment for myelodysplastic syndromes. Leuk Res. 2012;36:146-48.
7. Suzuki Y, Kuroda K, Kojima T, Fujita M, Iseki T, Shinkai H. Unusual cutaneous manifestations of myelodysplastic syndrome. Br J Dermatol. 1995;133:483-6.
8. Agrawal A, Arif SH, Kumarasan K, Janjua D. Sweet's syndrome: An update. Curr Pediatr Rev. 2022;18:265-73.
9. Matsumura Y, Tanabe H, Wada Y, Ohta K, Okamoto H, Imamura S. Neutrophilic panniculitis associated with myelodysplastic syndromes. Br J Dermatol. 1997;136:142.

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Our Dermatology Online

Case Report

Two subcutaneous cold abscesses after accidental bacillus Calmette–Guérin revaccination in an adult with urothelial carcinoma of the bladder

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ABSTRACT

The complications of bacillus Calmette–Guérin (BCG) revaccination are poorly described. The objective was to report a rare case of two subcutaneous abscesses caused by accidental BCG revaccination. A 63-year-old patient, followed for non-invasive urothelial carcinoma of the urinary bladder resected on two occasions with a recurrence, was scheduled for BCG immunotherapy. One month before admission, the patient, accidentally, received two subcutaneous injections of BCG in the left arm and periumbilical area. Three weeks later, the patient presented two subcutaneous cold abscesses at both injection sites. Ziehl–Neelsen stain found an acid-alcohol resistant bacillus. A culture showed *Mycobacterium bovis*. The patient received local isoniazid for two months with good evolution. Although adverse reactions are rare after BCG revaccination, it is crucial to continue monitoring to learn more and choose timely treatment if they occur.

Key words: Bacillus Calmette–Guérin immunotherapy, BCG vaccination, BCG revaccination, Subcutaneous cold abscesses, Urothelial carcinoma of the bladder

INTRODUCTION

Bacillus Calmette–Guérin (BCG) vaccine is a live-virus vaccine with attenuated strains of *Mycobacterium bovis* [1,2] employed in tuberculosis vaccination with an excellent safety profile. The local and systemic complications of BCG vaccination were well described in the literature. The frequency of these complications is low in relation to the large number of vaccinations performed. They are common in cases of overdosing and with poor vaccination techniques. They are mostly benign. The complications of revaccination, as in this observation, are much less described. The objective was to report a case of complications resulting from accidental BCG revaccination.

CASE REPORT

Herein, we report the case of a 63-year-old patient followed for non-invasive low-grade papillary urothelial carcinoma of the bladder, resected on two occasions with a recurrence. A decision was reached to treat the patient with BCG immunotherapy. The procedure consisted of administering BCG in liquid form into the bladder through a catheter once a week for six weeks in two-hour sessions. One month before admission, the patient received two subcutaneous injections of BCG (powder for intravesical suspension) in the left arm and periumbilical area following a misinterpretation of the prescription by the dispensing pharmacy. Three weeks after the injections, the patient presented two nodular

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and erythematous lesions, painless, of soft consistency, measuring 3 x 2.5 cm for the lesion of the arm and 5 x 5 cm for the periumbilical lesion, not improving under well conducted antibiotic therapy. The physical examination was normal, including pleuro-pulmonary, lymph node examination. Everything was evolving in a context of apyrexia and the conservation of the general state. Puncture of the lesions yielded frank pus. A search for pyogenic germs was negative. Ziehl–Neelsen stain found an acid-alcohol resistant bacillus. A culture showed *Mycobacterium bovis*. A skin biopsy from both sites revealed polymorphic granulation tissue rich in neutrophil with vascular neogenesis (Fig. 1). The two lesions ulcerated secondarily (Figs. 2a and 2b). Taking into account the risks of oral isoniazid monotherapy in a tuberculosis-endemic country such as ours, we decided to treat the patient with local isoniazid combined with local care (Figs. 3a and 3b) for two months with a good progression.

DISCUSSION

Over the past several decades, BCG therapy for non-muscle invasive bladder cancer has become more widely accepted, especially for intermediate- and high-risk patients. Intravesical BCG instillation continues to be the primary setting for the high-risk population at this time [3,4]. Our patient was a candidate for this therapeutic strategy, and by mistake, he received the BCG vaccine as a subcutaneous injection in the left arm and periumbilical area. In countries with high tuberculosis endemicity, localized BCG vaccine side effects, such as injection site abscesses, hypersensitivity reactions, and localized lymphadenopathy, are typically self-limiting [5]. *BCGitis* is a specific reaction to the BCG vaccine, described mainly in children. Depending on the location in relation to the injection site, a distinction is made between local, locoregional, distant, and disseminated forms. The WHO no longer recommends BCG revaccination since it is thought to have minimal or no efficacy [6-10]. The most frequently described complications following revaccination are subcutaneous abscesses and lingering ulcerations. In a retrospective study by Ouazzani et al. conducted in 2007 over a period of five years (between January 2000 and March 2005) including twelve patients presenting complications following revaccination with BCG, the most frequently noted complication was a subcutaneous abscess in two-thirds of the cases, followed by persistent secondary ulcerations in around one-third of the cases, including one case of

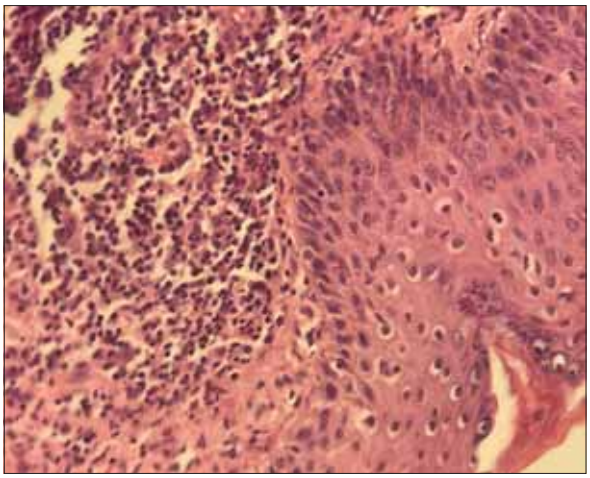

Figure 1: Histological section of the skin fragment from the periumbilical abscess. Microscopic observation of H&E-stained specimen in 40-fold magnification showing a polymorphic granulation tissue rich in neutrophils with vascular neogenesis.

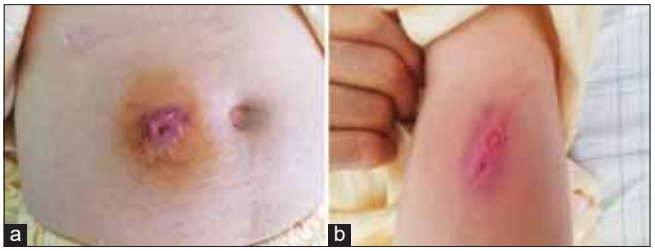

Figure 2: (a and b) The two lesions in (a) the periumbilical area and (b) The left arm ulcerating before the initiation of isoniazid.

Figure 3: (a and b) The evolution of the two abscesses five weeks after treatment with local isoniazid in (a) The periumbilical area and (b) The left arm.

osteitis [11,12]. Complications related to revaccination were reported in Brazil in thirteen children and adolescents, dominated by the occurrence of persistent ulcerations [12]. The mechanism of these accidents after revaccination has been poorly studied in the literature. Two pathophysiological mechanisms have been proposed: infectious and immunological. However,

the presence of *Mycobacterium bovis* in the wounds is compatible with an immunological phenomenon at the origin of these skin lesions. It may be a type III hypersensitivity reaction or a local Arthus phenomenon with excess antigen in an already immunized subject with precipitating circulating antibodies. It may also be a delayed hypersensitivity reaction induced by BCG revaccination with the appearance of an inflammatory erythematous reaction followed by central necrosis. The proportion of responsibility between the two main types of pathophysiological mechanisms—infectious and immunological—is difficult to assess.

In the literature, there is no consensus on the treatment for BCG as per side effects, and the management approach varies between cases and countries. According to some authors, the effectiveness of oral antibiotics, such as isoniazid, erythromycin, and an isoniazid and rifampicin combination, in treating BCG complications is debatable. The use of isoniazid monotherapy for the treatment of local BCG complications may be limited by the development of resistance during treatment [13,14]. Drainage and chemotherapy with erythromycin or isoniazid are typically effective treatments for injection site abscesses [14]. Taking into account the risks of oral isoniazid monotherapy in a tuberculosis-endemic country such as ours, we decided to treat the patient with local isoniazid and local care and noted good evolution. Topical isoniazid may be a reasonable option in this situation given that its use in our case was safe and effective. Future randomized controlled research should explore this hypothesis.

CONCLUSION

Revaccination is no longer recommended by the WHO, and several studies have concluded that revaccination is unnecessary. The favorable evolution of our case may have been related to a low virulence of the strain or the effectiveness of antibiotic therapy. In the case of accidental vaccination, preventive treatment is strongly recommended.

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. World Health Organization. BCG vaccines: WHO position paper. Weekly Epidemiological Record. 2018;93:73-96.
2. Andersen P, Woodworth JS. Tuberculosis vaccines-rethinking the current paradigm. Trends Immunol. 2014;35:387-95.
3. Liu G, Li B, Xu Z, Wang J, Ma S, Kan Y, et al. Bacillus Calmette–Guerin for the treatment of non-muscle invasive bladder cancer: History and current status. Discov Med. 2022;33:85-92.
4. Saluja M, Gilling P. Intravesical bacillus Calmette–Guerin instillation in non-muscle-invasive bladder cancer: A review. Int J Urol. 2018;25:18-24.
5. Sellami K, Amouri M, Kmiha S, Bahloul E, Aloulou H, Sfaihi L, et al. Adverse reaction due to the bacillus Calmette–Guerin vaccine: Twenty Tunisian cases. Indian J Dermatol. 2018;63:62-5.
6. Roth AE, Benn CS, Ravn H, Rodrigues A, Lisse IM, Yazdanbakhsh M, et al. Effect of revaccination with BCG in early childhood on mortality: Randomised trial in Guinea-Bissau. BMJ. 2010;340:671.
7. Glynn JR, Fielding K, Mzembe T, Sichali L, Banda L, McLean E, et al. BCG re-vaccination in Malawi: 30-year follow-up of a large, randomised, double-blind, placebo-controlled trial. Lancet Glob Health. 2021;9:1451-9.
8. Barreto ML, Pereira SM, Pilger D, Cruz AA, Cunha SS, Sant'Anna C, et al. Evidence of an effect of BCG revaccination on incidence of tuberculosis in school-aged children in Brazil: Second report of the BCG-REVAC cluster-randomised trial. Vaccine. 2011;29:4875-7.
9. Bolursaz MR, Lotfian F, Velayati AA. Bacillus Calmette–Guérin vaccine complications in Iranian children at a University Hospital. Allergol Immunopathol. 2017;45:356-61.
10. D'Aleo F, Bananno R, Costantino ALP, Arena S, Midiri A, Mancuso G, et al. A case of abscess after BCG vaccine in an immunocompetent child without other clinical signs. JMM Case Reps. 2015;2:1-3.
11. Bannister S, Sudbury E, Villanueva P, Perrett K, Curtis N. The safety of BCG revaccination: A systematic review. Vaccine. 2021;39:2736-45.
12. Gyldenlove M, Andersen AB, Halkjaer LB. Cutaneous necrotic ulceration due to BCG revaccination. Human Vacc Immunother. 2012;8:423-4.
13. Alrabiaah AA, Alsubaie SS, Bukhari EI, Gad A, Alzamel FA. Outbreak of bacille Calmette–Guérin-related lymphadenitis in Saudi children at a university hospital after a change in the strain of vaccine. Ann Saudi Med. 2012;32:4-8.
14. Cuello-García CA, Pérez-Gaxiola G, Jiménez Gutiérrez C. Treating BCG-induced disease in children. Cochrane Database Syst Rev. 2013:CD008300.

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Our Dermatology Online

Case Report

Disseminated eczema or CTCL: Usefulness of high-frequency ultrasonography in the assessment of skin lesions of cutaneous T-cell lymphoma

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ABSTRACT

Cutaneous T-cell lymphoma (CTCL) presents a diagnostic and prognostic challenge in evaluating disease progression. High-frequency ultrasound (HFUS) is a non-invasive imaging technique that has emerged as a valuable tool for assessing dermal alterations, including infiltrative intensity in CTCL. Herein, we report the case of a 74-year-old male patient with a long-standing history of neurofibromatosis type 1 (NF1) since childhood who was also diagnosed with Sézary syndrome (SS) and whose disease remission was confirmed through HFUS examination during PUVA and methotrexate therapy. HFUS facilitated the assessment of infiltrative intensity, visualization of tumor characteristics, and monitoring of disease progression and treatment response. The high-resolution imaging provided by HFUS gave detailed and precise information about the affected skin layers, contributing to the diagnostic process and aiding in the management of CTCL.

Key words: CTCL, Ultrasonography, Diagnostic imaging, Skin diseases, Sézary syndrome

INTRODUCTION

Cutaneous T-cell lymphomas (CTCLs) encompass a heterogeneous group of non-Hodgkin lymphomas characterized by the clonal expansion and infiltration of malignant T lymphocytes within the skin. CTCLs predominantly manifest as primary cutaneous neoplasms without evidence of extracutaneous involvement at the time of diagnosis [1]. The incidence rate of CTCL is reported to be 10.2 cases per million individuals [2], and the conclusive diagnosis of CTCL presents a diagnostic challenge due to the absence of pathognomonic clinical features especially in the early stage [1]. High-frequency ultrasound (HFUS) is an emerging diagnostic modality that holds promise for the evaluation and monitoring of CTCL. Despite being a safe, cost-effective, and non-invasive technique, its application in the assessment of skin neoplasms remains limited. However, preliminary evidence from the literature suggests that HFUS exhibits significant diagnostic value and potential in the management of CTCL, warranting further exploration and validation in clinical settings [3].

CASE REPORT

Skin sonographic examinations were conducted at the Department of Dermatology in Wrocław, utilizing a taberna pro medicum (tpm) GmbH device manufactured in Lüneburg, Germany. The device employed advanced high-frequency ultrasound (HFUS) technology operating at a frequency of 22.5 MHz. The transducer enabled deep tissue penetration up to a maximum depth of 8 mm, providing remarkable vertical (axial) resolution of 80 µm and impressive horizontal (lateral) resolution of 200 µm. To acquire and store data, the state-of-the-art DUBmicro®tpm software was effectively employed. This cutting-edge

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software facilitated the seamless recording and systematic storage of ultrasound data obtained during the meticulously performed examinations. For the evaluation of echogenicity measurements, both A-mode and B-mode imaging techniques were employed.

A 74-year-old male patient diagnosed with neurofibromatosis type 1 was urgently admitted to the Department of Dermatology in April 2023 due to the presence of erythroderma (redness and scaling of the skin) accompanied by generalized desquamation (skin peeling) suggestive of generalized eczema. The patient reported a history of occupational exposure to various irritants, including oils and coolant fluids related to car manufacturing, and intermittent mild skin changes. Additionally, the patient had had skin lesions associated with neurofibromatosis type 1 since childhood and eczema since 2018. The patient provided informed written consent to participate in our study and undergo photographic documentation.

In November 2018, the patient was initially diagnosed with palmoplantar eczema, which responded well to topical glucocorticosteroid treatment. However, the condition later recurred and extended to involve the entire body, prompting a skin biopsy in May 2020 that confirmed generalized eczema. Intravenous antihistamines led to rapid skin improvement. Abnormalities in peripheral blood morphology warranted a hematological consultation and bone marrow examination, which revealed lymphoid infiltration with polymorphic morphology.

Further investigations included erythropoietin assessment, trephine bone marrow biopsy, tryptase concentration measurement, and screening for specific genetic mutations, all yielding negative results. Abdominal and peripheral lymph node ultrasounds in October 2020 were unremarkable, except for a reactive lymph node in the left axillary region.

Dermatological treatment involved systemic glucocorticosteroids and antihistamines, initially resulting in local improvement. Despite continued systemic therapy and medication adjustments, the skin condition gradually worsened. A skin biopsy in March 2021 did not indicate lymphoma yet showed minimal lymphoid infiltration. Peripheral blood immunophenotyping was unremarkable. Treatment approaches included methotrexate, methylprednisolone, and gabapentin.

In May 2021, higher doses of methylprednisolone and gabapentin were administered, alongside methotrexate and topical therapy. Despite initial improvement, the patient discontinued medication, leading to symptom worsening. Methotrexate was reintroduced in August 2021, combined with systemic steroids, antihistamines, gabapentin, and topical treatments. Eventually, methotrexate was discontinued in July 2022 due to a significant improvement in skin lesions and itchiness.

During hospitalization in April 2023, a comprehensive physical examination revealed generalized cutaneous alterations characterized by erythroderma, hyperkeratosis, desquamation, fissuring of the hands and soles of the feet, and numerous neurofibromatosis tumors (Figs. 1a and 1b).

Pertinent laboratory investigations demonstrated leukopenia, elevated erythrocyte sedimentation rate (ESR), increased C-reactive protein (CRP) levels, fasting hyperglycemia (113.0 mg/dL), total bilirubinemia (2.0 mg/dL), elevated lactate dehydrogenase (LDH) activity (286 mg/dL), hyperuricemia (10.6 mg/dL), and raised B-microglobulin levels. Manual peripheral blood smear examination did not reveal the presence of Sézary cells. Furthermore, a histopathological evaluation of skin specimens obtained in February 2023, exhibited an epidermis that was slightly acanthotic with mild hyperkeratosis and focal parakeratosis. Epidermotropic proliferation of small to medium-sized pleomorphic (*cerebriform*) lymphocytes formed intraepidermal Pautrier's microabscesses (Fig. 2). In

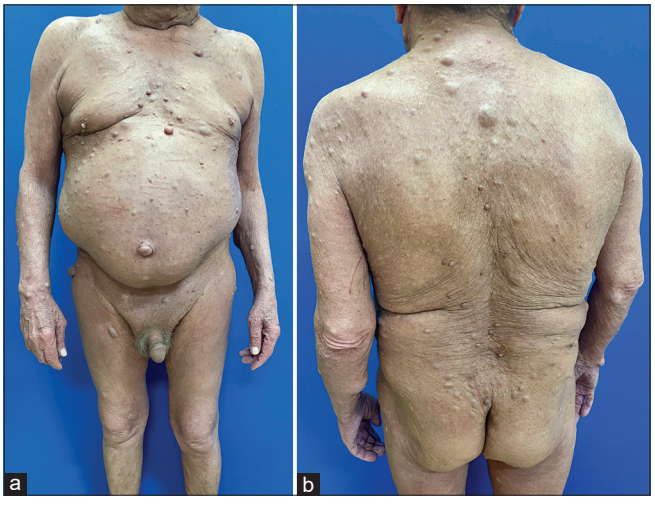

Figure 1: (a) Diffuse erythematous and infiltrated lesions on the trunk and extremities, a feature of CTCL and numerous neurofibromatosis tumors (front).(b) Diffuse erythematous and infiltrated lesions on the trunk and extremities, a feature of CTCL and numerous neurofibromatosis tumors (back).

immunohistochemistry, the neoplastic lymphocytes showed immunophenotype CD3+, CD4+, CD5+, CD8-, and CD7-/+ (partial loss). Cytotoxic markers such as TIA-1 and granzyme B were negative. In the course of employing HFUS to examine skin affected by Sézary syndrome, we ascertained pronounced infiltration within the dermal layer, coupled with notable augmentation of its thickness (Fig. 3a). Additionally, we also conducted an examination of neurofibromatosis lesions (Fig. 3b). During hospitalization, PUVA-therapy and topical therapies such as Encortolon ointment and urea ointment were administered, resulting in alleviation of pruritus. Nevertheless, due to an inadequate therapeutic response following PUVA treatment (total dose was 37.08 mJ/m^2 during ten sessions), methotrexate was reintroduced. Also, mSWAT was completed with a score of 51.

DISCUSSION

Despite the growing interest in HFUS as a diagnostic tool for patients with CTCL, there remains a limited number of studies in the literature focused on this particular area [4-7]. In a study conducted by Yazdanparast et al. [4] comprising a cohort of 21 CTCL patients, HFUS examination revealed significant differences in hydration, pH, melanin content, and erythema index between the lesional areas and unaffected skin. Moreover, the dermal echo density in the CTCL lesions was found to be significantly reduced compared to the adjacent normal skin. These findings underscore the potential utility of HFUS as a non-invasive and cost-effective modality for the diagnostic evaluation and longitudinal monitoring of CTCL. In a study conducted by Zi Han Niu et al. [5], involving a cohort of 62 patients presenting with erythema and scales, the investigation of epidermal thickness and subepidermal low-echo band (SLEB) thickness demonstrated a notable diagnostic significance in the differential diagnosis of early-stage mycosis fungoides from psoriasis vulgaris and eczema. A study conducted by Polańska et al. [6] demonstrated the significance of the subepidermal low-echo band (SLEB) parameter measured using high-frequency ultrasound (HFUS) in patients with CTCL. The investigation observed a notable decrease in SLEB thickness among patients undergoing phototherapy, implying that monitoring this parameter in CTCL patients could serve as a valuable tool for assessing the efficacy of treatment interventions.

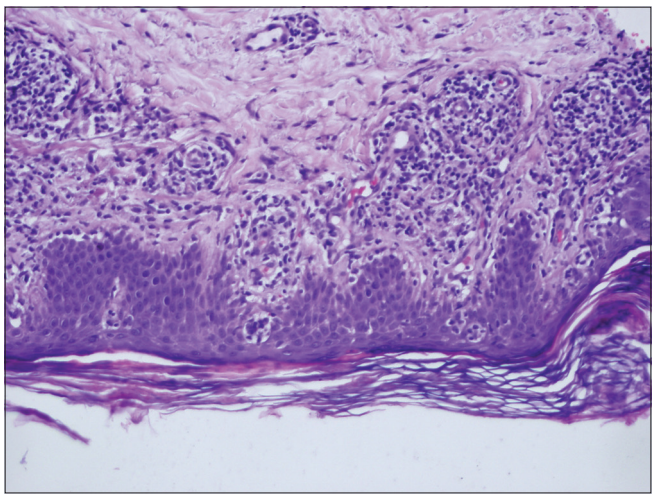

Figure 2: Dense upper dermal band-like epidermotropic infiltrate by atypical lymphocytes forming Pautrier's microabscesses (H&E).

In a study conducted by Iris Wohlmuth-Wieser et al. [7] comprising a cohort of thirteen patients, HFUS examination demonstrated an augmented epidermal thickness in individuals diagnosed with CTCL and psoriasis when compared to those with atopic dermatitis. Our observations indicated conspicuous dermal infiltration and heightened dermal thickness in regions affected by Sézary syndrome, thereby accentuating the informative capacity of HFUS in delineating disease-associated alterations.

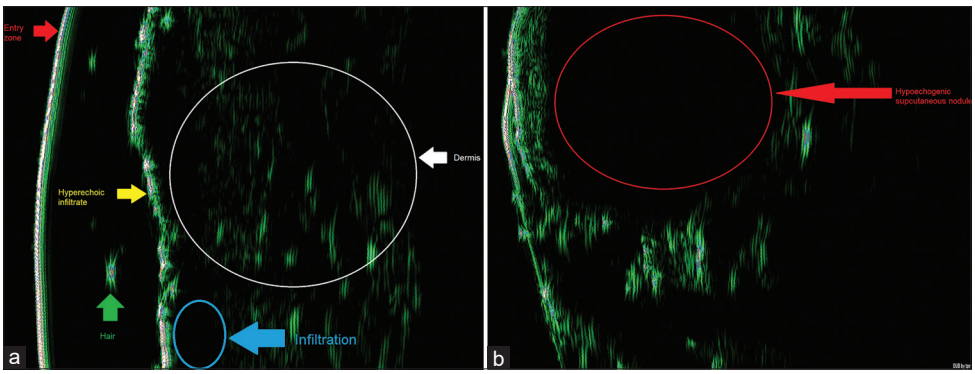

Figure 3: (a) Massive infiltration in the dermis (sonographic picture). (b) Sonographic feature of the neurofibroma in the skin.

CONCLUSION

The use of HFUS for the evaluation of CTCL furnishes valuable insights into both the underlying pathophysiology of the disease and its diagnostic prospects. While HFUS exhibits promising diagnostic utility in CTCL, the existing literature offers a relatively circumscribed exploration of its comprehensive capabilities. Noteworthy investigations conducted by disparate researchers have underscored HFUS's aptitude in discerning CTCL from other dermatological conditions based on parameters such as hydration, pH, melanin content, and echo density. Moreover, inquiries into the thickness of the subepidermal low-echo band (SLEB) have unveiled its potential as an indicator of treatment responsiveness and as a discriminator between CTCL and alternative skin disorders.

REFERENCES

1. Hristov AC, Tejasvi T, Wilcox RA. Mycosis fungoides and Sézary syndrome: 2019 update on diagnosis, risk-stratification, and management. Am J Hematol. 2019;94:1027-41.
2. Korgavkar K, Xiong M, Weinstock M. Changing incidence trends of cutaneous T-cell lymphoma. JAMA Dermatol. 2013;149:1295-9.
3. Wang Y, Niu Z, Liu J, Zhu Q, Liu Z, Liu Y, et al. Value of high-frequency ultrasound in accurate staging of mycosis fungoides/Sézary syndrome. J Ultrasound Med. 2020;39:1927-37.
4. Yazdanparast T, Yazdani K, Ahmad Nasrollahi S, Izadi Firouzabadi L, Humbert P, Khatami A, et al. Biophysical and ultrasonographic changes in early patch/plaque stage of mycosis fungoides, compared with uninvolved skin. Skin Res Technol. 2021;27:1029-34.
5. Niu Z, Wang Y, Zhu Q, Liu J, Liu Y, Jin H. The value of high-frequency ultrasonography in the differential diagnosis of early mycosis fungoides and inflammatory skin diseases: A case-control study. Skin Res Technol. 2021;27:453-60.
6. Polańska A, Dańczak-Pazdrowska A, Olek-Hrab K, Osmola-Mańkowska A, Bowszyc-Dmochowska M, Żaba R, et al. High-frequency ultrasonography: New non-invasive method in assessment of skin lymphomas. Skin Res Technol. 2018;24:517-21.
7. Wohlmuth-Wieser I, Ramjist JM, Shear N, Alhusayen R. Morphologic features of cutaneous T-cell lymphomas using dermoscopy and high-frequency ultrasound. J Clin Med. 2020;10:17.

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Our Dermatology Online

Case Report

Multiple squamous cell carcinomas complicating cocaine-induced morphea

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ABSTRACT

Localized cutaneous scleroderma, or morphea, is a highly heterogeneous group of autoimmune disorders that primarily affect the skin and adjacent tissues. Its pathogenesis remains unclear. Numerous factors, including genetics, drugs, infections, skin injuries, autoimmune diseases with abnormal cytokine production and/or such as vascular dysfunction, may play a role in the development of morphea. Fibrosis, inflammation, and chronic ulceration may ultimately contribute to skin neoplasia. Herein, we report a case of multiple metastatic squamous cell carcinomas complicating cocaine-induced morphea.

Key words: Squamous cell carcinoma, Induced scleroderma, Morphea, Drugs, Cocaine

INTRODUCTION

Morphea is a localized form of scleroderma that sometimes causes erosions and chronic ulcers on the skin. Herein, we report a case of multiple metastatic squamous cell carcinomas complicating cocaine-induced morphea.

CASE REPORT

A 54-year-old patient had been a cocaine sniffer for 22 years. He had been suffering from rapidly extensive skin sclerosis for sixteen years without Raynaud's phenomenon or other systemic signs. The initial clinical examination revealed scleroatrophic plaques on all four limbs and the trunk. The skin area was estimated at 50%. There were sclerodactyly and erosive plaques on the hands and feet, with synechiae and flessum of the limbs, resulting in functional impotence (Figs. 1a – 1d). Cocaine-induced generalized morphea was considered and immunosuppressive treatments were initiated. A combination of methotrexate and corticosteroids for six months did not yield an improvement, and the patient was put on imatinib. The evolution after two years was marked by the development of persistent erosions and ulcerations with hyper burgeoning, which led to taking a skin biopsy (Figs. 2a and 2b). A histological study confirmed the presence of a mature, well-differentiated squamous cell carcinoma with bone infiltration on the left hand and foot. An extension study revealed lymph node and lung metastases. The patient died before treatment was initiated.

DISCUSSION

Morphea, also known as llocalizeted scleroderma, is an inflammatory connective tissue disease with numerous clinical manifestations in adults and children. It is characterized by inflammation and fibrosis of the skin and underlying tissues, and sometimes even surrounding structures, such as the fasciae, muscles, bones, and the central nervous system [1].

Generalized morphea is characterized by at least four plaques measuring at least 3 cm that coalesce and affect two or more anatomical regions [2]. Although the etiology of the disease is unknown for certain, some stimuli (viruses, drugs, trauma) may cause vascular

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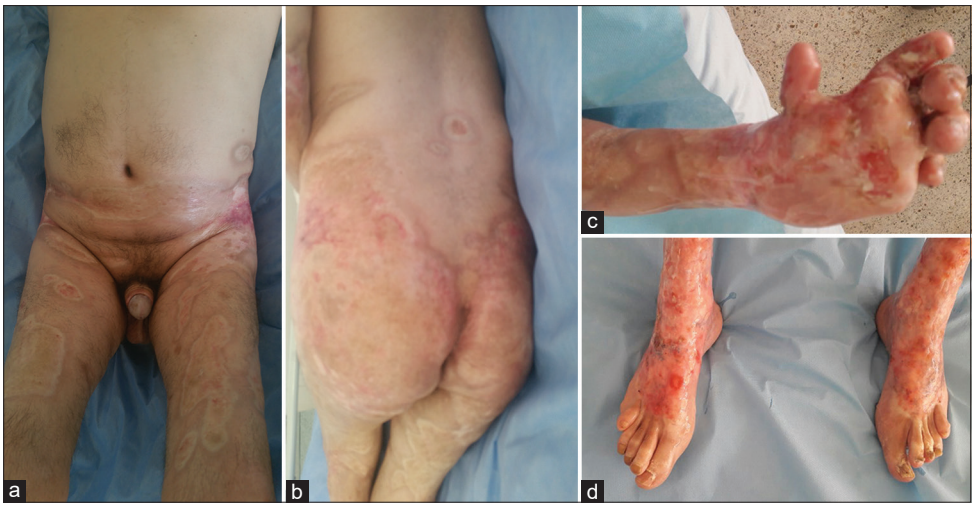

Figure 1: (a-d) Clinical presentation of generalized morphea: a defined, coalescing, pink erythematous patches with important central sclerosis on all four limbs and the trunk. Sclerodactyly and erosion of the hands and feet.

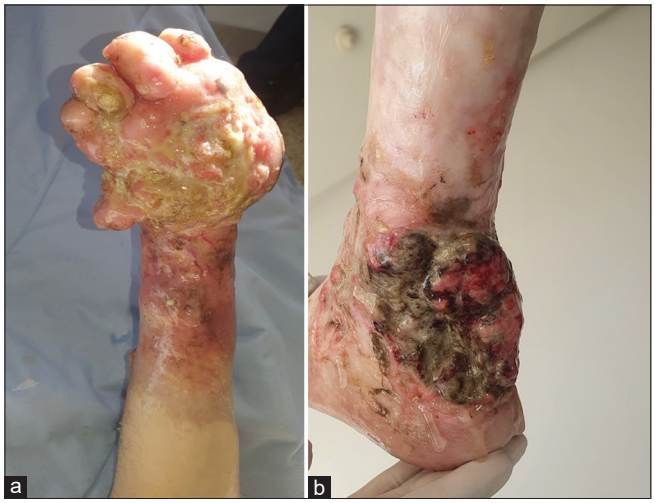

Figure 2: (a and b) Development of cutaneous squamous cell carcinoma (cSCC) in the 54-year-old male within a pre-existing lesion of morphea over the course of sixteen years. Clinical presentation of the patient's left hand and left lower leg.

and immune dysfunction in genetically predisposed patients [1].

Cocaine is a potent vasoconstrictor agent that has been associated with the appearance of scleroderma syndromes characterized by diffuse cutaneous sclerosis and acral vasospasm with Raynaud's phenomenon and a positive immunological assessment. Cocaine is known to produce vasoconstriction either by blocking the reuptake of norepinephrine and dopamine from the presynaptic space or by a direct vasoconstrictive effect independent of the vascular endothelium [3]. In our case, the diagnosis of cocaine-induced generalized morphea was retained given the negativity of the immunological and morphological workup and the chronological delay.

Malignant transformation of localized scleroderma is exceptionally rare and more associated with pansclerotic or generalized variants [4,5]. It occurs most often on the lower extremities of patients after a long evolution of the disease.

Immunosuppressive drugs used for the treatment of scleroderma may promote tumor formation [6]. Although carcinogenesis in scleroderma is a rare event, clinicians performing follow-up examinations should always be aware of the risk of tumor development on long-standing morphea lesions. In addition, common therapeutic strategies for morphea, such as immunosuppressive drugs and phototherapy, must be critically considered in light of their potential carcinogenic side effects.

CONCLUSION

Generalized morphea may be induced and maintained by cocaine as illustrated by our case. Although its malignant transformation is exceptionally rare, chronic ulcerations and hyper burgeoning should be examined with suspicion and benefit from histopathological evaluation at the slightest doubt.

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. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ. Morphea: The 2023 update. Front Med (Lausanne). 2023;10:1108623.
2. Andreussi R, Silva LMB, da Silva HC, Luppino-Assad AP, Andrade DCO, Sampaio-Barros PD. Systemic sclerosis induced by the use of cocaine: Is there an association? Rheumatol Int. 2019;39:387-93.
3. Kilaru P, Kim W, Sequeira W. Cocaine and scleroderma: Is there an association? J Rheumatol. 1991;18:1753-5.
4. Saleh DB, Williams AM, Smith IM. Cutaneous squamous cell carcinoma arising within generalised morphea. J Plast Reconstr Aesthet Surg. 2011;64:149.
5. Boozalis E, Shah AA, Wigley F, Kang S, Kwatra SG. Morphea and systemic sclerosis are associated with an increased risk for melanoma and nonmelanoma skin cancer. J Am Acad Dermatol. 2019;80:1449-51.
6. Heck J, Olk J, Kneitz H, Hamm H, Goebeler M. Long-standing morphea and the risk of squamous cell carcinoma of the skin. J Dtsch Dermatol Ges. 2020;18:669-73.

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Our Dermatology Online

Case Report

Large, rapidly growing, ulcerated tumor in the abdomen

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ABSTRACT

Mycosis fungoides is the most common primary T-cell tumor, usually CD4+. Clinically, three stages are described: patch, plaque, and tumor. There are rare variants such as granulomatous lymphoma, accounting for less than 1.8% of the cases. Herein, we present the case of a 27-year-old male, previously healthy, having a large tumor on the abdominal wall, for which the diagnosis was delayed for one year, with an especially poor response to chemotherapy treatments, and with transformation to large cell mycosis fungoides.

Key words: Mycosis fungoides, Cutaneous lymphoma, Hospital Dermatology

INTRODUCTION

Mycosis fungoides is the most common primary T-cell tumor, usually CD4+. Clinically, three stages are described: patch, plaque, and tumor. The World Health Organization and the European Organization for Research in Cancer Therapy recognize three variants of classic mycosis fungoides: pagetoid reticulosis, folliculotropic, and granulomatous lax skin [1]. However, there are other varieties such as granulomatous lymphoma, which is a rare variant, accounting for less than 1.8% of primary cutaneous lymphomas [2], which may present at initial diagnosis or years after the classical form [1]. Herein, we present a case of this atypical variety.

CASE REPORT

This was a 27-year-old patient, who was previously healthy, native of a rural area in Mexico. One year prior to the admission, he reported an erythematous dermatosis that was treated as cellulitis without a response, which grew rapidly over six months. An ultrasound was performed in the patient's birthplace, which revealed a soft tissue tumor. A skin biopsy was performed and Rosai–Dorfman disease was diagnosed. An additional biopsy of the tumor revealed non-Hodgkin's T-cell lymphoma. In view of the presence of lymphadenopathy, a biopsy of the inguinal lymph node was performed, which revealed chronic non-crossing granulomatous lymphadenitis and sinusoidal histiocytosis. During this period, the patient experienced occasional nocturnal diaphoresis and unintentional weight loss of 8 kg. When he was examined at our institution, he had a skin dermatosis located on the trunk, unilateral, affecting the abdomen in the lower right quadrant, characterized by a large exophytic cupuliform neoformation measuring 20 x 20 cm, with two ulcers on its surface, one measuring 10 cm and the other 3 cm, both with irregular, hyperpigmented, dark brown, undermined edges, with purulent secretion on the periphery and a dry-looking discharge in the center. The rest of the tumor had a soft consistency, with irregular, firm, ill-defined edges, brown erythematous hyperpigmentation on the surface, and areas of atrophy. The tumor led to pain and reduced

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ability to walk (Fig. 1). A skin biopsy was performed where, on H&E staining, atypical, small to medium-sized lymphocytes, histiocytes, and multinucleated giant cells were observed (Figs. 2a and 2b), with immunohistochemistry, with CD3+ (Fig. 3a) and CD20- (Fig. 3b), in the characterization of these lymphocytes with CD2+ (Fig. 3c), CD4+ (Fig. 3d), CD5+ (Fig. 3e) markers, and focally in histiocytes and CD68+ multinucleated giant cells (Fig. 3f), and CD8- (Fig. 3g). The pathology service reported granulomatous mycosis fungoides in the tumor phase.

In order to establish the stage, a PET-CT scan was performed. It showed an infiltrative lesion in the soft tissues of the right abdominal wall with associated hypermetabolism and hypermetabolic right axillary lymph nodes (Fig. 4), for which an axillary node biopsy was performed. The pathology report indicated infiltration by granulomatous mycosis fungoides with partial involvement ISCL/EORTC (International Society for Cutaneous Lymphomas and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer) NE/category 3 DUTCH system and no involvement was reported in the bone marrow aspirate revealed no abnormalities.

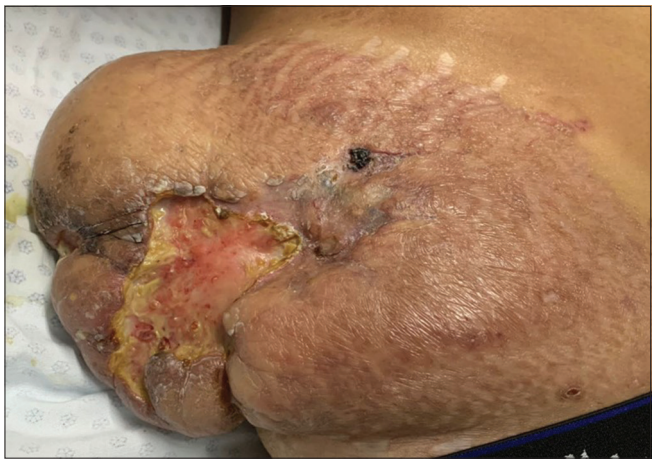

Figure 1: Dermatosis.

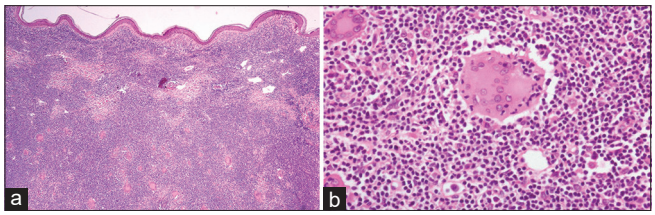

Figure 2: (a) Diffuse infiltrate of basophilic cells and multinucleated giant cells (H&E; 40x). (b) Magnification cells of intermediate to small size with blastic-looking chromatin with periadnexal involvement and even adipose tissue (H&E; 400x).

Based on these findings, the subject was classified as being in stage IVB.

The hematology and lymphoma department began treatment with gemcitabine for eight cycles, with little response and adverse reactions to chemotherapy (diarrhea, fever, tubulointerstitial necrosis) and malignant hypercalcemia. Due to the partial response, treatment with brentuximab, adriamycin, and cyclophosphamide was initiated with the aim of reducing the tumor load. One year after beginning the treatment, the patient manifested a new disseminated dermatosis on the trunk and four extremities, characterized by oval infiltrated plaques measuring 0.5 to 1.5 cm, erythematous, brown, with fine scaling on the surface, pruritic, with an evolution of one month (Fig. 5), in addition to the persistence of the initial lesion. A new biopsy was performed, which showed transformation to large cell mycosis fungoides with an immunophenotype CD3+, CD20-, CD2+, CD4+, CD5+, CD8-, CD56-, CD30 (60%). Treatment with brentuximab is currently awaiting initiation.

DISCUSSION

Clinical features of granulomatous mycosis fungoides are generally atypical. Patches or plaques may be absent [3]. Some features that may suggest this form of presentation are thick plaques or nodules, no scaling and no laxity. It may mimic granuloma annulare, sarcoidosis, or granulomatous rosacea. Other reported forms include psoriasiform or dermatofibroma-like plaques [3] and morphea-like plaques [2]. The form of presentation in this case was atypical, as it presented as a large, subcutaneous, exophytic tumor with central ulceration, with no previous patch or plaque stage. The initial presumptive diagnosis was sarcoma. The biopsy is characterized by CD4+ T-cell infiltrate, in different patterns such as lichenoid, perivascular, perivascular, and interstitial. Up to 33% lymphocytic infiltrate or nuclear atypia may be absent. If epidermotropism is observed, it is moderate and focal. Multinucleated giant cells, histiocytes, and granuloma formation are found. Immunohistochemistry is dominated by CD4+ cell population, CD4: CD8 > 4:1 and 50% loss of CD7 expression [2]. Histological criteria include a prominent granuloma formation of any type, with histiocytes and multinucleated giant cells. Loss of elastic fibers is common, yet elastophagocytosis is rare [1]. Histology of this tumor showed abundant histiocytes, multinucleated giant cells, and atypical lymphocytes.

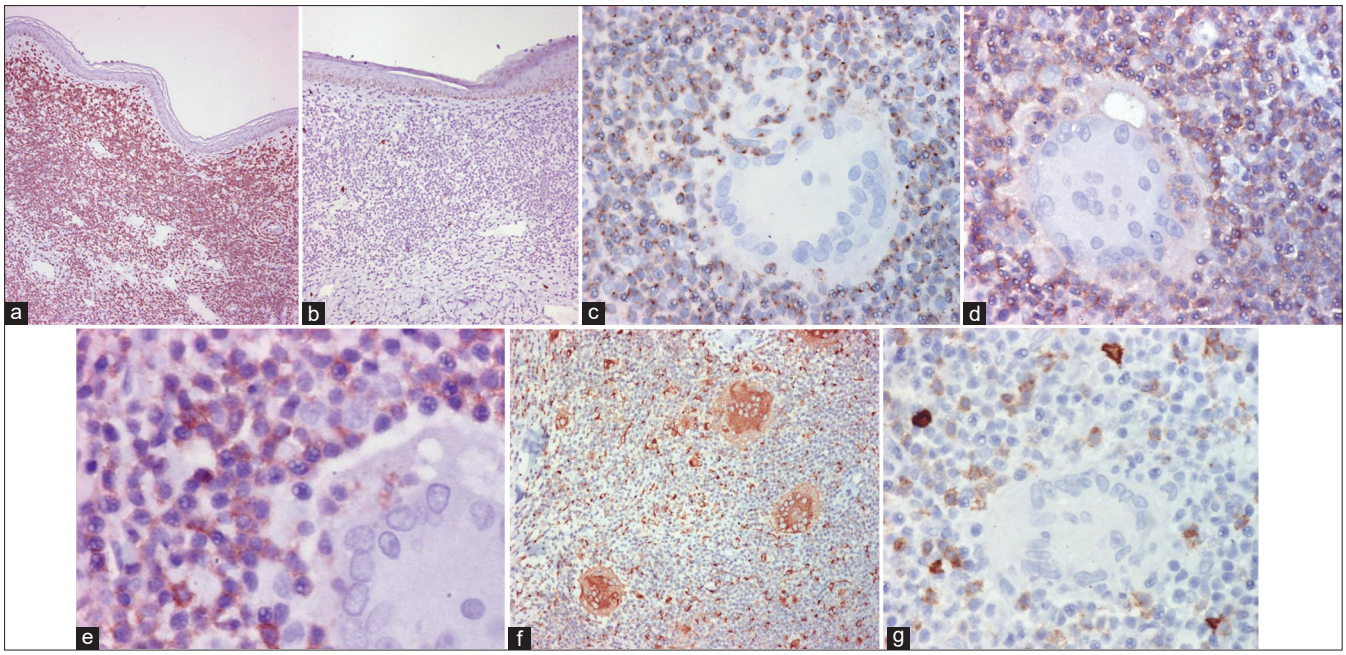

Figure 3: (a) Immunohistochemistry, CD3 intensely positive. (b) Immunohistochemistry, CD20 negative. (c) Immunohistochemistry, CD2 positive. (d) Immunohistochemistry, CD4 positive. (e) Immunohistochemistry, CD5 positive. (f) Immunohistochemistry, CD68 positive for multinucleated giant cells and interstitial histiocytes. (g) Immunohistochemistry, CD8 negative.

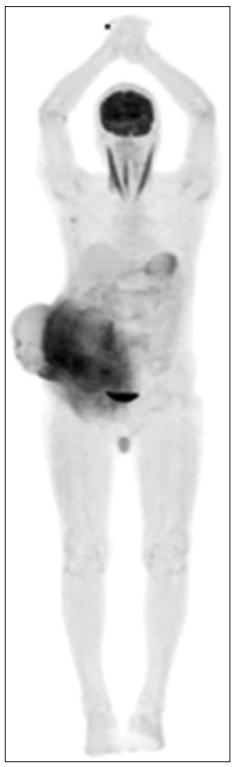

Figure 4: Hypermetabolism in the right abdominal wall and axillary adenopathies (PET 18F-FDG).

Immunohistochemistry was as expected. Diagnosis may be difficult because epidermotropism may be absent and because of the predominance of granulomatous infiltrate [1], as in this case, the initial biopsies were

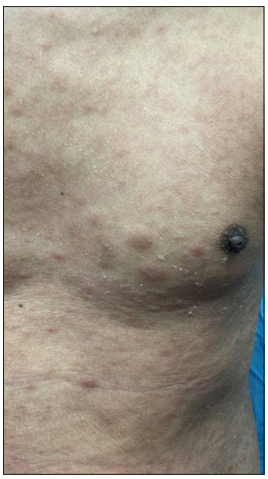

Figure 5: Progression: oval, erythematous, brown plaques with fine scaling on the surface.

diagnosed with granulomatous disease and Rosai–Dorfman disease. This showed how important it is that the diagnosis is made by pathologists with experience in this type of disease. Atypical presentations show a more rapid progression, worse prognosis, or transformation to cutaneous or extracutaneous large cell lymphoma [3], as in this case. The five-year survival rate is 66% in this form of presentation, with progression up to 46% [2]. This patient had a poor response to the first-choice treatment, gemcitabine. When the patient manifested a new disseminated dermatosis, the histology showed an infiltrate with more than 25% of cells of large

size and has now transformed to large cell mycosis fungoides, with a worse prognosis. This transformation is defined as more than 25% predominance of large cells with oval or irregular nuclei and prominent CD30 (+/-) nucleoli [4]. 50% occur in the tumor phase, and in 66%, the transformation occurs in the skin [5], as in this case. Overall survival in this phase is 12 to 20 months, and there is a mortality rate of 40% [4]. The patient is currently awaiting treatment with brentuximab.

CONCLUSION

Herein, we have presented an exceptional case due to the initial clinical presentation as a giant tumor in the abdomen, which progressed despite treatments. This form of presentation, which is rare, confers a worse prognosis.

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. Hodak E, Amitay-Laish I. Mycosis fungoides: A great imitator. Clin Dermatol. 2019;37:255-67.
2. Lenskaya V, de Moll EH, Hussein S, Phelps RG. Subtlety of granulomatous mycosis fungoides: A retrospective case series study and proposal of helpful multimodal diagnostic approach with literature review. Am J Dermatopathol. 2022;44:559-67.
3. Sidiropoulou P, Tsaoutou K, Constantinou A, Marinos L, Voudouri D, Iliakis T, Kanellis G, Pouliou E, Stratigos A, Nikolaou V. New insights into granulomatous mycosis fungoides (GMF): A single-center experience. Eur J Cancer. 2021;156 Suppl 1:S69-S70.
4. Vural S, Akay BN, Botsalı A, Atilla E, Parlak N, Okçu Heper A, Şanlı H. Transformation of mycosis fungoides/Sezary syndrome: Clinical characteristics and prognosis. Turk J Haematol. 2018;35:35-41.
5. Gómez Díez S, Fresno Forcelledo MF, Raya Aguado C, Vázquez López F, Rodríguez Vigil T, González López M, Rodríguez Prieto MA, Pérez Oliva N. Transformation of mycosis fungoides/Sézary syndrome to large cell lymphoma. Actas Dermo-Sifiliográficas Vol. 92. No. 9. Pages 391-396 (September 2001).

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Our Dermatology Online

Case Report

Favorable evolution of acute erythema nodosum leprosum under prednisolone and clofazimine at Dosso Regional Hospital in Niger

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ABSTRACT

During the course of leprosy, some patients will develop a reaction. Acute inflammatory events occur in approx. 25% of patients, usually during and sometimes at the end of treatment. There are two types of a leprosy reaction: type I or reverse reaction, and type II or erythema nodosum leprosum (ENL). It is a therapeutic emergency, and recurrence is frequent. ENL is treated with corticosteroids and other immunosuppressants such as thalidomide, azathioprine, and cyclosporine. Some patients respond favorably to treatment, while others become refractory. Herein, we report the case of a 49-year-old female with acute ENL treated with prednisolone and clofazimine for twelve months with a favorable evolution.

Key words: Leprosy, Leprous reaction, Corticosteroids, Clofazimine, Dosso

INTRODUCTION

Leprosy is a chronic, debilitating infection, known since ancient times, caused by *Mycobacterium leprae*. It is a slow-multiplying, *in vitro* non-cultivable germ with cutaneous and peripheral nerve tropism. Acute inflammatory manifestations occur in around 25% of patients, generally during and sometimes after treatment. A distinction is made between type 1, or reverse reaction, and type 2, or erythema nodosum leprosum (ENL), whose manifestations are varied, combining fever, painful acute neuritis with paralysis, edema, and redness of pre-existing skin lesions. It is a disseminated nodular erythema nodosum and is inflammatory, hence sensitive, and associated with uveitis, polyarthritis, adenitis, and orchiepididymitis. It constitutes a therapeutic emergency, and recurrence is frequent [1]. ENL affects around 50% of people with lepromatous leprosy and 5–10% of patients with lepromatous leprosy [2]. In the majority of patients, ENL is a chronic disease requiring prolonged immunosuppression. Thalidomide is effective in controlling ENL and is recommended by the WHO under strict medical supervision due to its serious teratogenic effects. However, it is not available in numerous countries where leprosy is endemic. Patients must, therefore, take high doses of oral corticosteroids, often for many years. The WHO recommends a high dose of clofazimine in combination with prednisolone for the management of severe ENL [3].

Our work was to report a case of acute ENL in a 49-year-old patient followed at our department with a favorable evolution.

CASE REPORT

A 49-year-old housewife with a history of multibacillary leprosy with grade II disability (ulnar claw) was treated

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with polychemotherapy for twelve months and declared cured. Two years later, she presented to our department with painful papulonodular lesions (Figs. 1a and 1b) of abrupt onset in a febrile context, with ocular redness, lacrimation, and altered general condition. These firm, sensitive papulonodular lesions of variable size, embedded in the dermis, predominated on the trunk and face, and coexisted with sometimes hyperpigmented, sometimes hypopigmented macules of variable shape and size, with blurred borders and a smooth, non-scaly surface. A standard laboratory work-up was requested yet returned normal. A nodular lesion was biopsied, yet histological examination was not performed due to insufficient technical resources in our context. The diagnosis of type II leprous reaction (erythema nodosum leprosum) was made on the basis of the patient's history of leprosy and the clinical picture. Treatment consisted of prednisolone 1 mg/kg/day corticosteroid therapy combined with clofazimine 300 mg/j inpatient and adjuvant therapy. An ophthalmology consultation for the management of iridocyclitis was conducted. The evolution was favorable, marked by an improvement in general condition, apyrexia, early regression, and progressive subsidence of the lesions after ten days, justifying a gradual reduction in corticosteroid therapy and, for clofazimine, a reduction of 100 mg every twelve weeks. After six months, outpatient follow-up was marked by clinical improvement, with progressive subsidence of the papulonodular lesions. Regular monthly monitoring of weight, blood pressure, blood glucose, creatinine, and blood ionogram revealed no abnormalities. After one year of treatment, all papulonodular lesions had completely subsided (Figs. 2a and 2b). No recurrence was observed after a two-year follow-up.

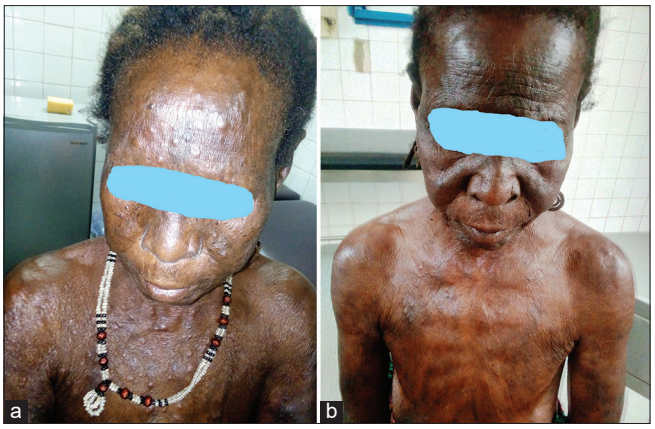

Figure 1: a) Papulonodular lesions on the face, thorax, and arms before treatment. b) Collapse of papulonodular lesions on the face, thorax, and arm after treatment.

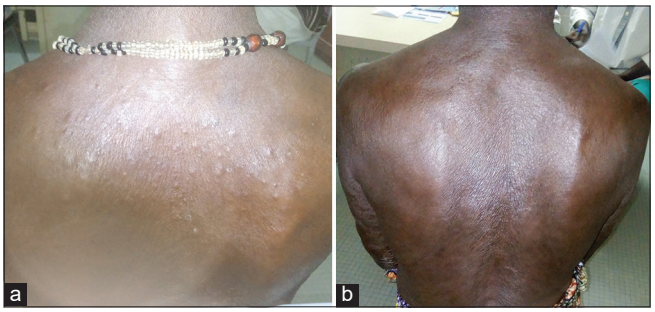

Figure 2: a) Papulonodular lesions on the back before treatment. b) Total collapse of the papulonodular lesions on the back after treatment.

DISCUSSION

Erythema nodosum leprosum (ENL) is a serious immune-mediated, multi-systemic complication of lepromatous and borderline leprosy. It causes high morbidity and mortality, and usually requires urgent medical attention [4]. Lesions are dermohypodermal inflammatory nodules of varying size. In contrast to classic erythema nodosum, generally confined to the declivities, ENL is often diffuse (trunk, upper limbs, face). The lesions are smaller and accompanied by fever. They tend to recur in the same location. Other reactive equivalents may be encountered: iridocyclitis, arthritis, orchiepididymitis, and glomerulonephritis. Oral corticosteroids are the first-line treatment. Immunosuppressants (methotrexate, azathioprine, cyclosporine), anti-TNF-alpha drugs (infliximab, etanercept), or pentoxyphiline are possible alternatives [5]. Several authors have reported a recurrence of ENL [6,7], unlike our case, which was the first episode occurring two years after treatment with multidrug leprosy therapy. We did not observe a recurrence of ENL in our patient two years after the end of treatment, yet some authors have reported a variable delay in the onset of recurrence, ranging from eighteen months to two years [6,8]. In our patient, progression was favorable with prednisolone and clofazimine, although a study in India [7] reported that the rate of ENL recurrence was lower with thalidomide than with clofazimine combination therapy. Most ENL patients respond well to these treatments, while those refractory to conventional therapies may suffer severe morbidity or mortality [9]. However, therapeutic options have expanded well beyond thalidomide and steroids [10].

CONCLUSION

The diagnosis and treatment of acute erythema nodosum leprosum is particularly important in order

to avoid numerous serious and disabling consequences. The particularity of our case was its early management and favorable evolution with no recurrence after two years.

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. SPILF, CMIT, SFMTSI, SMV. Lèpre. Dans: ePILLY Trop [En ligne]. 3e édition web. Paris: Alinéa Plus Ed; 2022. **[Cité le 10/04/2023]**. Disponible: https://www.infectiologie.com/fr/pillytrop.html
2. Walker SL, Balagon M, Darlong J, Doni SN, Hagge DA, Halwai V, et al. ENLIST 1: An international multi-centre cross-sectional study of the clinical features of erythema nodosum leprosum. PLoS Negl Trop Dis. 2015;9:e0004065.
3. Walker SL, Lebas E, Doni SN, Lockwood DNJ, Lambert SM. The Mortality associated with erythema nodosum leprosum in ethiopia: A retrospective hospital-based study. PLoS Negl Trop Dis. 2014;8:e2690.
4. Negera E, Tilahun M, Bobosha K, Lambert SM, Walker SL, Spencer J, et al. The effects of prednisolone treatment on serological responses and lipid profiles in Ethiopian leprosy patients with erythema nodosum leprosum reactions. PLoS Negl Trop Dis. 2018;12:e0007035.
5. Park L, Wallace CE, Vasile G, Buckley C. A case of lepromatous leprosy with erythema nodosum leprosum. Cureus. 2023;15:e33846.
6. Lastória JC, Almeida TSC, Putinatti MSMA, Padovani CR. Effectiveness of the retreatment of patients with multibacillary leprosy and episodes of erythema nodosum leprosum and/or persistent neuritis: A single-center experience. An Bras Dermatol. 2018;93:181-4.
7. P K Mishra SR, Samal R, Behera B. Thalidomide and steroid in the management of erythema nodosum leprosum. Indian J Pharmacol. 2022;54:177-82.
8. Tabassum S, Zia M, Khoja AA, David J, Iqbal M, Junaid M. Lepra reactions: A study of 130 cases from Pakistan. J Pak Med Assoc. 2021;71:2317-20.
9. Zhu J, Yang D, Shi C, Jing Z. Therapeutic dilemma of refractory erythema nodosum leprosum. Am J Trop Med Hyg. 2017;96:1362-4.
10. Bhat RM, Vaidya TP. What is new in the pathogenesis and management of erythema nodosum leprosum. Indian Dermatol Online J. 2020;11:482-92.

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Our Dermatology Online

Case Report

Madura's foot: A disabling evolution

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ABSTRACT

Mycetomas are pathological processes in which fungal or actinomycotic agents emit seeds. It is a chronic infectious disease, endemic in tropical countries, that affects the soft tissues and the skeleton with sometimes fatal visceral damage. Foot involvement is by far the most common, occurring in 80% of cases. The treatment of mycetomas depends on their etiology, medical or surgical. Herein, we report a rare case of a foot and leg eumycetoma. The purpose of this work was to recall this rare condition, often overlooked by practitioners, remaining a source of therapeutic difficulties.

Key words: Mycetomas, Madura's foot, Actinomycetomas

INTRODUCTION

Mycetomas are chronic infections responsible for inflammatory pseudo-tumor lesions due to fungal agents (eumycetomas) or aerobic bacteria (actinomycetomas). They evolve slowly. In addition to developing at the subcutaneous level, they may affect the bone structure, complicating management. Eighty percent of cases are located on the foot, thus known as Madura's foot [1,2].

CASE REPORT

A 53-year-old day laborer with the concept of walking barefoot as an antecedent was traumatized eleven years earlier by a sharp object at the level of the sole of his left foot, causing a wound, for which he was given undocumented local treatment without success. Four years later, a swelling of the foot gradually increased in size. He sought the trauma department, which performed MRI and an initial bone biopsy revealing subacute osteitis. He was given antibiotics. In response to the persistent nature of the disease and the disabling clinical worsening, as well as the appearance of new lesions, the patient sought multiple consultations at the traumatology department before being referred for additional care to our training. An examination preceding admission found that the patient was in good general condition yet had inflammatory pain in the left lower extremity responsible for lameness, with a pseudo-tumor swelling of the left foot, polyfistulized (Fig. 1a), dotted with multiple yellowish and reddish papules (Fig. 1b), and emitting pus and small, yellowish-white grains (Fig. 1c) associated with a painless mass under the skin of the ipsilateral leg. A long anatomopathological examination performed on a local sample from the foot led to the diagnosis of eumycetoma with positive PAS staining. A radiological assessment consisted of standard X-ray of the foot, an ultrasound of the lymph node areas objectifying bilateral inguinal and iliac lymph node formations, and MRI of the foot highlighting a bony extension of the lesions with multiple lacunae affecting all bony structures of the foot and leg, with infiltrations of the subcutaneous tissues, creating a point-in-the-circle appearance (Figs. 2a and 2b). MRI of the left leg showed an 8 cm mycetoma pedicle. The therapeutic decision was to perform a left trans-femoral amputation and to administer an antifungal. The patient unfortunately refused any treatment.

DISCUSSION

Mycetomas are indolent and deforming inflammatory pseudotumors often polyfistulized due to fungi

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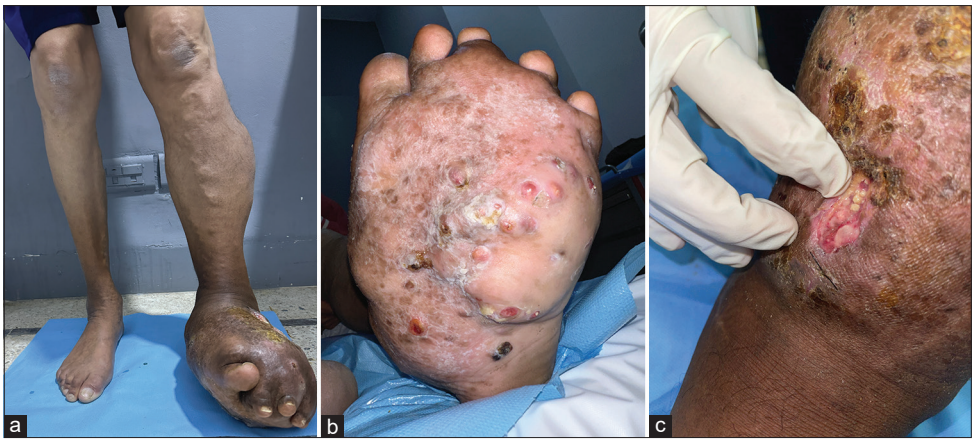

Figure 1: (a) Pseudo-tumor swelling of the left foot polyfistulized with an under-skin mass on the leg. (b) Multiple yellowish and reddish papules. (c) Pseudo-tumor emitting pus and small, yellowish-white grains.

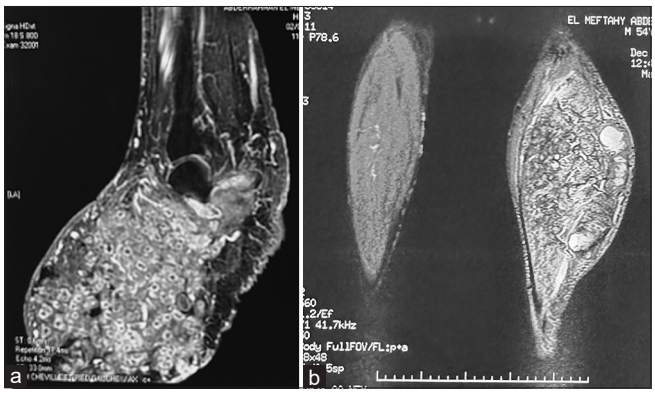

Figure 2: MRI of (a) the foot and (b) the leg highlighting a bony extension of the lesions with multiple lacunae, creating a point-in-the-circle appearance.

(eumycetoma) or aerobic bacteria (actinomycetoma) [1]. It most commonly affects young, male subjects engaged in manual labor, such as farmers and breeders in humid tropical climates [2].

Sixty percent of cases in the literature indicated anterior trauma. In general, the preferred site is the foot [3], as was the case in our patient. Nevertheless, various extrapodal locations have been described in the literature, including the trunk, hands, and knees [2,4].

Initially, eumycetoma manifests as a firm and painless subcutaneous nodule that evolves into an infiltration with fistulizations, from which intermittent pus and black or yellowish-white grains appear. It is essential to have an accurate biological diagnosis in order to confirm the diagnosis and guide treatment. The procedure is divided into several stages: direct examination and culture of the grains when these are emitted, followed by a biopsy and anatomical pathology examination [1,5].

Generally, mycetomas spread superficially, as well as in depth, gradually engulfing the surrounding tissues, particularly the bones and joints [5-7]. It is common for them to develop slowly and remain painless for a number of months, even years once they have appeared [8,9], which explains the delayed consultations [10,11].

The extent of the pathogenesis must be documented immediately after diagnosis. Plain radiographs may show non-specific lesions (geodes, reactive osteosclerosis), ultrasound or MRI may identify the mycelium by its characteristic morphology: single or multiple small grains appearing on hyperechoic images with posterior shadow cones confirming the context of a point in a circle that is pathognomonic [12-14]. The treatment of fungal infections depends on their etiology. Although there is no established consensus, treatment should be continued over a long period of time [15]. Eumycetoma is usually treated with the antifungal drugs itraconazole, amphotericin B, voriconazole, and terbinafine for a prolonged period of 12 to 15 months. Surgery remains the solution of choice for initial lesions and is strongly indicated in cases of bone lysis [1,10]. Lymph nodes are a route for the spread of pathogens with the possibility of inguinal localization [16,17]. There are no satisfactory criteria to confirm healing. The risk of postoperative recurrence is always present. Only long-term monitoring over several years may confirm the cure. In this case, the treatment should be continued at a reduced dose for several months [18]. Prevention is of great interest. It consists of wearing protective shoes, thoroughly and systematically disinfecting wounds, and avoiding injuries, especially thorns [16].

CONCLUSION

Fungal mycetomas are rare and recurring infections that may make them difficult to recognize. Treatment depends on the pathogen and the extent of the lesion. Immediate and early treatment is indicated to improve prognosis and avoid disabling sequelae.

Consent

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REFERENCES

1. Traore T, Toure L, Diassana M, Niang M, Ballo E, S Coulibaly B, et al. [Medico-Surgical treatment of mycetoma in the Somine Dolo hospital of Mopti (Mali)]. Med Trop Sante Int. 2021;1:mtsi.2021.170.
2. Ndiaye D, Ndiaye M, Sène PD, Diouf MN, Diallo M, Faye B, Sakho MG, Ndiaye JL, Tine R, Kane A, Ndir O. [Mycetomas diagnosed in Senegal from 2008 to 2010]. J Mycol Med. 2011;21:173-81.
3. Sigera LSM, Narangoda KUL, Dahanayake MY, Shabri ULF, Malkanthi MA, Somarathne V, et al. Mycetoma due to *Madurella mycetomatis*. IDCases. 2020;30;21:00857.
4. Dikhaye S, Afifi Y, Aoufi S, Tligui H, Mirrane H, Senouci K, et al. [Mycetoma]. Ann Dermatol Venereol. 2008;135:626-8.
5. Daghfous M, Mokhtar I, Fazaa B, Kamoun MR. [Anatomo-clinical study of mycetomas]. Tunis Med. 1993;71:529-34.
6. Omer RF, Seif El Din N, Abdel Rahim FA, Fahal AH. Hand mycetoma: The Mycetoma Research Centre experience and literature review. PLoS Negl Trop Dis. 2016;2;10:e0004886.
7. Gupta M. Maduromycosis of foot. Our Dermatol Online. 2017;8:92-3.
8. N'diaye B, Dieng MT, Perez A, Stockmeyer M, Bakshi R. Clinical efficacy and safety of oral terbinafine in fungal mycetoma. Int J Dermatol. 2006;45:154-7.
9. Ait Essi F, Akbari I, Najeb Y, Latifi M, Hokar O, Amal S. Le mycétome tumoral du pied. Med Chir Pied. 27:9-11.
10. Aounallah A, Boussofara L, Ben Saïd Z, Ghariani N, Saidi W, Denguezli M, et al. [Analysis of 18 Tunisian cases of mycetoma at the Sousse hospital (1974-2010)]. Bull Soc Pathol Exot. 2013;106:5-8.
11. Baha H, Khadir K, Hali F, Benchikhi H, Zeghwagh A, Zerouali K, et al. [Actinomycosic mycetoma of the foot in Morocco due to Actinomycetes viscosus]. J Mycol Med. 2015;25:76-80.
12. Dieng MT, Sy MH, Diop BM, Niang SO, Ndiaye B. [Mycetoma: 130 cases]. Ann Dermatol Venereol. 2003;130(1 Pt 1):16-9.
13. Messoudi A, Fnini S, El Andaloussi Y, Charafeddine A, Marouane S, Ouarab M, et al. [Madura foot: A rare pathology in Morocco (about 15 cases)]. Bull Soc Pathol Exot. 2013;106:9-12.
14. Fuentes-Nava AG, Fierro-Arias L, Araiza J, Benitez-Barradas MI, Peláez González HE, Bonifaz A. Actinomycetoma due to Actinomadura madurae: A therapeutic challenge. Case report. Our Dermatol Online. 2018;9:399-403.
15. Asly M, Rafaoui A, Bouyermane H, Hakam K, Moustamsik B, Lmidmani F, et al. Mycetoma (Madura foot): A case report. Ann Phys Rehabil Med. 2010;53:650-4.
16. Sarr L, Niane MM, Diémé CB, Diatta BA, Coulibaly NF, Dembélé B, et al. [Surgery in black grain mycetoma: About 44 patients treated at aristide le dantec hospital (Dakar, Senegal) from December 2008 to March 2013]. Bull Soc Pathol Exot. 2016;109:8-12.
17. Salim AO, Mwita CC, Gwer S. Treatment of Madura foot: A systematic review. JBI Database System Rev Implement Rep. 2018;16:1519-36.
18. Brufman T, Ben-Ami R, Mizrahi M, Bash E, Paran Y. Mycetoma of the foot caused by Madurella mycetomatis in immigrants from Sudan. Isr Med Assoc J. 2015;17:418-20.

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Our Dermatology Online

Case Report

Red lunula: A case report

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ABSTRACT

The red lunula has been associated with cutaneous, systemic, and immunological disorders. Other circumstances in which it has been described include corticosteroid and azathioprine therapy, malnutrition, and substance abuse. Doctors outside of dermatology are unaware of this entity, which shows us that dermatological examination is important to make a comprehensive clinical diagnosis. Herein, we present a male with scales on the neck and scalp and red spots that had appeared and disappeared on the arms. During the physical examination, we observed red lunulae on the left thumbnail, onychorrhexis on the fingernails, lentigo senile, dry skin, and seborrheic keratosis.

Key words: Nails, Nail diseases, Nail malformation

INTRODUCTION

The lunula is a white, semi-lunar shaped, visible part of the distal nail matrix. It is normally observed on the thumb, the index, and the great toe. It is responsible for producing the nail plate's keratin [1-6]. Color anomalies may appear in multiple shapes and sizes and may be idiopathic or related to systemic diseases [1-3,7-8]. Red lunulae have been seen in patients with cutaneous, cardiovascular, endocrine, gastrointestinal, hematologic, hepatic, infectious, neoplastic, neurologic, pulmonary, renal, and rheumatologic disorders [1-11]. Currently, the pathogenesis remains uncertain, yet different hypotheses suggest that red lunulae result from increased arteriolar blood flow and the vasodilatory capacitance phenomenon [2-8,10].

CASE REPORT

Herein, we present the case of an 81-year-old male who consulted the clinic for scales on the neck and scalp and red spots that began to appear and disappear on the arms four to five years previously. During the physical examination, we found a localized dermatosis on the scalp consisting of erythematous plaques and erythematous, violaceous spots on the arms with precise limits and variable size. The rest of the physical examination evidenced onychorrhexis at the level of the fingernails, pinkish-red lunula on the left thumbnail, senile lentigo, dry skin, and seborrheic keratosis. The patient reported a history of hyperuricemia and vasectomy and denied a family medical history.

The red lunula was an incidental finding on dermatological examination for another reason, with dermoscopy accentuating the coloration of the lunula (Figs. 1a and 1b). With these clinical features, the diagnosis of seborrheic dermatitis on the scalp, senile purpura, and the red lunula was established.

DISCUSSION

The lunula is the visible part of the distal nail matrix and defines the nail plate's shape. It has its histological features that allow it to produce keratin to form the nail plate. It is normally seen on the thumb, the index finger, and the great toe as a white half-moon [1-7]. It may present changes in its shape and size, such as macrolunula, microlunula, anolunula, non-convex lunula, and non-symmetric lunula, which may be an indication of trauma, deficiency, or infection [1-3]. Lunula dyschromia may be related to dermatological disorders, systemic diseases, or drug reactions.

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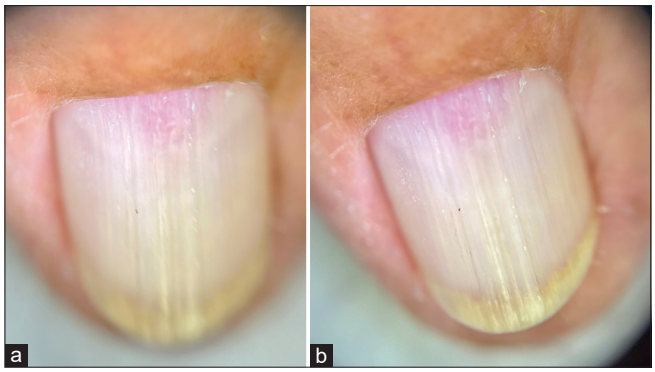

Figure 1: (a and b) Dermoscopy revealing the red coloration of the lunula on the left thumbnail.

Discolorations are variable in color and may be confluent, spotted, or form a longitudinal band [1-3,7].

The red lunula was first reported in 1954. Since then, it has been associated with cardiovascular disorders and endocrine and autoimmune conditions. It seems to occur more often in patients with rheumatoid conditions, such as rheumatoid arthritis, systemic lupus erythematosus, alopecia areata, primary Sjogren's syndrome, and systemic corticosteroid therapy [1-11]. In addition, a subungual tumor and trauma are thought to be the underlying causes of a single red lunula, and connective tissue disease is thought to be a major cause of multiple red lunula [4]. The etiology and histological examination of this onychopathology include increased arteriolar blood flow and dilated and tortuous blood vessels. Although the pathogenesis is unknown, some hypotheses have suggested an increased transparency of the lunula, causing exaggerated visualization of the underlying nail bed vasculature, or congested vasculature due to the inflammation of the nail bed [2-8,10].

This onychopathy is classified into three forms: complete, incomplete, and mottled. In the first one, the entire lunula is erythematous; in the second form, the proximal zone is affected, and the distal zone appears as a white arrow band; and the third one is characterized by a complete red lunula with whitish spots [3,7,8].

On the other hand, actinic purpura, also known as senile purpura, results from the fragility and atrophy of the skin caused by long-term sun exposure. The dermal connective tissue is incapable of holding the microvasculature, causing the extravasation of the blood into the dermis [12]. This microvascular damage may be related to capillary abnormalities, especially in the nail fold. It may be supposed that the red lunula in this patient could have developed as a symptom of senile purpura.

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. Cohen PR. The Lunula. J Am Aacad Dermatol. 1996;34:943-53.
2. Morrissey K, Rubin A. Histopathology of the red lunula: New histologic features and clinical correlations of a rare type of Erythronychia. J Cutan Pathol. 2013;40:972-5.
3. Wilkerson M, Wilkin J. Red lunulae revisited: A clinical and histopathologic examination. J Am Acad Dermatol. 1989;20:453-7.
4. Morrissey K, Rubin A. Histopathology of the red lunula: New histologic features and clinical correlations of a rare type of Erythronychia. J Cutan Pathol. 2013;40:972-5.
5. Wilkerson M, Wilkin J. Red lunulae revisited: A clinical and histopathologic examination. J Am Acad Dermatol. 1989;20:453-7.
6. Cohen P. Red lunulae: Case report and literature review. J Am Acad Dermatol. 1992;26:292-4.
7. Perez B, Sánchez B, Marinero S, Arsuaga C, Polimón I, Fernandez PL. Lúnulas rojas en alopecia areata. Med Cutan Iber Lat Am. 2010;38:207-9.
8. Kaur I, Jakhar D. Intraoperative onychoscopy and histopathological correlation of red lunula in nail lichen Planus: A case series. Clin. Exp. Dermatol. 2020;45:884-7.
9. Jorizzo J, Gonzalez DE, Daniels J. Red lunulae in a patient with rheumatoid arthritis. J Am Acad Dermatol. 1983;8:711-4.
10. Mai Y, Ujiie H, Iguchi A, Shimizu H. A case of red lunulae after haematopoietic stem cell transplantation. Eur J Dermatol. 2018;28:407-9.
11. Bergner T, Donhauser G, Ruzicka T. Red lunulae in severe alopecia areata. Acta Derm Venereol. 1992;72:203-5.
12. Rayner RL, Carville KJ, Leslie GD, Dhaliwal SS. Clinical purpura and elastosis and their correlation with skin tears in an aged population. Arch Dermatol Res. 2019;311:231-47.

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Our Dermatology Online

Case Report

Allergic contact dermatitis caused by azithromycin eye drops

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Sir,

Herein, we report three cases of unusual acute-type allergic reactions to topical 1.5% azithromycin ophthalmic solution in three patients.

Case 1: A seventy-year-old male presented with acute conjunctivitis and acute eczema affecting the eyelids and cheeks two weeks after using azithromycin eye drops for bilateral ocular hypertonia and blepharitis. He experienced redness, scales, itching, and burning (Fig. 1). Discontinuation of the eye drops and treatment with a topical dermocorticoid led to a significant improvement.

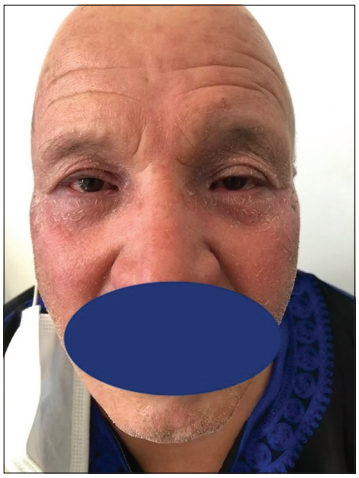

Figure 1: Acute conjunctivitis and acute eczema affecting the eyelids and cheeks.

Cases 2 and 3: A 76-year-old male and a 56-year-old female with diabetic retinopathy received intravitreal injections of bevacizumab followed by azithromycin eye drops. Both patients developed acute edematous eczema and conjunctival hyperemia within twenty-four hours (Figs. 2a and 2b). After withdrawing the eye drops and administering a topical dermocorticoid, their condition improved.

The discontinuation of the eye drops was recommended to all three patients, and treatment with a topical dermocorticoid led to a significant improvement.

Patch tests with azithromycin eye drops were positive in all patients and the pharmacovigilance report was in favor of allergic contact dermatitis.

Topical 1.5% azithromycin ophthalmic solution is a second-generation macrolide antibiotic with multiple benefits in treating eye infections. It combines bacteriostatic and bactericidal actions, possesses excellent intracellular penetration, and rapidly distributes in tissues. Moreover, it has a prolonged post-antibiotic effect, thereby enhancing its efficacy. Additionally, topical azithromycin offers extra anti-inflammatory and immunomodulatory functions [1,2].

While cases of non-occupational allergic contact dermatitis caused by azithromycin eye drops are rare, occupational allergic contact dermatitis has been documented in pharmaceutical workers handling azithromycin during synthesis and formulation. Patch testing with various concentrations of powdered azithromycin has shown positive reactions at lower concentrations (1% and 5%), indicating that higher

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Figure 2: (a) Bilateral acute edematous eczema of the eyelids and acute conjunctivitis. (b) Acute edematous eczema of the eyelids.

concentrations may be unnecessary for testing to avoid irritant reactions [3].

Interestingly, Lopez-Lerma et al. did not find positive reactions to erythromycin and clarithromycin in patients with allergic contact dermatitis to azithromycin, possibly due to the slight structural difference between these macrolides. However, in a series by Milkovic-Kraus et al., cross-reactivity with azithromycin intermediates, including erythromycin, was observed in some patients [4].

In summary, while allergic reactions associated with topical azithromycin eye drops are rare, ophthalmologists should remain vigilant about the potential for such reactions. As a precautionary measure, close monitoring of patients during the initial administration of the drug is recommended [5].

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. Blondeau JM, DeCarolis E, Metzler KL, Hansen GT. The macrolides. Expert Opin Investig Drugs. 2002;11:189-215.
2. Reiter J, Demirel N, Mendy A, Gasana J, Vieira ER, Colin AA, et al. Macrolides for the long-term management of asthma: A meta-analysis of randomized clinical trials. Allergy. 2013;68:1040-9.
3. López-Lerma I, Romaguera C, Vilaplana J. Occupational airborne contact dermatitis from azithromycin. Clin Exp Dermatol. 2009;34:e358-9.
4. Milkovic-KrausS,MacanJ, Kanceljak-Macan B. Occupational allergic contact dermatitis from azithromycin In pharmaceutical workers: A case series. Contact Dermatitis 2007:56:99-102.
5. Gedar Totuk OM, Yukselen A. Acute allergic reaction caused by topical azithromycin eye drops: A report of two cases. Saudi J Ophthalmol. 2019;33:180-2.

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Our Dermatology Online

Review Article

Skin diseases in the world`s indigenous peoples - with special focus on Greenland's Inuit`s population

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ABSTRACT

Providing health care in Greenland is a major challenge. Spanning 2,600 km from north to south and 1,050 km from east to west, Greenland is the largest island in the world and has the lowest population density on the globe. The geographical situation combined with, at times, extreme weather conditions make providing healthcare a logistical challenge in Greenland. Most Doctors working in Greenland are used to perform a very broad range of medical duties including various dermatological conditions. But not a single certified Dermato-venereologist at work in Greenland. Dermatological care at specialist level is provided by tele-dermatology. In this article we will describe some of the problems with skin diseases in Greenland with special focus on the Inuit population - based on challenges with access to care and challenges associated with diagnosis based on differences in baseline patient characteristics and correct treatment due to cultural differences influencing treatment preferences.

Key words: Arctic dermatology, Inuits, Atopic dermatitis, Psoriasis, Hidradenitis Suppurativa

INTRODUCTION

Dictionaries define indigenous as "originating in a particular region or country".

The word dates all the way back to the Latin word "indigena ", meaning native or original inhabitant.

Due to the diversity and difficult history experienced by these groups, including countries that don't recognize indigenous peoples in their lands, there is purposefully no official definition of "indigenous people".

The UN and other organizations working with indigenous peoples utilize an understanding based on self-determination that includes:

- Self-identification as indigenous peoples at the individual level and accepted by the community.
- Historical continuity with pre-colonial and/or pre-settler societies.
- Strong link to territories and surrounding resources.
- Distinct social, economic, or political systems.
- Distinct language, culture, and beliefs.
- Forms non-dominant groups of society.
- Resolve to maintain and reproduce their ancestral environments and systems.

Groups like Greenland's Inuit were included, because of their long history of colonial control as well as Danish influence.

This above map by "Bhabna Banerjee" (Fig. 1) uses data from the indigenous World 2010-2022 report to show the population distribution of the roughly 476 million Indigenous people around the world.

Please notice (according to the map) Greenland is a country territory with one of the

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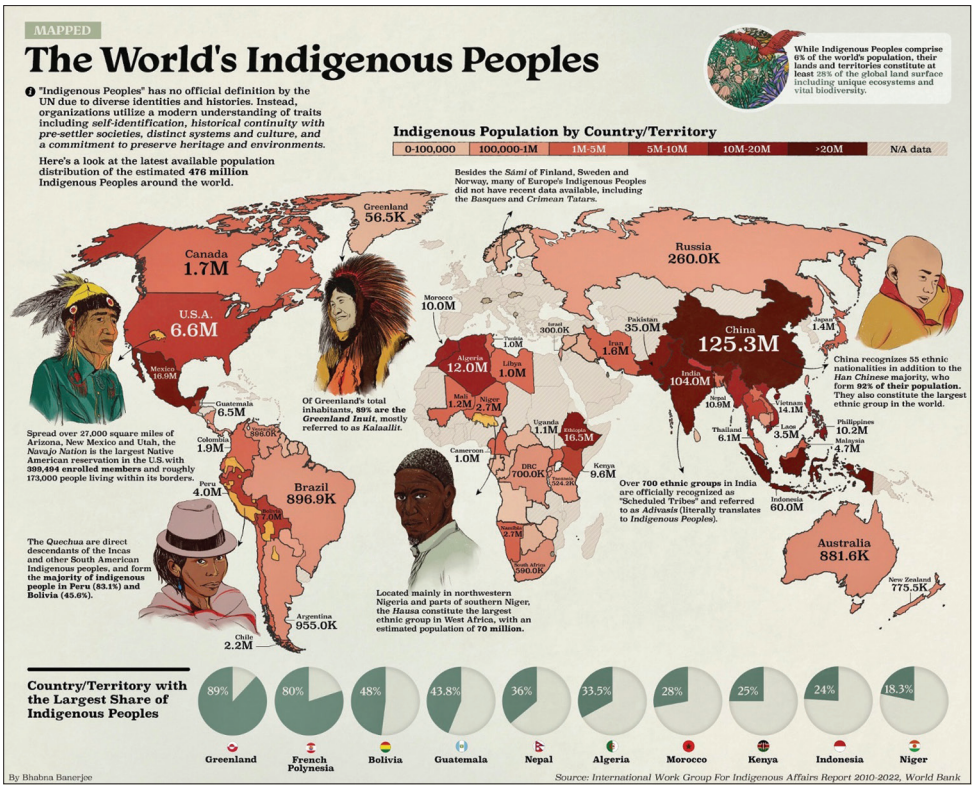

Figure 1: Source: International Work Group For Indigenous Affairs Report 2010-2022. World Bank.

largest shares of indigenous people with 89 % of Inuit ethnicity.

It is already evidence based that skin diseases are highly prevalent among indigenous people and greatly impacting their quality of life.

Unfortunately, skin diseases among indigenous populations have only been very poorly described in the literature [1].

Only few data on racial and ethnic differences in skin and hair structure, physiology, and function exist [2].

In the following we will focus on some of the most prevalent dermatological diseases among intuits in Greenland and the challenges because of few doctors in general in the country and no dermatologist at all working permanently in the region.

Providing health care in Greenland is a major challenge. Spanning 2,600 km from north to south and 1,050 km from east to west, Greenland is the largest island in the world [3,4]. Greenland has the lowest population density on the globe. The current population of Greenland in 2022 totals 56,466 inhabitants, and 19,394 people live in Nuuk alone. The majority of the population is of Greenlandic origin, while 2.4% are immigrants from the Philippines, Thailand, and Iceland. People live along the coastline, as the inner part of Greenland is covered with a permanent ice cap. There are 18 "larger" settlements and 120 small villages. No roads exist between these settlements, and travelling between settlements require transportation by helicopter, airplane, boat, snowmobile or sometimes even dog sled [3].

The weather conditions in Greenland can be extreme in wintertime [3]. Since most of the country is located north of the Arctic Circle, and due to the Arctic climate, temperatures regularly fall to –30°C to –40°C and can even drop to as low as –70°C in the coldest places. Besides the cold, Arctic storms, gale winds, heavy fog, and snowstorms can complicate travelling from one city to another.

Greenland's healthcare system consists of Queen Ingrid's Hospital in the capital city Nuuk (Fig. 2), and four regional hospitals in the next largest human settlements in Sisimiut, Ilulissat, Aasiaat and Qaqortoq. There are 13 physician-staffed health clinics/small hospitals and 48 rural health clinics staffed by nurses or healthcare workers in the smallest settlements.

Figure 2: The healthcare system in Greenland (Photo credit: Carsten Sauer Mikkelsen. Air Photo of Queen Ingrids Hospital in Nuuk) Mikkelsen CS , Poulsen CB, Hove LS. Best Practise Marts 2023.

Queen Ingrid's Hospital serves as a referral hospital for the whole country, and the regional hospitals serve as referral hospitals for the smallest hospitals [5].

In addition to these, the 48 rural health clinics are supervised by physicians and healthcare workers from regional hospitals and small hospitals. Physicians from the regional and small hospitals typically visit the rural settlements two to four times a year. There is an extensive telemedicine service, which allows for medical care to be provided at rural health clinics by a physician daily. This includes both store-and-move-forward applications, as well as live-video telemedical consultations.

The geographical situation combined with, at times, extreme weather conditions make providing healthcare a logistical challenge in Greenland. Physicians in Greenland are used to performing a very broad range of medical duties, the majority probably being within the field of general medicine, general surgery, gynaecology, paediatrics, psychiatry [5].

Physicians also frequently encounter conditions and diseases within the field of dermato-venereology. Dermatological care at specialist level is provided by tele -dermatology. This includes primarily a store-and-move-forward application of clinical photos sent to consultant dermatologists at a Copenhagen University Hospital. There is a provision for sending dermatoscopic images and for live video consultations.

There is also a skin clinic in Nuuk run by a General Practioner with special interest in Dermatology, who is responsible for the overall treatment and coordination of patients throughout Greenland. Now they bring patients in for treatment at the skin clinic in Nuuk to a much greater extent than just few years ago, as a result of the sad fact that there are no permanent working dermatologist and only very few GP`s on the coast outside Nuuk.

In our opinion it is very problematic and many skin diseases including associated co-morbidities can be overlooked and mistreated.

In the following section, we will describe how we feel more doctors and dermatologists in Greenland can make major positive changes within classical dermatology in Greenland, starting with a case from an inuit patient with severe atopic dermatitis.

CLINICAL REPORTS

A 25-year-old man has suffered from severe atopic dermatitis since early childhood. In addition, he had experienced a few episodes of acute urticaria. He was not asthmatic, and a skin prick test was negative. He was admitted to the Queen Ingrid's Hospital in Nuuk with severe infected widespread atopic dermatitis on arrival (Fig. 3a – 3c). Blood samples showed high C-reactive protein values and elevated leukocytes. Cultures turned out positive for staphylococcus aureus. He had no fever. He was treated with intravenous dicloxacillin and penicillin. In addition, he started topical treatment with a combined group III steroid and antibiotic cream together with application moisturizing cream (fat content 70%).

When the infection was cured, the patient continued treatment with daily application of a group IV steroid for 14 days followed by a tapering scheme. He also started high dosage prednisolone (37.5 mg) for 7 days. We took blood samples to be able to start azathioprine or methotrexate, and even discussed the possibility of starting cyclosporine treatment due to the severity of his condition. After 14 days of treatment, the patient's condition had improved significantly (Figs. 4a – 4c) and additional immunosuppressive treatment was not started.

He was seen at a follow-up visit in the clinic after 3 weeks. Unfortunately, he had not adhered to the prescribed treatment and experienced severe exacerbation of the condition, almost like the condition as seen in Figure 3a - 4c.

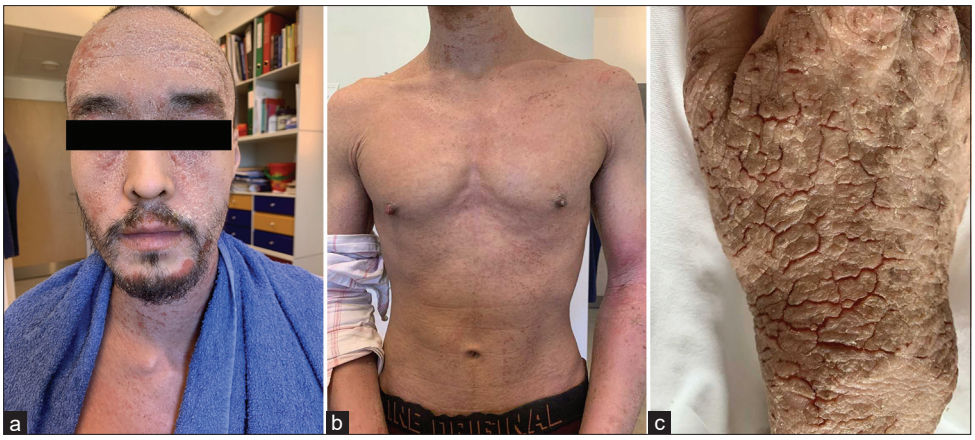

Figure 3: (a-c) Severe atopic dermatitis in an inuit patient from Greenland.

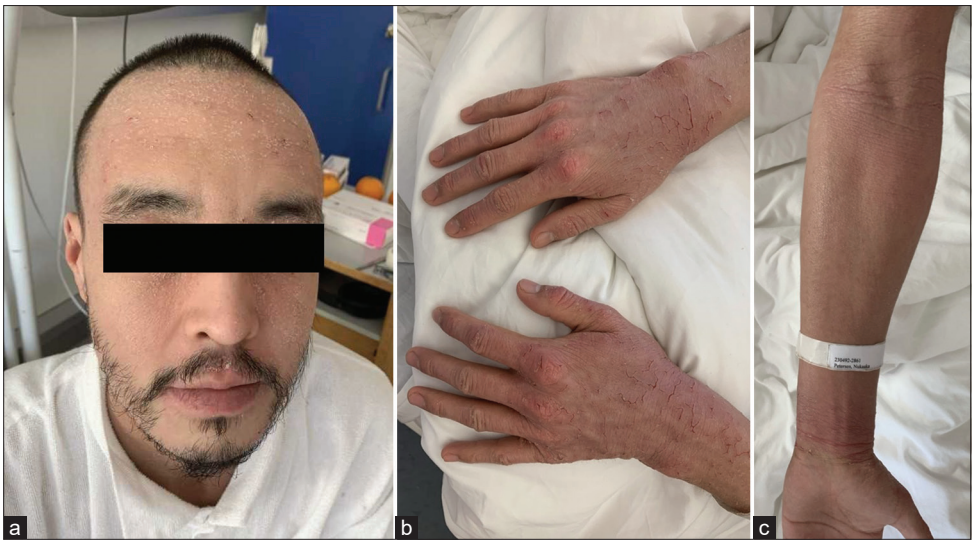

Figure 4: (a-c) Patient after the treatment.

DISCUSSION

Atopic dermatitis occurs in any geographical location and race, though it appears to be more frequent in urban areas and western countries (Fig. 5). The incidence of atopic dermatitis is increasing worldwide.

Unfortunately, only a few publications exist about Atopic Dermatitis in Greenland [6-8]. According to GADA (Global Atopic Dermatitis Atlas) gaps in data on atopic dermatitis are comparable with the African continent [9]. GADA is an international collaboration between the International League of Dermatological Societies (ILDS), the International Eczema Council (IEC), the International Society of Atopic Dermatitis (ISAD), the European Taskforce for Atopic Dermatitis (ETFAD), and The Global Alliance of Dermatology Patient Organizations (ADPO/GlobalSkin). GADA aims to make and maintain an atlas where all the data about atopic dermatitis is available, in all countries, answering the questions: how many people have it, at what age, how severe is it, and how is it treated?

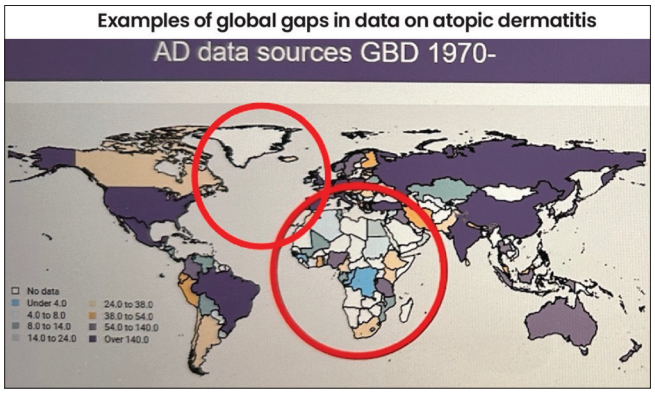

Figure 5: The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990-2017. Br J Dermatol. 2021 Feb;184(2):304-309.

The newest research, especially, shows atopic dermatitis is often very severe and has a high prevalence and incidence in Greenland. The most recent study about atopic dermatitis in Greenland showed a surprisingly high point prevalence and cumulative incidence of atopic dermatitis (28.2% and 35.2%) according to physicians' diagnosis and assessment [10].

In Greenland, there are many interesting aspects regarding the diagnosis and treatment of atopic dermatitis. This primarily involves aspects other than the topical, systemic, or biological treatment of atopic dermatitis. Particularly the importance of patient-centered values and issues.

Proper healthcare consists of clear information and communication with our patients. This is challenging in Greenland's healthcare system since many healthcare professionals come from abroad, primarily Denmark, and only have short-term contracts. This can result in communication problems between patients and healthcare professionals, who do not speak the Greenlandic Inuit language and are not familiar with Greenlandic culture and practice.

Health professionals often have a different perception of the possibilities within the healthcare system compared with patients. When this perception differs from Greenlandic patients' knowledge and other considerations about what is possible in their daily lives, this disconnection may have severe consequences for the individual patient's treatment [11].

Patient Empowerment

Patient empowerment is defined as helping patients to gain control over their own lives and increase their capacity to act on issues that they define as important [12,13]. Patient empowerment is crucial for proper treatment in Greenland, especially regarding the treatment of patients with chronic dermatological diseases. Patients should be encouraged to gain control over their disease: they should learn to take the initiative, solve problems, and make decisions.

These processes can be applied to different settings in healthcare, social care, and self-management [13]. As in other healthcare systems and societies, the shift from a biomedical model to patient-centered care is of the utmost importance in Greenland. This includes several aspects including taking a holistic approach, effective communication, information gathering, reflective listening, and exploration [12].

In addition, sufficient health literacy should be ensured. Patients should be given enough knowledge, understanding, skills, and confidence to use the given health information to take an active role in their wellbeing [11].

It is also important that health professionals actively explore the patients' own ways of handling their everyday life with illness or disabilities as an indicator of what kind of professional support is meaningful in individual cases. Lone Storgaard Hove and her staff are trying to improve the understanding of atopic dermatitis in the Greenlandic population through the development of the Eczema School called "Kalaallit Nunaat".

Atopic dermatitis is associated with several co-morbidities such as anxiety, depression, ADHD, autoimmune diseases, alopecia areata, vitiligo, rheumatoid arthritis, and inflammatory bowel diseases (Mb Crohn, colitis ulcerosa) [14].

These co-morbidities emphasize the importance of "patient empowerment" for those with atopic dermatitis and other chronic dermatological diseases in Greenland.

Cold and dry environment as seen in Greenland is a risk factor for increased prevalence of atopic dermatitis. The vast majority of patients require topical treatment with steroids and calcineurin inhibitors. Of course, emollient therapy is a must, especially in Greenland. It appeared that there is a possibility to use ultraviolet narrow band (UBV) in atopic dermatitis patients in Nuuk in Greenland and hopefully soon also in other more populated places like Sisimiut, Ilulissat, Asiaat and Qaqortoq. More severe cases are managed with systemic agents, including short courses of steroids, cyclosporine, and for the most severe cases dupilumab. All the participants agreed on the necessity of a holistic approach to this group of patients and the importance of patient education.

Eczema School in Greenland – "Kalaallit Nunaat Eczema School"

Dermatology area responsible in Greenland, specialized as a GP Lone Hove, her nurse Magdalene Korneliussen, and project manager Tillie Marinussen are busy

planning the teaching program and travel program and development of the Eczema School called "Kalaallit Nunaat". They are working on making educational and socially informative animations films and TV spots, in Greenlandic which will be included in near future teaching.

Psoriasis in Inuit populations from Greenland

Very few studies describe the prevalence and incidence of psoriasis among Inuit populations [15,16]. Higher prevalence rates have been reported at higher latitudes, and also in Caucasians compared with other ethnic groups [17]. In Greenland, the earliest mention of psoriasis stems from a book from 1940 based on observations done over 30 years by a doctor. Here, a girl in 1912 was described clinically as having psoriasis. Furthermore, an epidemiological study from 1980 found a low incidence of chronic diseases, including psoriasis, in the Upernavik district in northern Greenland in the years 1950-1974 [18].

The objective of a recent study was to estimate the age- and gender-specific prevalence of psoriasis in Nuuk. Sofia Hedvig Christina Botvid, Carsten Sauer Mikkelsen et al conducted the study [19]. Furthermore, we aimed to explore the common risk factors and co-morbidities for patients with psoriasis compared to an age- and gender-matched control group. The study was designed as a cross-sectional case-control study based on national high-quality data from medical records and population registers in Nuuk, from January 1, 2021, to January 1, 2022.

RESULTS

During the study period of 12 months, 175 patients (0.9%) were diagnosed with psoriasis in Nuuk, of which 79 (45%) were females and 96 (55%) were males. The prevalence of patients diagnosed with psoriasis in the adult population aged 20 years old or more in Nuuk was 1.1%. No overall gender-specific difference in prevalence was observed.

Chronic diseases including diabetes, hypertension, and obstructive lung disease were observed more frequently among patients with diagnosed psoriasis (28.6%) in Nuuk compared to controls (20.9%) ($p < 0.05$).

We found a low prevalence of patients with psoriasis in Nuuk.

We speculate that the prevalence found in this study is underestimated.

A prevalence of 1.1% is considered a low prevalence, as the overall global prevalence of psoriasis is 1.9% [20].

For psoriasis patients in Greenland, there is a need for individual/personalized treatment since every patient has his/her own psoriasis phenotype and every patient has his/her own profile of co-morbidities. Disease activity can fluctuate and vary over time.

Individualizing treatment is needed and a special focus on psoriasis in visible locations like the face, psoriasis of hands, nail psoriasis, pustular psoriasis, inverse psoriasis, and genital psoriasis. Doctors need to focus treatment plans on complaints: like bothering pruritus, severity, pain, and consider gender aspects.

When you live with one autoimmune disease, there is an increased risk of developing other autoimmune diseases. Patients can be associated with different specialist departments, and this can have major consequences for the patient, treatment, and society. Psoriasis patients may feel overlooked in their treatment course, and a reorganization of the treatment may be necessary. We need to optimize the treatment across the different specialties based on an interdisciplinary treatment principle and with an individual approach to the patients, where the psoriasis patient and his diagnoses control the treatment course.

Psoriasis is a chronic disease with a significant impact on a patient's quality of life. At the moment multiple treatment options are available. It is of utmost importance to provide every patient with the most appropriate therapy, holistic approach, and focus on personalized goals. Personalized treatment and dosage. In severe cases we need to consider precision medicine for the inuits in Greenland.

Hidradenitis suppurativa (HS) in Inuit populations from Greenland

Hidradenitis suppurativa (HS) is a chronic debilitating suppurative skin disease clinically manifested by abscesses, fistulas, and scaring with the predominant involvement of the intertriginous region. It is a painful and itchy disease with an unpleasant odour. It is not surprising that HS is a devastating condition leading to a significantly decreased quality of life and increased level of stigmatization. Secondary psychiatric comorbidities,

like depression and anxiety, are common. Moreover, a high level of self-destructiveness is observed in this group of subjects. HS is 3 times more common in women and often begins after puberty.

The prevalence of HS is not well known. The group of experts proposed the Worldwide project – The Global Hidradenitis Suppurativa Atlas (GHiSA). Greenland was the first region to join the project. Sofia Hedvig Christina Botvid and Gregor Jemec and their research group used a well-developed methodology that demonstrated that 3.2% of the population suffers from HS lesions [21]. This prevalence was found to be extremely high as in the previous European Guideline on HS the global prevalence of HS was provisionally estimated at the level of 1%.

The important issue is the delay in HS diagnosis. The international study showed that this delay is more than 7 years and visits to about 4 doctors are required to put the correct diagnosis. This delay may result in disease progression and the late introduction of necessary therapy. Therefore, it is of great importance to educate GPs on HS, especially in the early stages of the disease.

The treatment of HS depends on the disease severity. There is a place for conservative treatment as well as for different surgical procedures. Severe cases of HS, also in Greenland, may be managed with the first biological agent registered in HS – adalimumab. However, long-term (10-12 weeks) systemic antibiotic therapy (tetracyclines or combined clindamycin and rifampicin treatment) seems to be a standard for moderate to severe HS.

Hand Eczema in Inuits in Greenland

Hand eczema is a very common dermatological condition worldwide with a particularly rising prevalence post-COVID pandemic. There are multiple factors involved in developing hand dermatitis from atopic constitution to irritancy and allergy. Data on the prevalence and number of cases of hand dermatitis in Greenland are lacking given the relative lack of epidemiological studies and data due to the geographic isolation and occupational and research challenges on the island. Nevertheless, the practitioners in Greenland have all been dealing frequently with hand dermatitis in various clinical presentations and degrees of severity.

Given the multiple factors that Greenland faces from cold weather to intense manual handling (fishing, manual work, etc) hand dermatitis is a frequently encountered problem. One of the main challenges in the treatment of hand dermatitis in Greenland is the general lack of patient adherence and commitment to treatment, which is an essential part of the management. Frequent use of emollients and the avoidance of soaps and the use of soap substitutes are long-term commitments in patients suffering from hand dermatitis. The eczema school established by Dr Lone Storgaard Hove will likely change this in the future given its emphasis on patients' education which again is an important component of the treatment. The current treatment ladder which in addition to the aforementioned hand care measures starts with potent to very potent topical corticosteroids and systemic therapy as a second-line option. Currently, systemic alitretinoin (a retinoid) is licensed and available in Greenland for severe hand dermatitis unresponsive to topical therapy. It is envisaged that by enhancing awareness of hand dermatitis and emphasizing the importance of regular hand care and timely adherence to treatment in the acute stages to prevent chronicity that all of these measures will lead to a favourable outlook on hand dermatitis in Greenland.

Sexually Transmitted Diseases among Inuits

Venereal diseases in Greenland are very common, especially among teenagers. The incidence of gonorrhea and chlamydia has been slightly decreasing since the record years 2015 and 2017 respectively but is still very high with an incidence of 19.2 and 55.4 per person respectively. 1,000 inhabitants in 2018 [22]. For comparison, corresponding figures for gonorrhea and chlamydia in Denmark in 2018 are respectively 0.58 and 11.5 per 1,000 inhabitants [23]. In both Denmark and Greenland, the majority of those infected with chlamydia are young people under 25 years of age. During the past ten years, the number of reported syphilis cases in Greenland has increased significantly from no reports in 2010 to 118 reports in 2019.

Most reports are registered in larger cities on the west coast: Nuuk, Sisimiut and Ilulissat and in Tasiilaq on the east coast [23]. Another worrying observation is that the number of registered HIV-infected people in 2018 was nine, while the number of new HIV-infected people in Greenland has otherwise been five to six in the period 2015-2017 [23] and that the age of the new HIV-infected people is lower than what has been seen before. Since there are very few registered patients,

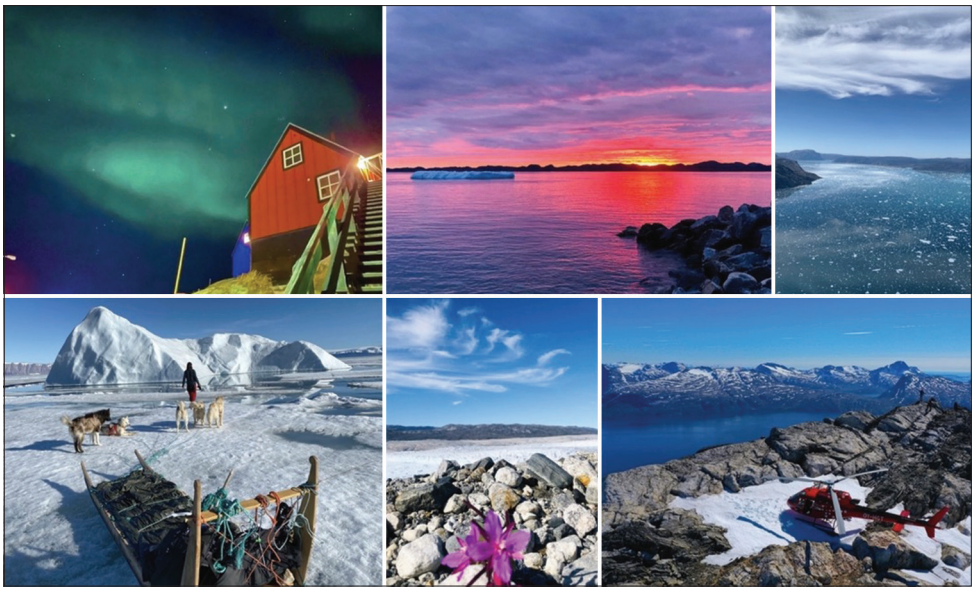

Figure 6: Photos from Greenland: Photo Credits: Carst en Sauer Mikkelsen.

it is however uncertain whether this is an actual development of the disease incidence.

A multi-pronged approach is suggested to be effective in order to reach as many of the sexually active persons in different age groups, social and cultural levels as possible. Rink et al. and Homøe et al. also suggest that education may be effective in reducing STI incidences [24,25] and should be considered included in a multi-pronged approach.

CONCLUSION

The Greenlanders call their own country Inuit Nunaat or Kalaallit Nunaat, meaning Land of the People or Land of the Greenlanders, respectively (Fig. 6). The Greenlandic people are warm, open-minded people. When healthcare personnel who have worked in Greenland are asked to name their greatest experiences, they often rank the meeting of the friendly and welcoming locals the highest. Unfortunately, it is now difficult to recruit doctors and especially certified Dermatologists. Greenland has many challenges in their health care system. Hopefully the future will improve the understanding, diagnosis, and treatment of dermatological diseases in Greenland.

We think it is very importantant to include a holistic approach and ensure adherence.

Ending Quotation

I would like to end this paper with some relevant words, in my opinion:

"When you want to succeed in leading a person to a certain place, you must, first of all, take care to find him where he is and start there. This is the Secret of all Helping Arts.

Anyone who can't do that is delusional when he thinks he can help someone else.

In order to be able to help someone else truly, I must be able to understand more than he does – but, of course, first and foremost, understand what he understands. When I don't, my more-understanding doesn't help him at all. If I still want to make my more-understanding valid, then it is because I am vain or proud, so instead of benefiting him, I want to be admired by him. But all true help begins with humiliation."

Søren Kierkegaard (1813 – 1855) was a Danish theologian, philosopher, poet, social critic, and religious author who is widely considered to be the first existentialist philosopher.

Consent

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

REFERENCES

1. Wu JSA, Florian MC, Rodrigues DA, Tomimori. Skin diseases in indigenous population: retrospective epidemiological study at Xingu Indigenous Park (XIP) and review of the literature. Int J Dermatol. 2017;56:1414-20.
2. Taylor SC. Skin of color: biology, structure, function, and

implications for dermatologic disease. J Am Acad Dermatol. 2002;46(2 Suppl Understanding):S41-62.
3. Lorentzen AK, Penninga L. Frostbite – A case series from arctic Greenland. Wilderness Environ Med. 2018;29:392–400.
4. Penninga, L., Lorentzen, A. K., Serup, J., & Mikkelsen, C. S. (2019). Teledermatology in Arctic Greenland. Forum for Nordic Dermato-Venereology, 24(3), 95-97. https://www.medicaljournals.se/forum/articles/24/3/95- 97.pdf
5. Penninga L, Lohrentzen AK, Mikkelsen CS. Kawasaki disease: Two episodes of recurrent disease in a Greenlandic Inuit Boy. Forum Nord Derm Ven. 2019;24:25-7.
6. Schultz Larsen F, Svensson A, Diepgen TL, From E. The occurrence of atopic dermatitis in Greenland. Acta Derm Venereol. 2005;85(2):140-3. doi:
7. Andersson AM, Kaiser H, Skov L, Koch A, Thyssen JP. Prevalence and risk factors for atopic dermatitis in Greenlandic children. Clin Exp Dermatol. 2023 Mar 22;48(4):352-360.
8. Tamsmark TH, Koch A, Melbye M, Mølbak K. Incidence and predictors of atopic dermatitis in an open birth cohort in Sisimiut, Greenland. Acta Paediatr. 2001;90:982-8.
9. Laughter MR, Maymone MBC, Mashayekhi S, Arents BWM, Karimkhani C, Langan SM et al. The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990-2017. Br J Dermatol. 2021 Feb;184(2):304-309. doi: 10.1111/bjd.19580. Epub 2020 Nov 29.
10. Andersson AM, Kaiser H, Skov L, Koch A, Thyssen JP. Prevalence and risk factors for atopic dermatitis in Greenlandic children. Clin Exp Dermatol. 2023 Mar 22;48(4):352-360
11. Aagaard T. Patient involvement in healthcare professional practice – a question about knowledge. Int J Circumpolar Health. 2017;76:1.
12. Patient empowerment--who empowers whom? Lancet. 2012 May 5;379(9827):1677. doi: 10.1016/S0140-6736(12)60699-0. Erratum in: Lancet. 2012 Aug 18;380(9842):650.
13. Mikkelsen CS, Jensen JN, Penninga L. Severe atopic dermatitis in arctic Greenland: The importance of patient empowerment. Best Practise, 2021:April.
14. Davis DMR, Eichenfield LF, Frazer-Green L, Paller AS, Silverberg JI, Sidbury R. American Academy of Dermatology Guidelines: Awareness of comorbidities associated with atopic dermatitis in adults. J Am Acad Dermatol. 2022 Jun;86(6):1335-1336.e18.
15. Harvald B. Genetic epidemiology of Greenland. Clin Genet. 1989 Nov;36(5):364-7. doi: 10.1111/j.1399-0004.1989.tb03214.x. PMID: 2689006
16. Kromann N. Green Epidemiological studies in the Upernavik district, Greenland: incidence of some chronic diseases 1950–1974. Acta Med Scand. 1980;208:401-6.
17. Farber EM, Nall ML. The natural history of psoriasis in 5,600 patients. Dermatologica. 1974;148(1):1-18. doi: 10.1159/000251595. PMID: 4831963.
18. Highlights from the first Dermatology Conference in Greenland Mikkelsen CS, Szepietowski JC, Hove LS, Korneliussen M, Firas Ai-Niami, Bjerring P Best Practise July
19. Botvid SHC, Storgaard Hove L, Backe MB, Skovgaard N, Pedersen ML, Sauer Mikkelsen C. Low prevalence of patients diagnosed with psoriasis in Nuuk: a call for increased awareness of chronic skin disease in Greenland. Int J Circumpolar Health. 2022 Dec;81(1)
20. Kimmel GW, Lebwohl M. Psoriasis: Overview and Diagnosis. Evidence-Based Psoriasis. 2018 Jul 1:1–16. doi:
21. Botvid SHC, Storgaard Hove L, Bouazzi D, Kjærsgaard Andersen R, Francis Thomsen S, Saunte DM, Jemec GBE. Hidradenitis Suppurativa Prevalence in Nuuk, Greenland: Physician Validation of a Hidradenitis Suppurativa Questionnaire in a Greenlandic Setting. Acta Derm Venereol. 2023 Jan 10;103:adv00847.
22. Landslægens rapport om seksuelt overførte sygdomme. 2018. https://nun.gl/nyheder/2019/05/seksuelt-overfoerte-sygdomme-i-groenland-i-2018?sc_lang=da
23. SSI. https://www.ssi.dk/sygdomme-beredskab-og-forskning/sygdomsovervaagning/g/gonorre-opgoerelse-over-sygdomsforekomst-2018 https://www.ssi.dk/sygdomme-beredskab-og-forskning/sygdomsovervaagning/k/klamydia—opgoerelse-over-sygdomsforekomst-2018
24. Rink E, Montgomery-Andersen R, Anastario M. The effectiveness of an education intervention to prevent chlamydia infection among Greenlandic youth. Int J STD AIDS. 2015;26:98–106.
25. Homøe AS, Knudsen AK, Nielsen SB, Grynnerup AG. Sexual and reproductive health in Greenland: evaluation of implementing sexual peer-to-peer education in Greenland (the SexInuk project). Int J Circumpolar Health. 2015 Oct 28;74:27941.

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Clinical Image

Dermoscopy of cutaneous lesion of pseudoxanthoma elasticum: A strength to clinical examination

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PXE is a rare hereditary disorder characterized by generalized fragmentation and progressive calcification of elastic tissue predominantly in the dermis, blood vessels and Bruch membrane of the eye affecting skin, eye, cardiovascular and digestive system [1].

A 26-year-old male presented with insidious onset gradually progressive asymptomatic lesions on lateral aspect of neck and axilla from last 5 years. Family history was non-contributory. Physical examination showed yellowish papules arranged in linear and reticulate pattern that tend to coalesce into confluent plaques on both side of neck and axilla (Fig. 1a). Systemic examination was unremarkable. Fundus examination was normal. 2D-echocardiography showed normal cardiac assessment. Stool for occult blood examination was normal.

Polarised light dermoscopy at 10X magnification (DermLite DL4) of skin lesions showed multiple linear yellowish area arranged in reticulate pattern alternating with multiple linear red to purplish areas (Fig. 1b). The yellowish linear areas were devoid of hair follicles (Dermalite DL4, non-polarised) (Fig. 1c). Histopathology shows accumulation of fragmented and faintly basophilic elastotic material in the mid and lower dermis (Fig. 1d). On the basis of clinical findings, histopathology and dermoscopy examination, final diagnosis of pseudoxanthoma elasticum (PXE) was made.

The yellowish papules are correspond to the dermal elastolysis and mineralisation of fragmented elastic fibres. The red to purplish reticulate background correspond to the rearranged dilated superficial vessels due to elastolysis on dermoscopy [2]. To conclude dermoscopy is a useful aid to clinical examination for a non-invasive, prompt diagnosis of PXE for early detection and intervention.

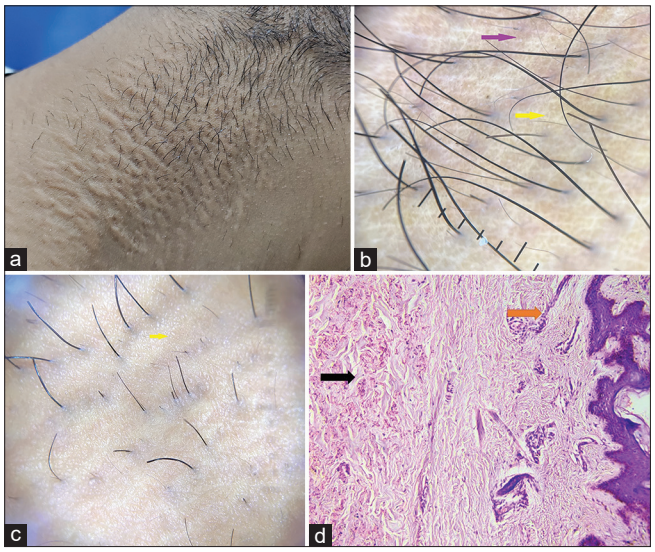

Figure 1: (a) Yellowish papules and linear plaques present in a reticulate manner on lateral side of neck. (b) Multiple yellowish areas in reticulate pattern (yellow arrow) alternating with multiple linear purplish areas (purple arrow). (DermLite DL4, 10X, Polarised). (c) Yellowish linear areas were devoid of hair follicles (yellow arrow). (DermLite DL4, 10X, Non-Polarised). (d) Histopathologic findings of the section of biopsy specimen (Hematoxylin and eosin stain; 40X). Brown arrow shows mild perivascular chronic inflammatory infiltrate in upper dermis. Black arrow shows fragmented and faintly basophilic elastotic material in lower dermis.

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

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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 A, Bhari N, Bhari A. BMJ Case Rep. 2017:2017:bcr2017221365.
2. Kawashima S, Togawa Y, Miyachi H, Matsue H. Dermoscopic features of pseudoxanthoma elasticum. Clin Exp Dermatol. 2018;43:175-9.

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Our Dermatology Online

Case Letter

Ibrutinib-induced pyoderma gangrenosum in a patient with chronic lymphocytic leukemia

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Sir,

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis of undetermined etiology. The pathophysiological mechanism is not fully understood. It is most often associated with systemic diseases: inflammatory bowel diseases, hematologic disorders, and solid tumors [1]. Drug-induced PG is an uncommon cutaneous reaction with no specific clinical or histopathologic features [2]. Herein, we describe a new case of ibrutinib-induced PG in a patient with B-cell chronic lymphocytic leukemia.

A 64-year-old male with a history of B-cell chronic lymphocytic leukemia was diagnosed three years earlier, treated with chemotherapy for two years, and achieved an incomplete remission. Thus, he was started on the Bruton tyrosine kinase inhibitor ibrutinib at the recommended dose of 420 mg/day with significant improvement. After eight months, the patient consulted for several painful, palpable, red-to-violaceous skin lesions in the lower limbs and feet. The lesions began one month after ibrutinib initiation with a vesicular appearance and evolved into nodules and painful ulcers with violaceous borders, sometimes associated with pustules (Figs. 1a and 1b). He also presented dyschromic and cribriform scars on his right leg (Fig. 2). A biopsy of the ulcer margin and pustules revealed massive lymphocyte and neutrophil infiltration with few apoptotic bodies. No histopathologic signs of vasculitis were observed (Fig. 3). The complete blood count did not reveal any leukocytosis, and the bacterial and fungal cultures were negative. After consultation with hematologists and pharmacologists, PG was diagnosed, and ibrutinib was suspected as the causative agent. In addition to ibrutinib discontinuation, the patient received topical corticosteroids, and an improvement in the skin lesions was observed.

PG is a neutrophilic dermatosis clinically defined by painful ulcers with a violaceous border, usually located in the lower limbs. It may also appear as aseptic pustules or, less frequently, nodules [1]. Histopathology is not specific; its main purpose is to exclude other potential diagnoses. PG typically imitates an abscess or cellulitis by displaying considerable neutrophilic infiltration, bleeding, and epidermal necrosis. Sometimes, vessel wall infiltration may be noticed [3]. Innovative therapies that focus on B-cell receptors and their signaling pathways are quickly improving the treatment options for B-cell malignancies. Ibrutinib is an example of a drug that has been approved for the treatment of mantle cell lymphoma, chronic lymphocytic leukemia, and other malignant hematologic conditions. It acts by inhibiting Bruton tyrosine kinase (BTK), which is necessary for B cells to survive and reproduce [4]. The most commonly reported side effects are cytopenia, diarrhea, fatigue, bruising, and upper respiratory tract infections. Only several cases of ibrutinib-induced neutrophilic dermatosis, including two cases of PG, have been reported in the literature [5,6]. Ibrutinib has a good safety profile and few adverse effects because of its BTK receptor specificity. The epidermal growth

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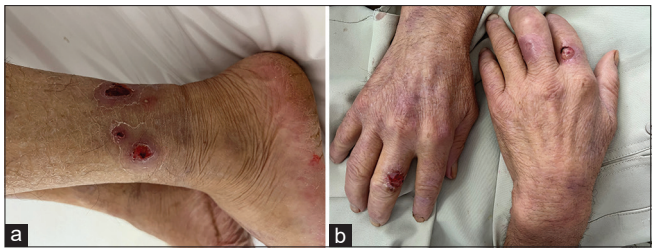

Figure 1: (a) Painful ulcers with a violaceous border and perilesional pustule. (b) Painful ulcers on the hands.

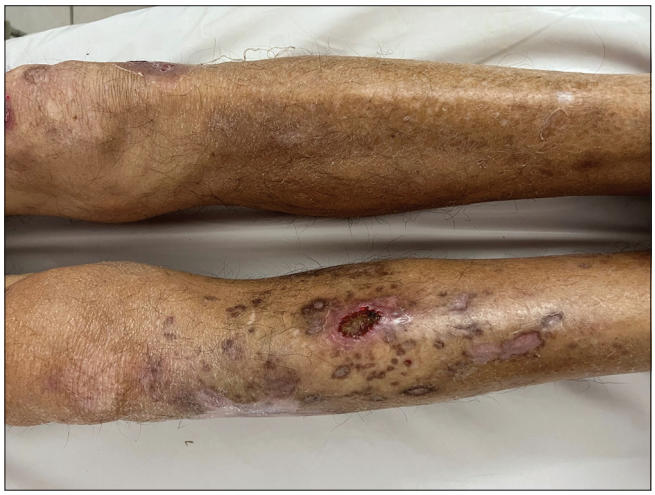

Figure 2: Dyschromic and cribriform scars.

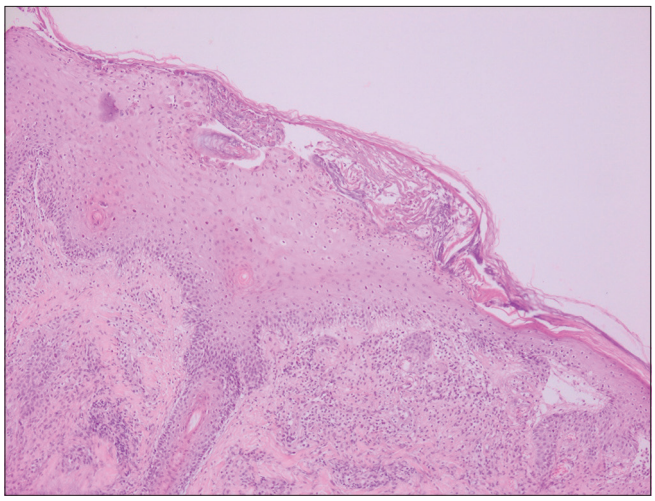

Figure 3: Pustule with lymphocyte and neutrophil infiltration and few apoptotic bodies.

factor receptor, which is expressed in the basal layer of the epidermis, is another target of its function. Inhibition of this receptor has a negative effect on tissue regeneration and is responsible for a pro-inflammatory reaction that may explain the occurrence of PG, which is more common in areas susceptible to repeated trauma [3]. Another theory contends that host immune cells are exposed to peptides conjugated to ibrutinib through the major histocompatibility complex, which triggers a T cell-directed immune response leading to tissue damage and destruction [2].

Ibrutinib, a BTK inhibitor, could lead to neutrophilic dermatosis, which is explained by the drug-induced immune process. Ibrutinib-dose tapering, low-dose corticosteroids, and dapsone remain the most effective options to treat this condition and prevent recurrence. Switching from ibrutinib to another medication could be suggested in the case of resistance.

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. Kridin K, Cohen AD, Amber KT. Underlying systemic diseases in pyoderma gangrenosum: A systematic review and meta-analysis. Am J Clin Dermatol. 2018;19:479-47.
2. Khoshnam-Rad N, Gheymati A, Jahangard-Rafsanjani Z. Tyrosine kinase inhibitors-associated pyoderma gangrenosum: A systematic review of published case reports. Anti-Cancer Drugs. 2022; 33:e1-e8.
3. Marzano AV, Ishak RS, Saibeni S, Crosti C, Meroni PL, Cugno M. Autoinflammatory skin disorders in inflammatory bowel diseases, pyoderma gangrenosum and Sweet's syndrome: A comprehensive review and disease classification criteria. Clin Rev Allergy Immunol. 2013;45:202-10.
4. Shaikh H, Khattab A, Faisal MS, Chilkulwar A, Albrethsen M Sadashiv S, et al. Case series of unique adverse events related to the use of ibrutinib in patients with B-cell malignancies: A single institution experience and a review of literature. J Oncol Pharm Practice. 2018;0:1-6.
5. Giovanni B, Ibatici A, Sola S, Maria A, Brunasso G, Massone C. Ibrutinib and pyoderma gangrenosum in a patient with b-cell chronic lymphocytic leukemia. Am J Dermatopathol. 2020;42:148-50.
6. Sławińska M, Barańska-Rybak W, Sobjanek M. Ibrutinib-induced pyoderma gangrenosum. Pol Arch Med Wewn. 2016;126:710-11.

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Our Dermatology Online

Case Letter

Rifampicin-induced Sweet's syndrome following erythema induratum of Bazin

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Sir,

Sweet's syndrome is a neutrophilic dermatosis characterized by abrupt infiltration of the superficial dermis by neutrophils in the absence of local infection. It is classified as classic, malignancy-induced, or drug-induced [1,2]. Medications are responsible for approx. 12% of Sweet's syndrome presentations with granulocyte colony-stimulating factor, all-trans retinoic acid, and vaccines cited as the most common causes [3]. Unlike the rest of antituberculous drugs, rifampicin is usually well tolerated by most patients, although severe digestive intolerance sometimes requires the discontinuation of the treatment. Cutaneous adverse effects have been described, including occasional flushing and maculopapular exanthema [4]. Herein, we report a case of rifampicin-induced Sweet's syndrome in a patient with erythema induratum of Bazin (EIB).

A 45-year-old female patient, with a history of chronic, recurrent, nodular lesions on the lower limbs treated as erythema nodosum, was treated with non-steroidal, anti-inflammatory drugs, then corticosteroids, without improvement. She had no personal or family history of active tuberculosis. The diagnosis of EIB was, then, reached based on the clinical morphology and evolution, histopathology, a tuberculin test, and QuantiFERON-B Gold Plus were also all positive. Antituberculous (ATB) treatment was then initiated. The patient reported a cutaneous rash ten days after the initiation of the treatment. All ATB drugs were stopped and reintroduced progressively with a two-week interval, starting with isoniazid (H), ethambutol (E), pyrazinamide (Z), and lastly rifampin (R) at a dose of 150 mg. After the reintroduction of rifampicin, the patient developed malaise, fever, chills, and arthralgia. Two days later, a tender non-pruritic rash characterized by painful, swollen, erythematous plaques and subcutaneous nodules symmetrically distributed on the thighs, legs, and upper arms was observed (Figs. 1a and 1b), leading to the discontinuation of the treatment by the patient. Biological assessment revealed hyperleukocytosis (14.2 × 10^3/mm^3) with 80% of neutrophils, an inflammatory syndrome with a high level of C-reactive protein (at 228), and the erythrocyte sedimentation rate at 42. A diagnosis of Sweet's syndrome was confirmed by the histological findings of a dense dermal neutrophilic infiltrate extending deeper to the hypodermis in a lobular distribution, focal leukocytoclasia, and papillary dermal edema. After a consultation with pneumoallergists, the patient was put back on ATB with progressive administration.

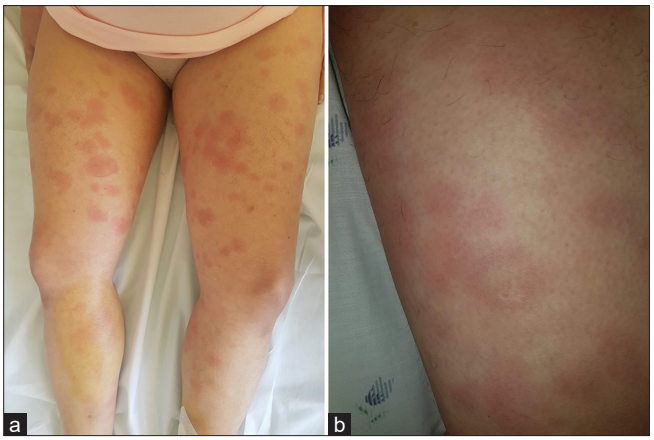

Figure 1: Swollen, erythematous plaques and subcutaneous nodules symmetrically distributed (a) on the thighs and legs; (b) shows a close-up of the thigh.

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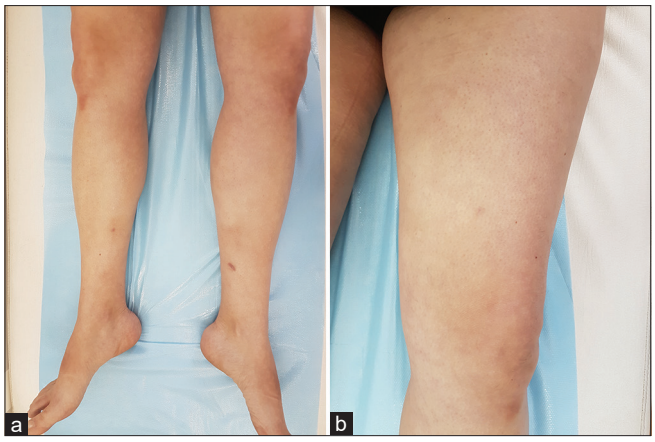

Figure 2: A complete regression of all lesions occurring three months later in (a) the legs and (b) the thighs.

Along with close monitoring, oral corticosteroids were initiated at a dose of 1 mg/kg/day with tapering over six months. A marked improvement occurred over the next month with the regression of EIB lesions. A minimal flare-up following the reintroduction of rifampicin was noted, characterized by painful, swollen plaques in the legs, rapidly resolving after three days, and a complete regression of all lesions occurred three months later (Figs. 2a and 2b).

Along with the clinical and histopathological description, a temporal relationship between drug ingestion and the onset of symptoms as well as the resolution of symptoms after drug withdrawal and treatment with systemic steroids confirmed the diagnosis of rifampicin-induced Sweet's syndrome in our patient.

Consent

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REFERENCES

1. Shaikh MB, Krunic AL. Drug-induced Sweet syndrome. J Allergy Clin Immunol Pract. 2019;7:2400-1.
2. Belmourida S, Khallayoune M, Palamino H, Meziane M, Ismaili N, Benzekri L, Hassam B, Senouci K. Sweet syndrome revealing a leukemia. Our Dermatol Online. 2020;11:e139.1-2.
3. McNally A, Ibbetson J. Azathioprine-induced Sweet's syndrome: A case series and review of the literature. Australas J Dermatol. 2017;58:53-7.
4. Campbell JR, Trajman A. Adverse events in adults with latent tuberculosis infection receiving daily rifampicin or isoniazid: Post-hoc safety analysis of two randomised controlled trials. Lancet Infect Dis. 2020;20:318-29.

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Case Letter

Cutaneous rash in patients receiving imatinib: Lichenoid drug eruption or induced lichen?

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Sir,

Imatinib is a tyrosine kinase receptor inhibitor used in the treatment of chronic myeloid leukemia, gastrointestinal stromal tumors, and Darier–Ferrand dermatofibrosarcoma.

Several cutaneous side effects were described with this molecule, including lichenoid eruptions, which remain rare. Herein, we report a new observation.

A 61-year-old female patient had a history of chronic myeloid leukemia and was put on imatinib by her hematologist. She received 400 mg per day for six months with good tolerance so far. The patient presented with a generalized itchy rash persistent for a month.

A dermatological examination revealed general xerosis and several erythematous and squamous plaques that were well-limited, shiny, and lichenified in some areas. Cutaneous lesions were of different sizes, sometimes confluent and symmetrically distributed on the trunk, arms, and thighs sparing the face (Figs. 1a and 1b).

An examination of the oral mucosa showed enanthema with a fine reticulated network of the inner surface of the right cheek.

A skin biopsy revealed orthokeratotic hyperkeratosis, necrotic keratinocyte cells (Civatte bodies), pigmentary incontinence, and a dense lichenoid lymphoid infiltrate consisting of lymphocytes and eosinophils. In addition, blood work found no abnormalities and hepatitis B and C serologies were negative.

Therapeutic management consisted of an emollient, antihistamines, and a local corticosteroid for the skin and oral lesions.

A follow-up after eight weeks of treatment noted the disappearance of pruritus, the absence of new lesions, post-inflammatory hyperpigmentation (Fig. 2). Imatinib was continued at the same dose of 400 mg per day. No recurrence was observed for two years (Fig. 3).

The cutaneous side effects of imatinib are frequent and occur between 9% and 69% [1]. They include xerosis, alopecia, facial edema, and photosensitivity [2]. Lichenoid drug eruption under imatinib is rare, with around thirty published cases [3]. The period between imatinib initiation and the rash onset typically ranges from one to twelve months [2].

The clinical presentation of this drug eruption is polymorphic, associating psoriasiform, lichen-like, and sometimes even eczema-like lesions. Oral lesions manifest with erythema or ulcerated whitish plaques that may have a reticulated form and linear streaks [4].

A distinction between a lichenoid drug eruption and induced lichen planus may be challenging. Clinically, lichenoid drug eruption is associated with a more symmetrical arrangement of lesions on the trunk and extremities, located on photo-exposed areas, without Wickham's streaks and evolving toward post-inflammatory hyperpigmentation. Meanwhile, histology rather shows focal parakeratosis and eosinophilic infiltrate with a perivascular arrangement [5].

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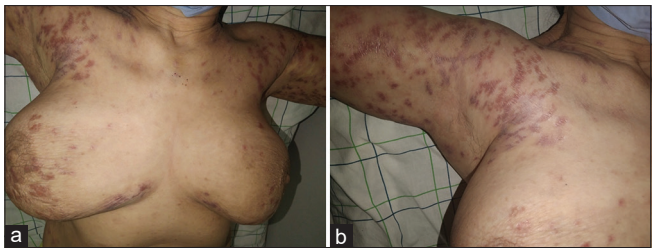

Figure 1: (a) Multiple, symmetrical, erythematous and squamous plaques on the trunk and upper arm. (b) Erythematous and squamous plaques on the shoulder (note the shiny and purplish aspect).

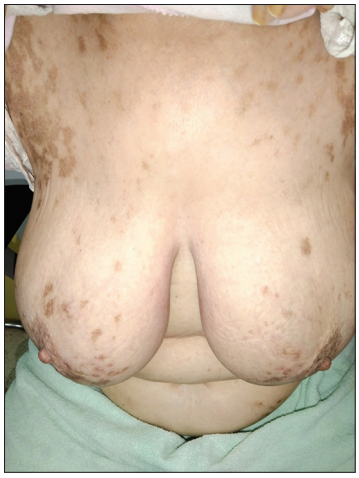

Figure 2: Follow-up after eight weeks of local treatment (note post-inflammatory pigmentation).

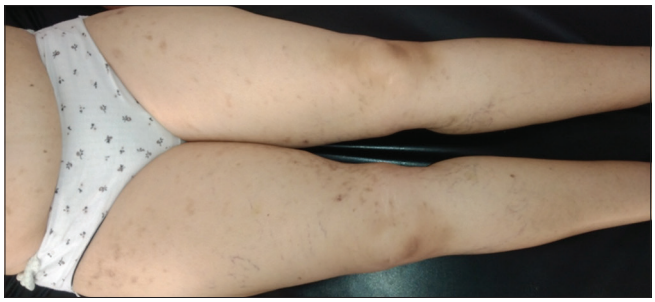

Figure 3: Follow-up at six months noted no new lesions and clarification of the hyperpigmentation.

In our case, there was an overlap between the clinical and histological appearance of these two entities. Similar observations have been reported in the literature.

Imatinib withdrawal is not mandatory, and dose reduction with a local symptomatic treatment based on topical corticosteroids usually allows improvement. In more resistant cases, other treatments are suggested. Dalmau et al. recommended acitretin [4].

Imatinib-induced lichenoid drug eruption is generally benign. However, severe or treatment-resistant forms require dose reduction or even treatment discontinuation, which risks aggravating the underlying pathology. The definitive discontinuation of imatinib should, therefore, be discussed based on the benefit/risk ratio of each patient.

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. Bouabdella S, Sof K, Khouna A, Zizi N, Dikhaye S. Éruptions lichénoides induites par l'Imatinib: A propos de deux cas. Presse Médicale Form. 2021;2.
2. Penn EH, Chung HJ, Keller M. Imatinib mesylate-induced lichenoid drug eruption. Cutis. 2017;99:189-92.
3. Frioui R, Faten R, Asma B, Jaber K, Dhaoui MR. Toxidermies lichénïdes sous inhibiteurs des tyrosines kinases: un effet indésirable à ne pas méconnaître. Rev Méd Interne. 2021;42:A412.
4. Meddeb Z, Souissi A, Derbel F, Bellakhal S, Jellouli A, Mestiri A, et al. La toxidermie lichénoïde à l'imatinib: un effet indésirable à ne pas méconnaître. Rev Méd Interne. 2015;36:A867.
5. Pascual JC, Matarredona J, Miralles J, Conesa V, Borras-Blasco J. Oral and cutaneous lichenoid reaction secondary to imatinib: Report of two cases. Int J Dermatol. 2006;45:14713.

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Our Dermatology Online

Case Letter

Anti-MDA5 dermatomyositis

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Sir,

A 44-year-old male presented to emergency department at Basildon University Hospital with a two-week history of fatigue, fever, severe joint pain primarily in his jaw and shoulders, and progressive loss of muscle strength in his upper and lower body. He reported increasing respiratory distress with difficulty with swallowing. Additionally, he developed a papulovesicular rash on his knuckles, followed by a scaly rash on his hairline and both elbows. Swelling around his eyes (Figs. 1a – 1e) and oral ulceration accompanied the rash.

The patient claimed to have no recent travel history, weight loss, underlying medical conditions, or regular medication usage. During examination, the patient's skin was of Fitzpatrick Skin Type V1 with a resolving papulovesicular rash and ulcerations over the metacarpophalangeal and interphalangeal joints of both hands. He showed painful, keratotic papules on the palmar surfaces of both hands and peri-orbital swelling with a scaly rash on the frontal hairline and elbows (Figs. 1a – 1e). Muscular examination revealed upper and lower limb girdle weakness.

Investigation results showed high levels of serum ferritin, LDH, CK, ALT, AST, positive ANA test, positive MDA-5 antibodies, and low haemoglobin. MRI scan of the thigh showed subtle changes with increased signal in the vastus lateralis muscle bilaterally.

Electromyography was done and it showed evidence of inflammatory myopathy. A muscle biopsy subsequently revealed an increase in HLA-ABC's upregulation and membrane attack complex surrounding capillaries. The changes were highly suggestive of inflammatory myositis.

Pulmonary function tests showed an FVC of 79% and a TLCO of 65% of the predicted reading.

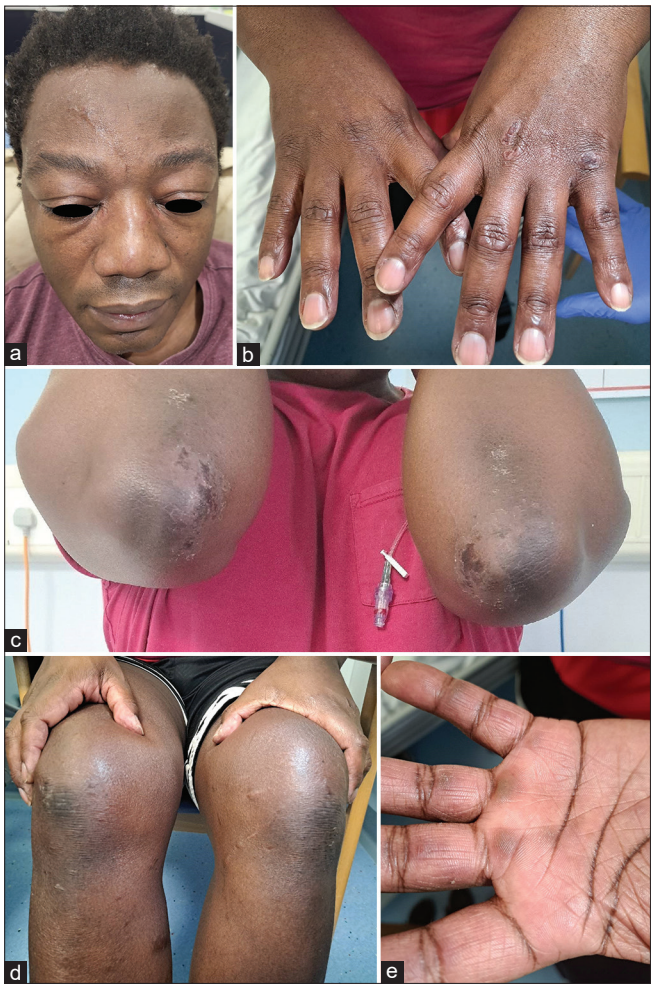

Figure 1: (a) Bilateral peri-orbital swelling (b) Red-violet, slightly raised papules (Gottron papules) on the metacarpophalangeal and interphalangeal joints with healing ulcerations, (c and d) Redness over the back of the elbows and knees (Gottron sign) (e) Painful, keratotic papules on the palmar surfaces of both hands (Mechanic's Hands).

The clinical presentation matched that of Anti-MDA-5 dermatomyositis (previously known as CADM-140). The presence of this antibody has been associated with rapidly progressive interstitial lung disease and high mortality rate especially in the Asian population.

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It also affects the prognosis for the patient who may have a lower likelihood of achieving remission [1,2]. Anti-synthetase antibodies might also be associated with interstitial lung disease, however the course of it is usually slowly progressive as opposed to rapidly progressive interstitial lung disease in Anti MDA5 dermatomyositis [3]. The clinical presentation of Anti-MDA5 dermatomyositis includes skin ulceration which usually occurs at the site of Gottron papules and might include elbows and lateral nailfolds. It is also associated with tender palmar papules (mechanics hands), oral pain and/or ulceration and arthritis [4,5].

The patient received oral prednisolone and mycophenolate mofetil treatment that resulted in a gradual improvement of symptoms, and a decrease in muscle markers including CK, ALT, and LDH. The patient was screened for associated malignancy and his chest, abdomen and pelvis CT scan was unremarkable apart from some basal atelectasis involving both lungs.

This case highlights the importance of certain antibodies in suggesting increased risk of serious complications of dermatomyositis. Patients with anti-MDA5 dermatomyositis need specific attention and monitoring of the pulmonary function tests as they carry important prognostic factors and might be associated with increased morbidity and mortality in patients with dermatomyositis.

Consent

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REFERENCES

1- Nombel A, Fabien N, Coutant F. Dermatomyositis with anti-MDA5 antibodies: bioclinical features, pathogenesis and emerging therapies. Front Immunol. 2021;12:773352.

2- Wu W, Guo L, Fu Y, Wang K, Zhang D, Xu W, et al. Interstitial lung disease in anti-MDA5 positive dermatomyositis. Clin Rev Allergy Immunol. 2021;60:293-304.

3- Sawal N, Mukhopadhyay S, Rayancha S, Moore A, Garcha P, Kumar A, et al. A narrative review of interstitial lung disease in anti-synthetase syndrome: a clinical approach. J Thorac Dis. 2021;13:5556-71.

4- Gupta R, Kumar S, Gow P, Chang L, Yen L. Anti-MDA5-associated dermatomyositis. Intern Med J. 2020;50:484-7.

5- Yamaguchi K, Yamaguchi A, Onuki Y, Itai M, Kashiwagi C, Takehara K, et al. Clinical features of dermatomyositis associated with anti-MDA5 antibodies by age. Mod Rheumatol. 2021;31:177-85.

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Our Dermatology Online

Case Letter

Mucosal involvement in the context of mycosis fungoides revealing a cicatricial pemphigoid

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Sir,

Cicatricial pemphigoid (CP), also known as cicatricial pemphigoid, is a rare, synechial, subepidermal autoimmune bullous dermatosis characterized clinically by its elective involvement of mucous membranes, most often the oral and ocular mucosae. Because of the risk of serious complications, such as blindness and airway involvement, early and aggressive treatment may be warranted. Recent studies have shown the association of CP with an increased risk of solid cancer.

Herein, we report a sixty-year-old female who had been followed at our department for four years for a mycosis fungoid at tumor stage transformed classified as T3N0M0 or stage IIB. The patient received nine courses of gemcitabine followed by localized radiotherapy on two persistent nodules on the left thigh with complete remission. Sixteen months later, the patient developed oral erosions, epistaxis with high dysphagia, and bilateral ocular redness.

Clinical examination found two well-limited, erythematous ulcerations on the soft palate in the process of healing (Fig. 1a), conjunctival hyperemia with bilateral pterygium (Fig. 1b), and an inflammatory nasal mucosa with a well-limited, rounded erosion on the right nostril mucosa (Fig. 1c).

An ophthalmological examination revealed fibrotic conjunctivitis evoking cicatricial pemphigoid at first. Laryngoscopy revealed whitish ulcerations at the base of the tongue and on the laryngeal surface of the epiglottis. A biopsy with a histological study and direct immunofluorescence of an oral bulla was compatible with cicatricial pemphigoid.

The patient was put on corticosteroid bolus and then low-dose corticosteroid therapy associated with a course of rituximab. The evolution was marked by an improvement in oral, ocular, and nasal involvement.

Cicatricial pemphigoid (CP) is an autoimmune disease characterized by the presence of various autoantibodies directed against basement membrane antigens, most frequently BP180 yet also BP230 or β4 integrin, with a minority against laminin 5 [1].

In the literature, several retrospective studies have reported an association between CP and malignancy, especially solid tumors.

Egan et al. described 35 patients with CP followed over a twelve-year period; ten patients (28.6%) developed solitary cancer. Eight of these patients developed cancer after the onset of CP, most within 12 to 14 months, and all deaths were cancer-related [2].

Associated malignancies included three lung, three stomach, two colon, and two endometrial cancers.

In addition to solid cancers, CP was described by Sadler et al. in a patient with mycosis fungoides treated for twelve years with topical clobetasol, who developed oral and nasal erosions. Histopathology confirmed the

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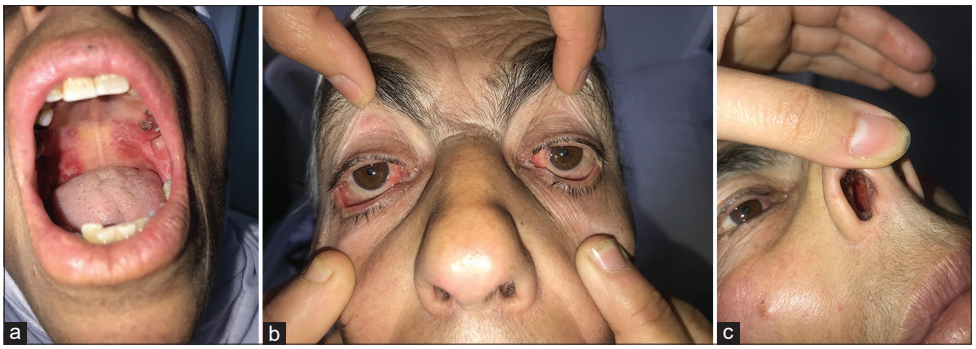

Figure 1: (a) Two well-limited, erythematous ulcerations on the soft palate in the process of healing.(b) Conjunctival hyperemia with bilateral pterygium.(c) An inflammatory nasal mucosa with a well-limited, rounded erosion on the right nostril mucosa.

diagnosis of CP. This was the first association between CP and lymphoma [3].

This association was later documented in another patient, with diffuse large B-cell non-Hodgkin's lymphoma in a series by Shannon et al. [4].

Our case was the third reported association between CP and lymphoma.

Most studies found the association between CP with laminin-5 and neoplasia.

Some reports suggested that CP may represent a paraneoplastic syndrome.

Various pathogenetic hypotheses have been put forward, including the theory that tumor cells secrete anti-laminin-5 antibodies directed against the skin and cause bulla formation [5].

In our case, the patient presented CP sixteen months after the diagnosis of mycosis fungoides with oral, ocular, nasal, and laryngeal involvement, which may be considered a paraneoplastic syndrome.

Various studies have demonstrated the correlation between laminin-5 in CP and cancer, emphasizing the importance of the immunological diagnosis of these autoantibodies.

However, the absence of this antigen in other cases casts doubt on this hypothesis, hence the need for further studies.

Consent

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REFERENCES

1. Kartan S, Shi VY, Clark AK, Chan LS. Paraneoplastic pemphigus and autoimmune blistering diseases associated with neoplasm: Characteristics, diagnosis, associated neoplasms, proposed pathogenesis, treatment. Am J Clin Dermatol. 2017;18:105-26.
2. Amber KT, Bloom R, Hertl M. A systematic review with pooled analysis of clinical presentation and immunodiagnostic testing in mucous membrane pemphigoid: Association of anti-laminin-332 IgG with oropharyngeal involvement and the usefulness of ELISA. J Eur Acad Dermatol Venereol. 2016;30:72-7.
3. Balestri R, Magnano M, La Placa M. Malignancies in bullous pemphigoid: A controversial association. J Dermatol. 2016;43:125-33.
4. Ding DC, Chu TY, Hsu YH. Remission of anti-epiligrin cicatricial pemphigoid after excision of cervical adenocarcinoma. J Cutan Pathol. 2014;41:692-3.
5. Taylor J, McMillan R, Shephard M. World workshop on oral medicine VI: A systematic review of the treatment of mucous membrane pemphigoid. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;120:161-71.

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Our Dermatology Online

Case Letter

Cultural and aesthetic considerations in patients with skin of color

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Sir,

Culture is influenced by the prevalent art, customs, religion and social institutions in an environment. As the population continues to evolve, the world is becoming more multicultural and, vice versa, cultures are becoming more multiethnic. By the year 2050, approximately 50 percent of the US population will be people with skin of color, demonstrating the importance of cultural sensitivity and awareness on the lives of our patients [1].

Religion is a significant component of cultural practice. For example, Muslim women who wear headscarves require a private establishment for their haircuts. These establishments are far and few in Western countries, and most Muslim women therefore develop expertise in cutting and styling their hair at home. As hair stylists are often the scouts for abnormal hair loss and complications of daily styling, such as traction alopecia, early stages could therefore be missed resulting in late presentation to a dermatologist and subsequently, irreversible scarring. The same applies to men wearing turbans.

In patients of African descent, certain hairstyles such as braiding and cornrows are practiced from childhood. Caregivers experience unnecessary judgement if their child's hair is deemed 'messy', resulting in braids often being done too tight. With these repeated insults, patients are predisposed to traction alopecia and possibly central centrifugal cicatricial alopecia (CCCA) [2]. Alternatively, chemical relaxers have been found to be associated with the development of uterine cancer in the postmenopausal population [3].

East Asians have a more prevalent culture of wearing sun-protective clothing compared to Asian Americans [4]. This leads to implications in research as studies examining skin cancer in East Asia may not reflect the lifestyles and risk of Asian Americans, thus underestimating the frequency in the latter. Regarding sunscreen and many cosmetic therapies, Hispanics/Latinx represent the "heaviest buyers" in skincare yet many feel underrepresented in the media [5]. Additionally, there is room for growth in the formulation of sunscreens for patients with skin of color as the absence of a residue, low price and suitable SPF and broad spectrum coverage are important factors for patients [6].

It is always an important reminder to keep an open mind and ask a patient to identify their most important concern. A woman wearing a Niqab may have multiple cosmetic concerns but her most important may be the lifting of the brows, the presence of tear troughs, or the health of the hands and nails, as these are the areas seen by most of the people that she interacts with. The psychosocial impact and stigmatization of skin conditions in different communities is also important to remember. While the scientific research and cultural awareness towards vitiligo is increasing, in South Asian communities, it is still unfortunately associated with significant ostracization. The role of psychodermatology should therefore be addressed in these consultations with a low threshold for psychiatric referrals.

The structural competencies that influence the social determinants of health also need to be heeded. Factors such as transportation, housing instability, and the distribution of how skin diseases present in

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different skin types all affect the care that is provided to patients. For example, patients living in highly segregated communities were significantly associated with a higher odd of developing atopic dermatitis [7]. Different measures to address these inequities include redistribution of resources to directly and indirectly increase the accessibility of care to underserved populations. Direct measures include establishing clinics in underserved communities, and indirect measures include standardized skin of color training throughout residency programs.

In conclusion, cultural competence is increasingly mandated in the context of dermatology consultations and should be compounded by cultural humility to address the lifelong dynamism of identities and eliminate our own implicit biases.

Consent

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REFERENCES

1. Nijhawan RI, Jacob SE, Woolery-Lloyd H. Skin of color education in dermatology residency programs: does residency training reflect the changing demographics of the United States? J Am Acad Dermatol. 2008;59:615-8.
2. Lawson CN, Hollinger J, Sethi S, Rodney I, Sarkar R, Dlova N, et al. Updates in the understanding and treatments of skin & hair disorders in women of color. Int J Womens Dermatol. 2017;3:S21-S37.
3. Bertrand KA, Delp L, Coogan PF, Cozier YC, Lenzy YM, Rosenberg L, et al. Hair relaxer use and risk of uterine cancer in the Black Women's Health Study. Eviron Res. 2023:117228.
4. Bowers JM, Hamilton JG, Wu YP, Moyer A, Hay JL. Acculturation, sun tanning behavior, and tanning attitudes among asian college students in the northeastern USA. Int J Behav Med. 2022;29: 25-35.
5. Dow AA, Murphy MJ. Hispanic/Latinos and skincare: disparities in product development, marketing, and toxicity. J Drugs Dermatol. 2020;19:1258-60.
6. Song H, Beckles A, Salian P, Porter ML. Sunscreen recommendations for patients with skin of color in the popular press and in the dermatology clinic. Int J Womens Dermatol. 2021;7: 165-70.
7. Williams J, Amerson EH, Chang AY. How dermatologists can address the structural and social determinants of health—from awareness to action. JAMA Dermatol. 2022;158:351-2.

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Case Letter

Leprosy in Morocco: A disease not to be forgotten in the twenty-first century

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Sir,

Leprosy, also known as Hansen's disease, is a chronic granulomatous disease caused by infection by *Mycobacterium leprae*. It affects the skin, peripheral nerves, mucosa of the upper airways, and other tissues. The disease shows polar clinical forms depending on the patient's immune response, as well as other intermediate forms [1]. The diagnosis, based on clinical suspicion, is confirmed by bacteriological and histopathological analyses. The WHO has decided to interrupt the transmission of leprosy globally by 2020. Leprosy is highly rare in Morocco, yet some cases are reported [2].

Herein, we report a case of borderline lepromatous leprosy revealed by a maculopapular rash and successfully treated with multidrug therapy.

A 71-year-old female patient was referred to our department for the etiological assessment of a chronic maculopapular dermatosis evolving since 2017, located on the back and limbs. She had no medical history.

The patient reported sensitivity disorders of the extremities, such as paresthesia with gloves and socks without associated motor disorders.

A clinical examination revealed infiltrated, reddish-brown plaques (Figs. 1a and 1b), without hypoesthesia or anhidrosis. A mucosal examination was normal. The general condition was preserved. The examination showed no adenopathy. A neurological examination revealed no peripheral nerve hypertrophy. An ophthalmologic examination was without abnormalities.

The skin histology of a papule revealed a dermal inflammatory infiltrate of lymphocytes and histiocytes with clear perivascular and adnexal cytoplasm. On Ziehl–Neelsen staining, multiple acid-fast bacilli clustered together, suggestive of Hansen's bacillus, were observed. Bacteriological sampling of the ear lobule was positive, with a bacteriological index of 4 crosses.

As the patient had multibacillary leprosy, the treatment regimen recommended by the WHO in countries with high leprosy endemicity such as Morocco was administered based on a triple therapy, including dapsone, clofazimine, and rifampicin.

Clinical and bacteriological improvement was obtained after six months of treatment (Figs. 2a and 2b).

Active screening of the patient's close contacts was performed.

Leprosy, or Hansen's disease, is a chronic infection with cutaneous and nervous tropism caused by *Mycobacterium leprae*. Although it remains a major public health problem in some countries, it is rare in Morocco and occurs in the rural and remote areas of the north. Clinical expression depends on the quality of the patient's immune response to *M. leprae*. It is polymorphic and represents a continuum in which two extreme forms are tuberculoid leprosy and lepromatous leprosy. Tuberculoid leprosy develops when the patient's immunity is relatively strong and is characterized by a low number of lesions and by the histological presence of a lympho-epithelioid granuloma with a low number of Hansen's bacilli. In contrast, lepromatous leprosy is marked by low immunity, hence the richness of the clinical-bacteriological picture. In this case, the

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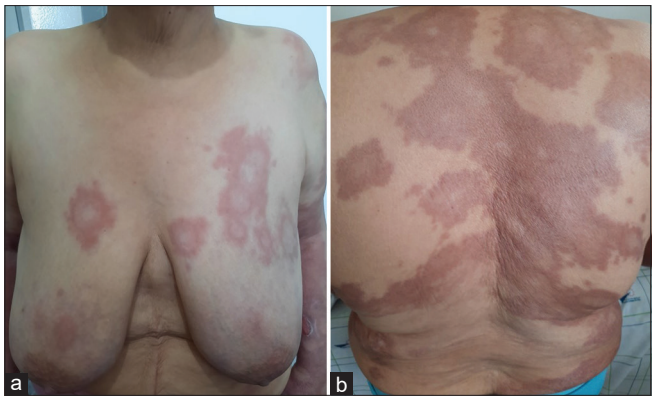

Figure 1: (a-b) Multiple, infiltrated, reddish-brown plaques.

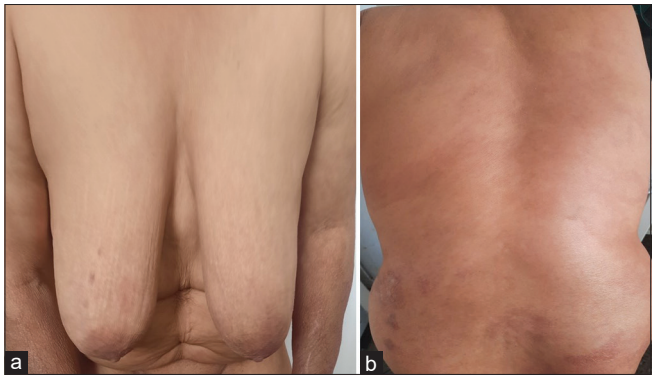

Figure 2: (a-b) Clinical improvement after six months of treatment.

cutaneous lesions are numerous, small, and not hypoesthetic [3-5].

According to the WHO classification, our patient had multibacillary leprosy as it had more than five symmetrical, poorly limited, confluent skin lesions on the trunk. In the Ridley and Jopling classification, the patient was classified, according to the clinical, bacteriological, and histological criteria, as falling between the polar lepromatous form (LL) and the borderline lepromatous form (BL) [3-6].

The treatment of leprosy has been based on polychemotherapy (rifampicin, dapsone, clofazimine) since the recommendations of the WHO in 1981. The combination and duration of treatment vary depending on the form of leprosy [5-7].

In spite of the progress made at the national level in the fight against leprosy, leprosy is still far from having disappeared. This observation confirms the necessity, in a patient originating from a leprosy endemic country, to evoke the diagnosis of leprosy in front of any unexplained atypical cutaneous lesions associated or not with sensorimotor disorders.

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. Ridley DS, Jopling WH. Classification of leprosy according to immunity: A five group system. Int J Lepr Other Mycobact Dis. 1966;34:255-73.
2. WHO. Global leprosy update, 2018: Moving towards a leprosy-free world. Wkly Epidemiol Rec 2019;94:389–412 https://www.who.int/publications-detail-redirect/who-wer9435-36/. accessed 15 April 2021.
3. Gupta R, Kar HK, Bharadwaj M. 2012. Revalidation of various clinical criteria for the classification of leprosy: A clinic-pathological study. Lepr Rev 83:354-62.
4. Singh A, Weng X, Nath I. Skin biopsy in leprosy. In: Khopkar U, ed. Skin Biopsy- Perspectives. London: IntechOpen; 2011:74-86.
5. Moschella SL. An update on the diagnosis and the treatment of leprosy. J Am Acad Dermatol 2004;51:417-26.
6. World Health Organization. 2013. WHO multidrug therapy (MDT). World Health Organization, Geneva, Switzerland. http://www.who.int/lep/mdt/en
7. De Carsalade G, Wallach D, Spinler E, Pennec J, Cottenot F, Flageul B. Daily multidrug therapy for leprosy: Results of a fourteen-year experience. Int J Lepr Other Mycobact Dis. 1997;65:37-44.

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Our Dermatology Online

Case Letter

Unusual presentation of a rare skin tumor: Glomangioma

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Sir,

Glomus tumor is a benign neuromyoarterial tumor of mesenchymal origin that arises from glomus bodies [1]. It may be of two types: glomangioma and glomangiomyoma depending on the amount of glomus cells, blood vessels, and smooth muscles in the tumor. In 1935, Bailey first described the term *glomangioma* as those glomus tumors that had wide vascular lumen. On the other hand, the term *glomangiomyoma* was coined for those tumors in which spindle shaped smooth muscle cells were seen with typical glomus cells [2]. Glomangioma is a rare, slow-growing benign tumor of the dermis or subcutaneous tissue occurring most commonly in the distal phalanx. The extradigital location of the tumor has rarely been reported.

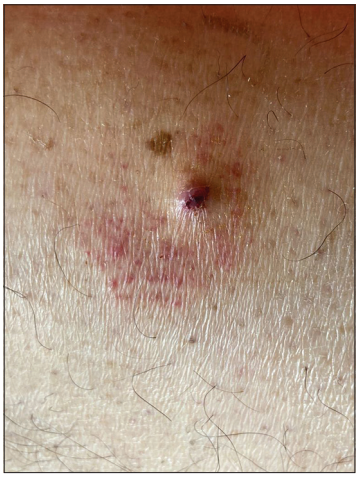

Figure 1: Single well-defined, hyperpigmented to erythematous papule on the lateral aspect of the upper one-third of the right leg.

A 64-year-old female presented to the dermatology department on an outpatient basis with a six-year history of a painful, raised lesion on the right leg, which was gradually progressive, not associated with itching or any fluid discharge and had no preceding history of trauma. There was a history of an increase in pain from the lesion on exposure to cold temperature. She had done various home remedies yet never consulted for the same. On examination, a single well-defined, hyperpigmented to erythematous, firm, tender papule measuring nearly 0.5 cm in diameter with surrounding erythema was noted on the lateral aspect of the upper one-third of the right leg (Fig. 1). Routine investigations were within normal limits. An excision biopsy was done to exclude the differentials of painful skin tumors such as dermatofibroma, pyogenic granuloma, neurilemmoma, neuroma, and angiolipoma. The histopathology report demonstrated a non-epithelial neoplasm in the deep dermis made of irregular vascular channels showing monomorphous, rounded cells with abundant pink cytoplasm and oval nuclei in the vessel walls and was consistent with glomangioma (Figs. 2a and 2b). MRI of the leg was conducted and demonstrated a soft tissue mass extending deeper into the extra muscular layer. The patient was then referred to the surgery department for further management.

The incidence of glomus tumors is 1–5% of all soft tissue tumors of the upper extremities, occurring mostly in the nail bed [1]. The various unusual sites reported in the literature to date have been the ankle, foot, knee, thigh, and hip [3]. Histopathology of the tumor shows a variable number of glomus cells, blood vessels, and smooth muscles, depending on which they are classified as glomangioma or glomangiomyoma [4]. Although the previous concept of this classification was widely accepted, subsequent ultrastructural analysis and

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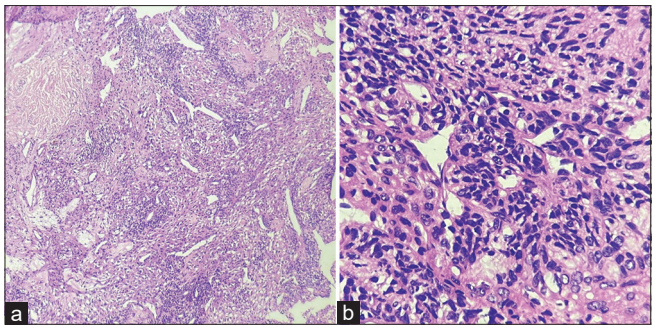

Figure 2: (a) Irregular vascular channels and monomorphous, rounded cells with abundant pink cytoplasm and oval nuclei (H&E; 10x). (b) Non-epithelial neoplasm in the deep dermis made of irregular vascular channels showing monomorphous, rounded cells with abundant pink cytoplasm and oval nuclei in the vessel walls (H&E; 40x).

Masson's theory on glomus tumors have disproved this categorization of glomus tumors, according to which both glomangioma and glomangiomyoma have only minor quantitative differences [5]. Nonetheless, these terms are still being used as separate entities. A solitary glomus tumor classically presents with the triad of pain, cold sensitivity, and point tenderness [6], and is, therefore, a differential of painful skin tumors [7].

The true incidence of glomus tumors could be higher due to misdiagnosis. Therefore, it is imperative to consider this differential whenever such a patient presents to the OPD to prevent mismanagement. As a dictum, any painful papulo-nodular lesion presenting with a long-standing history, not regressing spontaneously, rather progressively increasing, in size should be considered as a differential for painful skin tumors and subjected to a biopsy.

Consent

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REFERENCES

1. Rao G, Indira D, Kamal J. Extra digital glomangioma. Indian J Dermatol. 2010;55:397.
2. Chalise S, Jha A, Neupane PR. Glomangiomyoma of uncertain malignant potential in the urinary bladder: A case report. JNMA J Nepal Med Assoc. 2021;59:719-22.
3. Kumar T, Jamal I, Nigam JS, Pandey JK. Malignant glomus tumor of the index finger. Autops Case Rep. 2020;10:e2020184.
4. Mravic M, LaChaud G, Nguyen A, Scott MA, Dry SM, James AW. Clinical and histopathological diagnosis of glomus tumor: An institutional experience of 138 cases. Int J Surg Pathol. 2015;23:181-8.
5. Senhaji G, Gallouj S, El Jouari O, Lamouaffaq A, Rimani M, Mernissi FZ. Rare tumor in unusual location–glomus tumor of the finger pulp (clinical and dermoscopic features): A case report. J Med Case Rep. 2018;12:1-5.
6. Tang CY, Tipoe T, Fung B. Where is the lesion? Glomus tumours of the hand. Arch Plast Surg. 2013;40:492-5.
7. Cohen PR, Erickson CP, Calame A. Painful tumors of the skin: "Calm hog fled pen and gets back." Clin Cosmet Investig Dermatol. 2019;12:123-32.

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Our Dermatology Online

Case Letter

Cutaneous leishmaniasis of the neckline mimicking squamous cell carcinoma

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Sir,

Cutaneous leishmaniasis is a parasitic infection with cutaneous tropism linked to the inoculation of leishmaniasis transmitted by sandfly bites [1]. It is characterized by its ability to clinically simulate other pathological entities [2,3]. This highlights the need for a good dermoscopic analysis and extensive exploration to avoid diagnostic errors. Herein, we report the case of a patient presenting with an ulcerated, crusted lesion of the trunk revealing cutaneous leishmaniasis and mimicking squamous cell carcinoma [4,5].

A 29-year-old female patient from an endemic region to Leishmania tropical, followed in our training for neurofibromatosis type 1, presented for two years before her admission with localized pruritus on the trunk with the self-medication of a topical corticosteroid. The evolution was marked by the later appearance of an ulceration of centrifugal evolution in the trunk with a notion of spontaneous healing then recurrence without other associated signs. A dermatological examination revealed a patch of scarring in places and erosive in others at the level of the slightly sclerotic trunk, poorly limited, irregular contours, infiltrated border with a budding bottom topped and an adherent crust (Fig. 1a). A dermoscopic examination found ulcerations, scabs, a yellow teardrop appearance, linear and point vessels, and an erythematous background. The rest of the somatic examination was normal (Fig. 1b).

The skin smear and the anatomopathological examination found some amastigote forms of Leishmania. PCR was positive. HIV serology was negative, the search for visceral leishmaniasis doesn't find abnormality The diagnosis of cutaneous leishmaniasis was retained.

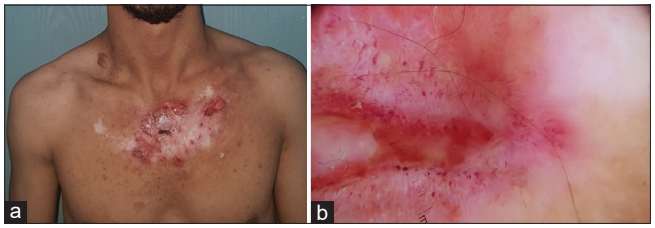

Figure 1: Trunk cutaneous leishmaniasis before treatment (a) Clinical image showing sclerotic and ulcerated plaque (b) dermoscopy showing ulcerations, yellow teardrop appearance Starry white appearance and linear vessels.

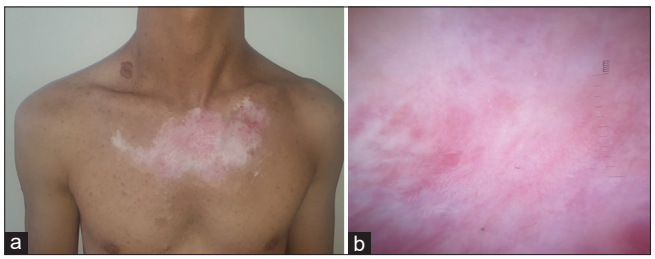

Figure 2: (a) Clinical image and (b) dermoscopy showing complete disappearance of the lesions after six weeks of treatment.

A pre-therapeutic assessment (NFS, renal, hepatic and cardiac assessment) was performed before putting the patient on systemic glucantime at a dose of 70 mg/kg/day associated with sessions of dynamic phototherapy with methylene blue. A clear regression marked by the subsidence of the lesions was obtained after treatment for six weeks (Figs. 2a and 2b).

Consent

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

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REFERENCES

1. Mokni M. Cutaneous leishmaniasis. Ann Dermatol Venereol. 2019;146:232-46.
2. Mancy A, Awad KM, Abd-Al-Majeed T, Jameel NF. The epidemiology of cutaneous leishmaniasis in Al-Ramadi, Iraq. Our Dermatol Online. 2022;13:402-7.
3. Paudel V, Parajuli S, Chudal D. Cutaneous leishmaniasis in Nepal: An emerging public health concern. Our Dermatol Online. 2020;11:76-8.
4. Wollina U, Koch A, Bitel A. Deep chronic cutaneous New World leishmaniasis due to Leishmania guyanensis and trichinellosis in a German returnee from Ecuador. Our Dermatol Online. 2019;10:272-4.
5. Mehmet S Gl, Burak T, Soner U. Cutaneous leishmaniasis: A great imitator. Clin Dermatol. 2020;38:140-51.

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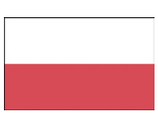





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