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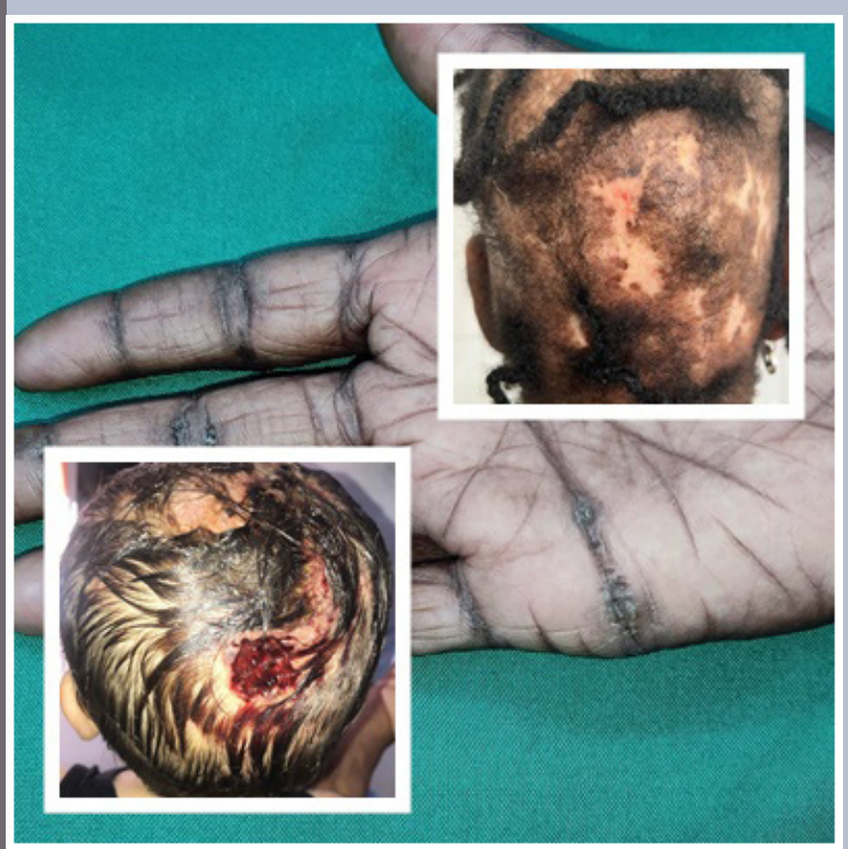

- A clinical study of striae emphasizing co-morbidities;

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- The role of phytotherapy in the management of dermatological conditions: The case of the northern region in Morocco;

- Hidden behind the mask: An observational study of mask-induced acne during the COVID-19 pandemic in south India;

- Characteristics of lupus erythematosus in dermatology: Analysis of a series of 72 hospital cases in Abidjan, Côte d'Ivoire;

- Severe cutaneous adverse drug reactions: A search for the culprit in a retrospective study of 107 patients;

- Beyond the skin: Unraveling the connection between atopic dermatitis and obsessive-compulsive disorder;

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Editorial Pages

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Original Article

A clinical study of striae emphasizing co-morbidities

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ABSTRACT

Background: Striae are a disfiguring cutaneous condition characterized by linear smooth bands of atrophic-appearing skin that occur in areas of dermal damage produced by stretching. They occur about twice as frequently in women as in men. They commonly occur during pregnancy, puberty, and obesity. **Aims of the Study:** The aim was to study the clinical profile and co-morbidities associated with striae and to study the correlation between striae and obesity with grading of obesity based on BMI. **Methods:** A complete evaluation of 107 patients with striae attending the Department of Dermatology of Rajarajeswari Medical College and Hospital was done over a period of one year. The data was collected by history taking and clinical examination. **Results:** This study comprised 107 patients, with a female preponderance. The majority of the patients (38.3%) belonged to the age group of 20–29 years. Striae alba was present in 66.4% of the patients. Striae because of pregnancy was present in 31.8%, followed by 22.4% who gave a history of steroid use. In adult female patients, the sites commonly involved were the abdomen (42.1%), thigh (30.8%), and breast (12.1%), whereas the thigh (50%) and buttocks (22.7%) were sites more commonly involved in adolescent female patients. In adult male patients, the sites commonly involved were the thigh (12.1%) and abdomen (8.4%), whereas in adolescent male patients, the sites most involved were the lower back (31.8%), thigh (9.1%), knee (9.1%), and buttocks (9.1%). Obesity was the major co-morbidity associated with striae, present in 39 (36.4.%) patients. Most of these obese patients belonged to obesity class I. **Conclusion:** Pregnancy is the most common cause of striae in females. Steroid abuse is the most common cause of developing striae in males in the present era, which is a multi-faceted problem that needs multi-dimensional interventions. Obesity is the major comorbidity associated with striae, followed by diabetes mellitus. In obese individuals, it is most often seen in obesity class I. Hence, a modification of lifestyle is the key to preventing obesity, which may, to a certain extent, prevent the development of striae.

Key words: Striae, Obesity, BMI, Co-morbidities

INTRODUCTION

Striae are a disfiguring cutaneous condition characterized by smooth, linear bands of atrophic-appearing skin that occur in areas of dermal damage produced by stretching [1].

Striae usually develop between 5 and 50 years of age. They occur about twice as frequently in women as in men [2]. They may have differing etiologies yet commonly occur during pregnancy, puberty, and obesity [3-5]. They occur in numerous other conditions such as connective tissue disorders, Cushing's syndrome, Marfan syndrome, hypercortisolism, diabetes, and long-term systemic or topical steroid use or exposure [6]. Although frequently encountered, the prevalence of striae distensae cited in the literature varies tremendously, ranging from 11% to 88% [7]. Anatomical sites affected vary widely, with the commonly affected areas being the abdomen, breast, thighs, and buttocks [3,4].

They rarely cause significant medical concern. However, they pose a psychological burden for the patients. Striae poses a considerable challenge to clinicians in terms of evaluation and treatment. A proper understanding of striae is essential for a rational approach. Hence, this study was undertaken to study the clinical profile and co-morbidities associated with striae and to study the correlation between striae and obesity with grading of obesity based on BMI.

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METHODS

Ethical clearance was taken from the institutional ethical committee. In the present study, we included 107 patients with striae, attending as outpatients and admitted as inpatients at the Department of Dermatology, Rajarajeswari Medical College and Hospital, over a period of one year. Patients of both sexes and all age groups with striae were included in the study. Pregnant female patients were excluded. Post-pregnancy patients were included after 6 months post-partum.

Consent was taken from the patient or from the parent or guardian (in case of a minor patient). A detailed history, including information on the patient's demographics, clinical presentation, along with a history of associated medical and surgical condition were obtained. We classified the patients based on the number of sites involved as localized and multiple site involvement.

Localized: patients who had a single site involved bilaterally.

Multiple: when two or more sites were involved bilaterally.

A diagnosis of striae was made based on clinical presentation, histopathology, and exclusion of other diseases that may have a similar presentation. BMI was calculated for every patient taking the patient's weight and height into consideration. Every patient was categorized based on the international classification of adult underweight, overweight, and obesity according to BMI (Adapted from WHO 1995, WHO 2000, and WHO 2004) (Table 1).

Investigations such as complete hemogram, fasting and post-prandial blood sugar levels, lipid profile, liver function test, renal function test, thyroid profile, ultrasonogram, serum cortisol, serum adrenocorticotropic hormone, luteinizing hormone, follicle-stimulating hormone, total and free testosterone, prolactin, dehydroepiandrosterone sulfate, chest X-ray, magnetic resonance imaging, electrocardiogram, and echocardiogram were done where required to exclude other comorbidities. Skin biopsy for histopathology was done if required. The results of the investigations were documented.

Statistical Analysis

A descriptive study of the patients with striae was performed. The collected data was analyzed with IBM SPSS Statistics, version 23.0. To describe the data, descriptive statistics, frequency analysis, and percentage analysis were used and depicted in the form of graphs and pie charts wherever necessary.

Table 1: Classification of obesity

Classification	BMI (kg/m²)	
	Principal cut-off points	Additional cut-off points
Underweight	< 18.50	< 18.50
Severe thinness	< 16.00	< 16.00
Moderate thinness	16.00–16.99	16.00–16.99
Mild thinness	17.00–18.49	17.00–18.49
Normal range	18.50–24.99	18.50–22.99
		23.00–24.99
Overweight	>= 25.00	>= 25.00
Pre-obese	25.00–29.99	25.00–27.49
		27.50–29.99
Obese	>= 30.00	>= 30.00
Obese class I	30.00–34.99	30.00–32.49
		32.50–34.99
Obese class II	35.00–39.99	35.00–37.49
		37.50–39.99
Obese class III	>= 40.00	>= 40.00

RESULTS

A total of 107 patients were examined during the period of the study. There were 71 female and 36 male patients. The female-to-male ratio was 2:1. The peak period of age at presentation was between 20 and 29 years, constituting 38.3% of all patients. In our study, 20.6% of the patients belonged to the adolescent age group (10–19 years), among which 15 were female, and the remaining were male, with a female-to-male ratio of 2.1:1. The average age of the adolescent females in our study was 14.7 years, whereas in the adolescent males, it was 15.8 years.

In our study, the majority of the patients presented with striae alba (66.4%), 27.1% with striae rubra, and 4.7% with hyperpigmented striae. One patient had both striae alba and striae rubra, and one patient had purple striae (Fig. 1). Among the adolescent patients, the majority (68.2%) presented with striae alba.

Post-pregnancy striae were seen in 31.8%, 22.4% developed it following steroid abuse, 19.6% because of weight gain, 11.2% due to exercise, 5.6% due to pubertal growth spurt, 4.7% due to both exercise and steroids, and 4.7% because of weight loss. Striae following pregnancy was the most common cause among female patients present in 47.9 % whereas steroid abuse was the main cause of developing striae in male patients present in 41.7% (Fig. 2). Among patients with striae

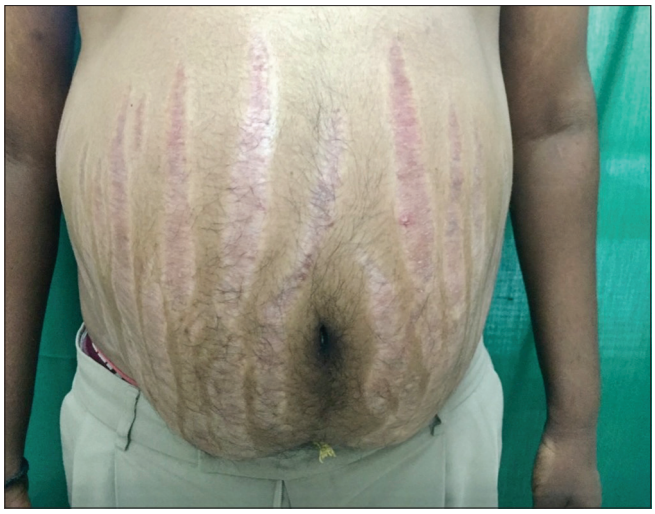

Figure 1: Purple striae involving the abdomen in iatrogenic Cushing syndrome.

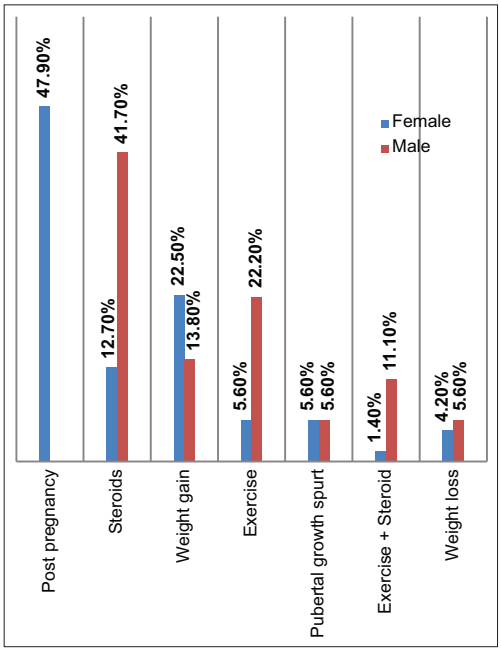

Figure 2: Sex distribution of striae vs. their etiology.

due to steroid abuse, topical steroid was abused by 18.7% of all patients for a duration of three months to two years. The causes for topical steroid abuse were fungal infections, intertrigo, and pruritus. Among these patients, the most common site of development of striae was the medial aspect of the thigh, followed by the axilla (Figs. 3a and 3b).

Localized striae were seen in 36.4% of the patients, among which 13.1% was due to topical steroid abuse (Table 2), whereas multiple sites were involved in 63.6% of the patients (Fig. 4). The thigh (50%) and buttocks (22.7%) were sites more commonly involved

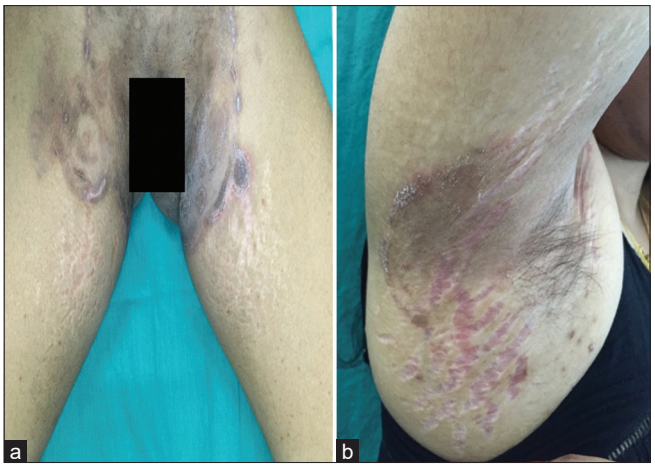

Figure 3: (a and b) Medial aspect of the thigh and axilla, sites commonly involved following topical steroid abuse.

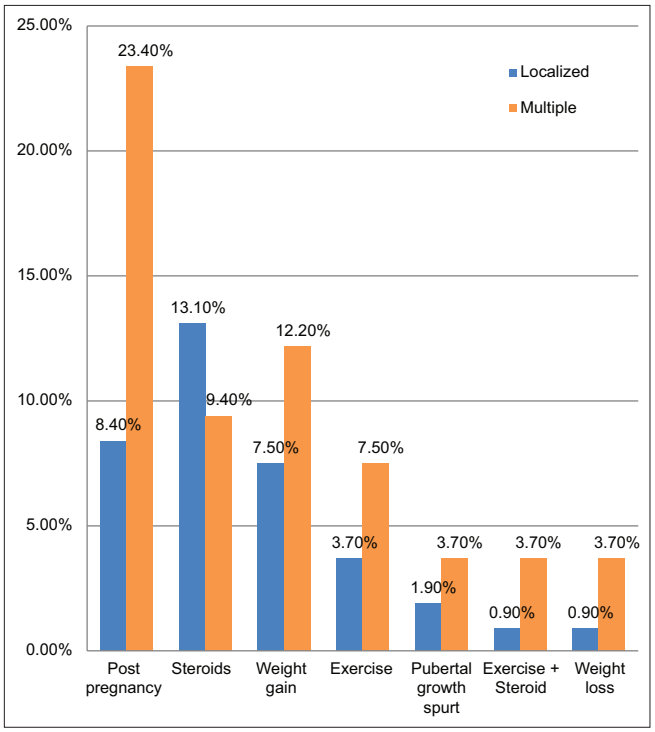

Figure 4: Distribution of the number of sites involved vs. etiology.

Table 2: Distribution of the number of sites involved based on the formulation of the steroid

Etiology (Steroid)	Number of sites	
	Localized	Multiple (2/>2)
Topical steroid	14 (13.1%)	6 (5.6%)
Systemic steroid	0 (0.0%)	4 (3.7%)
Total	14 (13.1%)	10 (9.3%)

in adolescent female patients. In adolescent male patients, the sites most often involved were the lower back (31.8%), thigh (9.1%), knee (9.1%), and buttocks (9.1%). Sites commonly involved in adult female patients were the abdomen (42.1%), followed by the

thigh (30.8%) and breast (12.1%), whereas in adult male patients, sites more commonly involved were the thigh (12.1%) and abdomen (8.4%). The abdomen was the most common site, involved in 33 (97.1%) patients who developed post-pregnancy striae, followed by the thigh (52.9%) and breast (35.3%).

In our study, obesity was the main comorbidity associated with striae, present in 39 (36.4%) patients (Fig. 5), among which 13 obese patients belonged to the age group 30–39 years. Most of these obese individuals belonged to obesity class I, accounting for 20.6% of the patients (Fig. 6). Other co-morbidities associated with striae were diabetes mellitus (8.4%), hypertension (5.6%), polycystic ovarian syndrome (5.6%), both diabetes mellitus and hypertension (1.9%), iatrogenic Cushing syndrome (0.9%), and pituitary microadenoma (0.9%).

Other comorbidities present in patients with obesity were diabetes mellitus, present in six obese patients, followed by PCOS, present in five obese patients (Fig. 7).

DISCUSSION

Striae is a connective tissue disorder due to cutaneous atrophy affecting a good proportion of the global population. Although it is not usually an impairing medical problem, it causes psychological distress, hence affects the quality of life. Most of the patients in our study were female, with a female-to-male ratio of 2:1. Among adolescent patients (10–19 years), the female-to-male ratio was 2.1:1. This was in accordance with a study by Sisson [4], who found that, in adolescent children, striae occur in girls about 2.5 times more frequently than in boys. The average age of the adolescent females was 14.7 years, whereas in the adolescent males, it was 15.8 years. This was in concordance with Al-Himdani et al. [7], who stated that the average age of the adolescent females developing striae was 13–14 years whereas that of adolescent males was 14 years. Striae alba was present in 68.2% of adolescent patients. This was similar to a study by Cho et al. [3], in which, out of 131 adolescent subjects with striae, 69.5% had striae that were white in color.

Pregnancy was the cause attributed by 31.8% of the patients who developed striae. Steroid abuse by 22.4% of the patients was the second major cause for developing striae, and in male patients, it was seen in

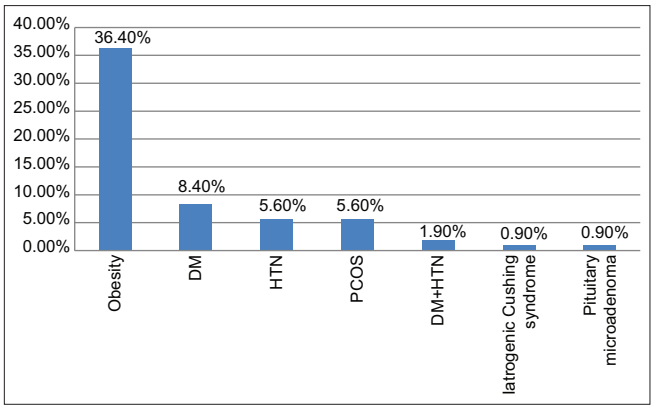

Figure 5: Comorbidities associated with striae.

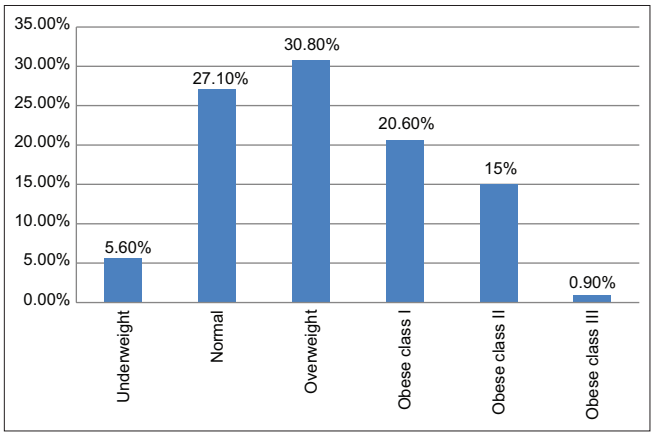

Figure 6: Distribution of striae vs. BMI.

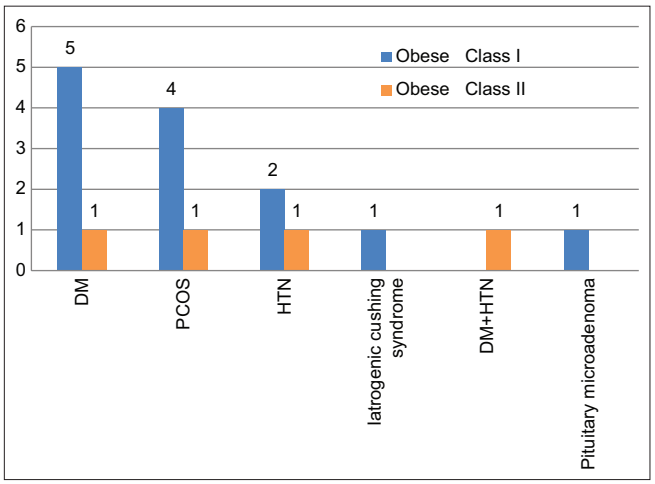

Figure 7: Comorbidities associated with obesity.

41.7%. Twenty patients gave a history of using topical steroids for a duration varying between three months to two years. Pavithran [8] showed the development of pinkish atrophic striae at the sites of prolonged application of topical corticosteroid in two male and one female patient. The duration of application in the three cases was 4, 22, and 18 months, which was

concordant with our study. A study by Nnoruka and Okoye [9] on topical steroid abuse as a depigmenting agent showed the presence of striae in 28.3% of cases because of steroid abuse. The median duration of use was nine years. Gupta [10] reported a case where a patient with vitiligo developed striae following the application of topical steroids for just 25 days. The main cause for steroid abuse may be attributed to their lack of information and severe withdrawal dermatitis that results from the withdrawal of the offending steroid, which makes discontinuation difficult for the patient.

The thigh (50%) and buttocks (22.7%) were the most common sites of striae development in adolescent female patients, whereas the lower back was the most common site involved, in 31.8% of the adolescent male patients, followed by the thigh, buttocks, and knee. In a study by Cho et al. [3], in adolescents of both sexes, the buttock was the most prevalent area of striae development, followed by the lower back and knee in boys and by the thigh and calf in girls. Striae were significantly more common on the thigh of girls and on the knee of boys. Al-Himdani et al. [7] stated that thighs, buttocks, and breasts are sites involved in adolescent females, whereas the thighs, buttocks, calves, and back are sites most often involved in adolescent males. These studies were concordant with our study. In our study, the sites most often involved in adult female patients were the abdomen (42.1%), thigh (30.8%), and breast (12.1%), whereas the thigh (12.1%), abdomen (8.4%), and axilla (7.5%) were the sites most often involved in adult male patients. The breast and thigh are sites commonly involved in adult females, whereas the buttocks is the site mostly involved in adult males, as stated by Al-Himdani et al. [7]. The difference in site involvement in adolescents and adults in either sex may be explained based on the difference in etiology. Striae during adolescence mainly occur because of rapid deposition of adipose tissue or muscular hypertrophy beneath the dermal layer [11], whereas as stated by Al Himdani et al. [7], striae in adult women occur mainly post-pregnancy and, in adult males, is a result of sudden weight gain/loss and muscular exercise.

The abdomen was the most common site involved (97.1%) in patients who attributed the development of striae to past pregnancy assessed not earlier than six months postpartum. This was followed by the thigh in 52.9% and the breast in 35.3%, which was in concordance with most previous studies [5,12]. Mechanical distention and rapidly developing obesity are associated mostly with striae formation during pregnancy. It is suggested that relaxin and estrogen, perhaps in combination with the raised cortisol levels of pregnancy, may cause the accumulation of mucopolysaccharides, increase the water absorption of connective tissue [13] and prime it for cleavage in the presence of mechanical stress [14]. The axilla and the medial aspect of the thigh were the most common sites involved following topical steroid abuse, which was similar to most previous studies [8,10,15]. The involvement of the axilla and groin may be explained by the fact that increased warmth, maceration, inflammation, and close approximation of the skin of the groin enhance penetration of corticosteroids because the physiological state of the skin at these sites is similar to that which results from occlusive therapy [8]. This, in turn, leads to systemic absorption of enough medication to produce a state of hyperadrenalism with subsequent striae formation as a sequela [15].

In the present study, obesity was the main co-morbidity associated with striae present in 39 (36.4%) patients. Among these, 13 obese patients belonged to the age group of 30–39 years at the time of presentation. Among all our patients, 20.6% had class I obesity (30–34.99). This contrasts with previous studies. A study by Divyashree et al. [16] in Karnataka on 100 patients with obesity showed a higher prevalence of striae among class II obesity patients (30.4%) with most of the obese patients with striae belonging to the age group 21–30 years. In another comparative study, done by Boza et al. [17], which included 76 cases (obese patients) and 73 controls, striae were the most prevalent dermatosis in obese patients (68.4%). The presence of striae was positively correlated with the increase in the degree of obesity. Most (83.3%) of grade III obesity patients had striae followed by grade II (70.4%) and grade I (52%). Other major comorbidities associated with striae that we came across in our study were diabetes mellitus present in nine (8.4%) patients, hypertension present in six (5.6%) patients, and both present in two (1.9%) patients.

Co-morbidities associated with obesity were diabetes mellitus present in six obese patients, hypertension present in three obese patients, and both diabetes mellitus and hypertension in one patient. Five patients had PCOS. Iatrogenic Cushing syndrome and pituitary microadenoma were present in one patient, each. This was consistent with a study by Divyashree et al. [16], in which associated diseases present in obese patients with striae were diabetes mellitus and hypertension.

To the best of our knowledge, there is a paucity of large-scales studies on patients with striae.

CONCLUSION

Pregnancy as a cause of striae is inevitable. However, the rising number of cases following steroid abuse is alarming. Steroid abuse is a multi-faceted problem and because of its easy over-the-counter availability and the immediate short-term relief for various dermatological conditions, it is more often abused than used. Hence, a multi-dimensional approach is required. Obesity is the major comorbidity associated with striae, followed by diabetes mellitus. Both, most often, point toward an unhealthy lifestyle, and a modification of the same may be a useful tool in avoidance of the development of striae.

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.

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Our Dermatology Online

Original Article

Topical use of olive oil to treat dermatological diseases: A systematic review

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ABSTRACT

Background: *Oleae europaea* (olive tree) and its derivatives have been used for centuries in traditional medicine for a variety of ailments, including skin conditions. This systematic review summarizes the current literature on the topical effects of *O. europaea* derivatives on skin. **Methods:** A comprehensive search of the PubMed database was conducted using 36 search terms. Studies were included if they met the inclusion and exclusion criteria and analyzed for their content. **Results:** 21 studies met the inclusion criteria. Most studies reported positive outcomes, indicating that *O. europaea* derivatives have a wide range of potential therapeutic uses for skin, including wound healing, dermatitis management, prevention and treatment of pressure ulcers and skin cancers, improvement of epidermal barrier function, relief from pruritus, and reduction of friction between the skin and personal protective equipment. **Discussion:** Several limitations were identified across the reviewed studies, including limited sample sizes in some cases, a lack of control groups in certain trials, and variability in the quality of evidence. Despite the limitations, this review provides evidence to support the use of *O. europaea* derivatives as a safe and effective treatment for a variety of skin conditions. **Conclusion:** O. europaea and its derivatives have the potential to improve the outcomes and experiences of numerous dermatological patients soon.

Key words: *Oleae europaea*, Topical treatments, Wound healing, Dermatitis management, Complementary and alternative medicine

INTRODUCTION

With over 600 species, *Oleacae* is a taxonomic family comprising over 30 genera of deciduous trees and shrubs and grow best in the tropical and temperate regions of Asia and Malaysia. *Olea europaea* is the most notable of the genus, popularly consumed across various regions and has been widely implicated in a number of traditional and contemporary ailments, including dermatological disorders [1-4].

While widely used for human consumption, *O. europaea* has been recognized for its therapeutic properties in traditional medicine and has been used to treat various ailments, most notably hypertension, diabetes, hypercholesterolemia, diarrhea, and respiratory and urinary tract infections. It has also been used as treatment for stomach and intestinal diseases, asthma, hemorrhoids, rheumatism, laxative, mouth cleanser, as a vasodilator, and to reduce inflammation [5].

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O. europaea extracts are primarily composed of phenolic compounds, represented by phenolic alcohols hydroxytyrosol, tyrosol, and secoiridoids, which include oleocanthal, oleacein, oleuropein, and ligstroside [3]. These compounds have been the focus of attraction for many scientists due to their antioxidant, anti-inflammatory, and anti-proliferative properties [3,6]. Oleuropein, the main component of olive oil and olive leaf extract, has been particularly studied because of a variety of reported health benefits including cardioprotective, anti-inflammatory, antioxidant, anti-cancer, anti-angiogenic, and neuroprotective function [7]. Oral gavage of olive oil has been shown to decrease inflammatory response and oxidative damage in pressure ulcers by accelerating ROS and NO synthesis *in vivo* [4]. Decreased aging has been found in mechanistic studies displaying increased autophagy activation in beta amyloid deposition rat models fed with oleuropein aglycon, a derivative of *O. europaea* [8]. The anti-aging and healing effects of *O. europaea* have prompted further insight to their potential in skincare.

O. europaea extracts have been used in contemporary medicine for prevention of dermatological ailments and promotion of skin health. Oleuropein extract has been shown to accelerate skin wound healing in aged male mice via increased collagen fiber deposition and reduce cell infiltration in wound sites [9]. Super virgin olive oil was found to significantly reduce the number of skin cancers when topically applied immediately after UVB radiation [2]. Uvaol, a natural pentacyclic triterpene widely found in olives and virgin olive oil, has also been found to stimulate endothelial cell growth and promote fibroblast function in vitro and in vivo [1].

There are currently various products on the market containing *O. europaea* derivatives, all containing marketing claims that may not be validated by current literature. According to INCI Decoder, there are over 100 olive containing products including skin creams, serums, and toners as of December 2022 currently on the market [10]. These products have been marketed under various claims including "skin rescuing" [11], "reparative" [12-14], "hydrating" [11-13], and "anti-aging" [11,12,15]. Companies describe it to "enhance collagen," "absorbs into skin quicker," "reduced trans-epidermal water loss" and provide "environmental protection" [14]. Current claims like this warrant further investigation to determine their validity.

Fortune Business Insights projects an economic increase in the skincare market, worth around 100.13 billion USD in 2021 to 145.82 billion USD by 2028 [16]. This sets the environment for further promotion of skincare products, many including *O. europaea* based products. With the extensive unsubstantiated claims in the current market, false advertising may be further promoted in the following years. We consolidated current literature on the topical effects of *O. europaea*-based products to determine the validity of their use in modern commercial skincare products.

In this paper, we gathered all current publications regarding the topical effects of derivatives and performed a systematic review on its cosmetic effects on the skin, including treatment of dermatologic diseases. We addressed both harmful and beneficial effects on the skin, and the limitations of each study to promote informed consumer decisions.

MATERIALS AND METHODS

Created using boolean operators, 36 possible search terms were used to search on Pubmed, as of July 4th, 2022 (Table 1). Literature from the search results is collected, and duplicates were removed. Inclusion criteria included clinical trials measuring the topical use of olive derivatives (including but not limited to oils, essential oils, extracts, pumices, oxidized) on the skin, hair, nails, and other dermatological features *in vivo*, including human only, published at any point in time, by itself or in combination with other variables. Exclusion criteria included trials without a control; trials that mainly focused on in vitro and ex vivo results; trials that mainly focused on histological parameters; trials that used olive oil as mainly a vehicle; reviews or any publications that do not present any original data; commentaries, editorials, and reviews that did not present any original data; and articles not written in English.

This method produced 439 unique papers. The abstracts were then reviewed to determine relevant papers, and irrelevant articles were taken out of the final line-up. As a result, 63 final papers fit the exclusion and inclusion criteria.

These publications were then read and parsed for their content, and how they fit their inclusion and exclusion criteria, leading to a final 21 papers. Different data points were collected from these publications, shown in Table 2.

Figure 1 shows a visual representation of the paper and data collection discussed here.

Table 1: List of search terms used for Pubmed search on July 4, 2022.

Skin* topical* olive	Derm* topical* olive	Cosmetic* topical* olive	Hair* topical* olive	Nail* topical* olive	Beaut* topical* olive
Skin* topical* "olea europaea"	Derm* topical* "olea europaea"	Cosmetic* topical* "olea europaea"	Hair* topical* "olea europaea"	Nail* topical* "olea europaea"	Beaut* topical* "olea europaea"
Skin* apply* olive	Derm* apply* olive	Cosmetic* apply* olive	Hair* apply* olive	Nail* apply* olive	Beaut* apply* olive
Skin* apply* "olea europaea"	Derm* apply* "olea europaea"	Cosmetic* apply* "olea europaea"	Hair* apply* "olea europaea"	Nail* apply* "olea europaea"	Beaut* apply* "olea europaea"
Skin* application olive	Derm* application olive	Cosmetic* application olive	Hair* application olive	Nail* application olive	Beaut* application olive
Skin* application "olea europaea"	Derm* application "olea europaea"	Cosmetic* application "olea europaea"	Hair* application "olea europaea"	Nail* application "olea europaea"	Beaut* application "olea europaea"

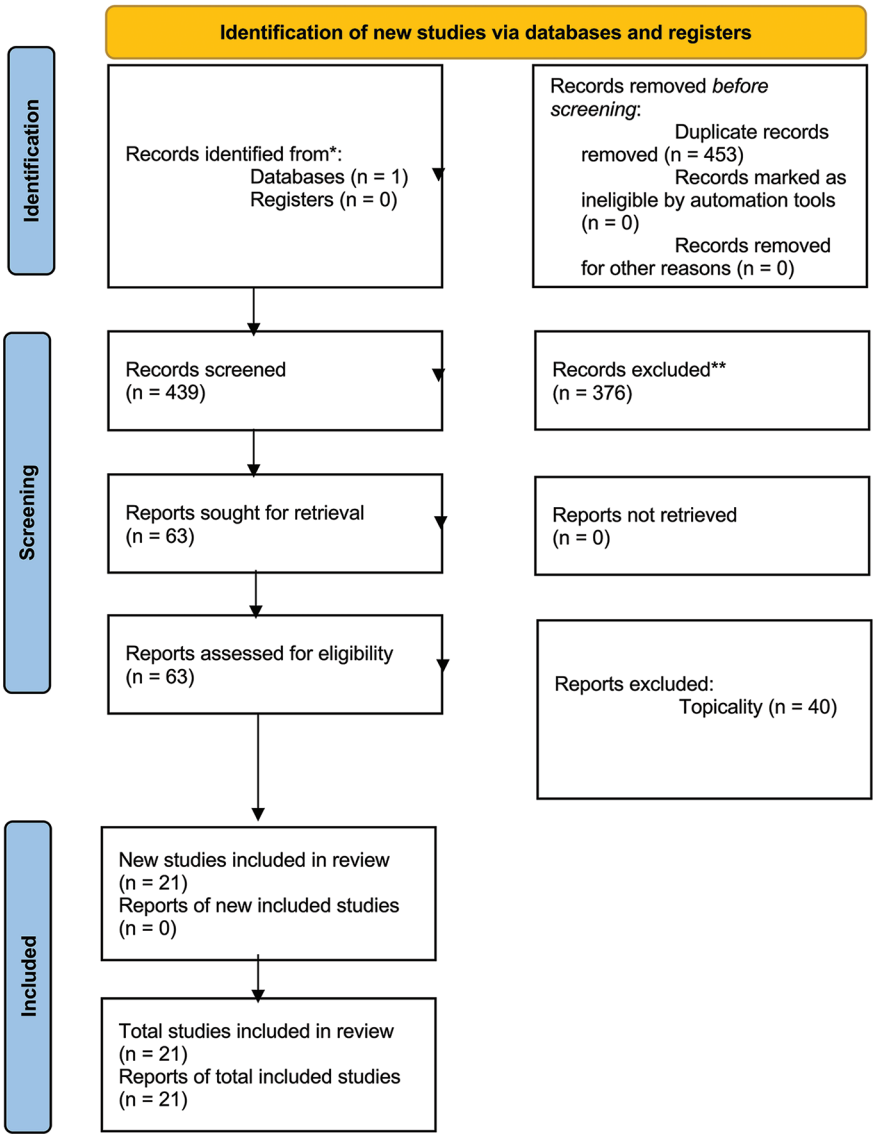

Figure 1: Flow Chart on the methods of literature search current to July 2022.

RESULTS

Types of Publications

A total of 21 papers were included in the literature review that fit the inclusion criteria. The study designs of these publications include multi-center, randomized, single, double, and triple-blind clinical trials, basic science experiments, animal trials, randomized controlled clinical trials, comparative studies, quasi-experimental pilot studies, and non-randomized clinical trials.

Table 2: Compiled and organized collected data from 21 papers resulted from the systematic review of literature from Pubmed.

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
Effectiveness and safety of olive oil preparation for topical use in pressure ulcer prevention: Multicentre, controlled, randomised, and double-blinded clinical trial [17]	Pressure Ulcer	Extra virgin olive oil solution	Hyperoxygenated fatty acids solution	283 in olive oil group, 288 in HOFA group	Non-inferiority. Multicentre, randomized, controlled, double-blind clinical trial.	Test agent was applied using atomizer spray	Olive oil as a preventative method for PU at-risk populations was found to be at least as effective as the use of HOFA. Pressure ulcer incidence was 4.18% in treated group vs 6.57% in the control group, with a -2.39% (95% CI = -6.40 to 1.56%) incidence difference, which is within the pre-established non-inferiority margin of ±7%.	No adverse effects	2019	30 days or until pressure ulcer onset	Humans	Yes	Yes
Effect of Olive Oil in Preventing the Development of Pressure Ulcer Grade One in Intensive Care Unit Patients [18]	Pressure Ulcer	Olive oil	Control (without olive oil)	36 in control, 36 in treatment group	randomized single-blind trial study	15 ml of olive oil was applied topically for 7 days, and ulcer healing status was assessed on the 1st, 4th and 7th day	The olive oil group had a smaller mean area of pressure ulcer than the control group and a decreased mean score of the pressure ulcer scale for healing (PUSH) tool. Olive PUSH score was lower (7.50 ± 2.823 and 5.44 ± 3.806) than the control's (9.50 ± 1.732 and 8.83 ± 2.864) (P-value <0.001)	None	2020	7 days	Humans	Yes	Yes
Effectiveness and Tolerability of Natural Herbal Formulations in the Prevention of Radiation-Induced Skin Toxicity in Patients Undergoing Radiotherapy [19]	Radiation Induced Dermatitis	Olive oil with beeswax, Calendula, Hypericum oil and Aloe gel.	None	59	Clinical trial	RDC was applied topically 2-3 times daily, RDO before bed, and RDSG one daily to cleanse the area.	The herbal formula was found to have statistically significant results in reducing the intensity of radiation dermatitis. At the end of the study, the majority (66.1%) of patients were at 0 to 1 DLQI scale, while using prophylactic herbal agents. It was statistically significant in reducing the intensity of radiation-induced skin toxicity up to 4 weeks postirradiation.	No adverse effects	2020	Not specified in abstract: Formula applied daily, regularly during radiotherapy, 2 weeks after treatment end (conducted toxicity tests 4 weeks after)	Humans	No	No

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
Olive Oil, Sunflower Oil or no Oil for Baby Dry Skin or Massage: A Pilot, Assessor-blinded, Randomized Controlled Trial (the Oil in Baby SkincaRE [OBSeRvE] Study) [20]	Atopic Dermatitis	Olive oil	No oil	30 in treatment, 30 in control group	Randomized controlled trial	4 drops applied to infant forearm, left thigh, and abdomen twice a day for 4 weeks	no significant differences for TEWL, significant improvements in hydration, significant improvement in lipid chain conformation after 4 weeks of treatment,	No adverse effects reported	2016	4 weeks	Human Neonates	Yes	Yes
Comparing the Therapeutic Effects of Aloe vera and Olive Oil Combination Cream versus Topical Betamethasone for Atopic Dermatitis: A Randomized Double-blind Clinical Trial [21]	Atopic dermatitis	Olivederma (combination of virgin olive oil and aloe vera)	Betamethasone	36	Randomized double-blind clinical trial	Topical application of Olivederma or betamethasone twice daily for 6 weeks	Olivederma is superior to topical Betamethasone after 6 weeks of therapy with regard to quality of life (Dermatology Life Quality Index (DLQI) questionnaire), eosinophil count, and disease severity (SCORAD), with statistical significance	Patients with adverse reactions to the medication were excluded.	2005	6 weeks	Humans	Yes	Yes
Comparison the effects of topical application of olive and calendula ointments on Children's diaper dermatitis: A triple-blind randomized clinical trial [22]	Diaper Dermatitis	Olive ointment	Calendula ointment	39 in calendula group, 37 in olive group	Triple-blind randomized clinical trial	Topical application of 1.5% olive ointment or 1.5% calendula ointment for 7 days	No statistically significant difference was found between the groups of olive ointment and calendula ointment in terms of the severity of diaper dermatitis on the days 0 (before the intervention) and 3, 5, and 7 days after the intervention.	No adverse effects reported	2018	7 days	Human (children)	Yes	Yes
Topical use of olive oil preparation to prevent radiodermatitis: results of a prospective study in nasopharyngeal	Acute radiodermatitis	Olive oil	None	47 in control group, 47 in treatment group	Random controlled double blind clinical trial	Topical treatment of olive oil thrice daily beginning on the first day of radiotherapy and continuing for 2 weeks after completion of radiotherapy.	Olive oil showed a statistically significant decrease in severity acute radiodermatitis in patients with nasopharyngeal carcinoma undergoing chemotherapy after	No adverse side effects reported.	2015	9 weeks	Human	Yes	Yes

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
carcinoma patients [23]							9 weeks. Use of olive oil significantly decrease skin injuries ($P < 0.01$).						
Effects of olive oil on striae gravidarum in the second trimester of pregnancy [24]	Striae Gravidarum	Olive oil	None used	35 in treated, 35 in control	Random controlled clinical trial	Test agents were applied topically twice daily	40% of women using olive oil developed striae whilst 50% of the control group developed striae. The use of olive oil did not show any statistically significant difference in the occurrence of SG when compared to controls.	No adverse effects	2010	8 Weeks	Humans	No	Yes
The effect of olive oil and the Saj® cream in prevention of striae gravidarum: A randomized controlled clinical trial [25]	Striae Gravidarum	Olive oil	No intervention	50 in control, 50 in the treated	Parallel randomized controlled clinical trial	Subjects were asked to apply the 1cm^3 oil twice daily on the skin of the abdomen without massage.	In the olive oil group, striae occurred in 72% of the participants, with 32% mild, 26% moderate, and 6% severe. For the control group, striae occurred in 60% of the participants, among which striae were 22% mild, 24% moderate, and 14% severe. Olive oil is not shown to be effective in preventing the occurrence of striae gravidarum or affect its severity.	No adverse effects reported	2014	22 Weeks	Humans	No	Yes
The effect of olive oil on prevention of striae gravidarum: a randomized controlled clinical trial [26]	Striae Gravidarum	Olive oil	Control group received no treatment	50 in the control, 50 in the treated	Randomized control clinical trial	Topical application of olive oil twice daily	Frequency of severe striae gravidarum lower in users of olive oil compared to control group, however it does not statistically significantly reduce the incidence and the severity of striae gravidarum	No side effects were reported in the study	2012	8 Months	Humans	No	Yes

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
Observer-blind randomized controlled study of a cosmetic blend of safflower, olive and other plant oils in the improvement of scar and striae appearance [27]	Scars and striae	Oils formulated with safflower and olive oils rich in omega-6 linoleic acid and omega-9 oleic acid (Bio Skin Oil®)	Untreated scar/ stretch mark region	80	Controlled randomized study	80 volunteers with non-hypertrophic scars (40) or stretch marks (40) that were not older than 3 years applied a cosmetic face and body oil for 8 weeks.	The application of the test agent led to a notable decrease in mean scores on the Observer Scar Assessment Scale (OSAS) by 5% ($P = 0.0006$) in the treated area, while no discernible changes were observed in the untreated region. Similarly, the Patient Scar Assessment Scale (PSAS) demonstrated a reduction of approximately 20% in scar appearance for the treated area and 6% for the untreated control area. The cumulative effect of the product was a significant overall reduction of 14% ($P = 0.0001$). The majority of volunteers attested to the beneficial effects of the test agent, with only 17% reporting no noticeable impact from the oil.	Side effects were not reported. 17% of subjects however considered that their scars/ stretch marks did not improve	2017	8 Weeks	Humans	No	Yes
Anti-Inflammatory and Tissue Regenerative Effects of Topical Treatment with Ozonated Olive Oil/Vitamin E Acetate in Balanitis Xerotica Obliterans [28]	Inflammation-Balanitis Xerotica Obliterans	Ozonated olive oil with vitamin E acetate	Control group received no treatment	30	Clinical study	Topical application of ozonated olive oil with vitamin E acetate (OZOILE) to foreskin tissue	A marked decrease in mRNA levels of IL-1β, TNF-α, INF–γ, transglutaminase 2, and NOS2 was observed in foreskins treated with OZOILE® compared to untreated samples ($p < 0.001$). Conversely, no significant variances were noted in NF-κB activation between treated and untreated specimens.	No adverse reactions reported	2018	7 Days	Male Children	No	No

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
							Consequently, treatment with OZOILE® resulted in an up-regulation of hypoxia-inducible factor (HIF)-1alpha, vascular endothelial growth factor (VEGF), and E-cadherin gene expression ($p < 0.001$).						
Topical treatment with oleocanthal extract in reducing inflammatory reactions after photodynamic therapy: a prospective quasi-experimental pilot study [29]	Inflammation - field cancerization	Phenolic oleocanthal extracted from extra virgin olive oil	emollient oily fluid base	24 treated, 23 control	Quasi-experimental pilot study	Topical application of oily fluid enriched with oleocanthal extract three times a day for a week on photodynamic therapy treated areas	After 48 hours post-treatment assessment, inflammation showed more pronounced improvement among patients treated with OC (median: 25%, 95% CI: -5.3 to 28.5) compared to those in the non-OC group (median: 0%; 95% CI: -45.2 to -6.2). This disparity was statistically significant ($p < 0.01$), with a Cohen's d value of 0.89, indicating a large effect size. Three months following PDT, a complete response was achieved by 60.9% of OC-treated patients versus 29.2% in the non-OC group, approaching statistical significance ($p = 0.059$).	No adverse effects reported	2018	3 Months	Humans	No	No
Blocking or enhancing effects of some basic emollients in UVA penetration [30]	minimal phototoxic dose -Psoralen UVA	Olive oil	None	29	Single blind vehicle-controlled study	Topical. 5 parallel rows of skin were tested after the application of different topical agents	Compared to pure PUVA, there is no significant increase or decrease in the values after application of olive oil ($P = 0.799$).	None stated	2018	72 hrs [Results were evaluated after 72 hrs by a binded investigator.]	Humans	Yes	No

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis [31]	Staphylococcus Aureus infected Atopic Dermatitis	Virgin olive oil (VOO)	Virgin coconut oil (VCO)	52	Double blind controlled trial	Two outpatient dermatology clinics with adult AD patients were randomized to apply VCO or VOO twice a day at two non-infected sites (52 subjects in all, 26 per oil). Topical application was done with 5 mL of whichever agent was given to the patients. They were instructed to massage the skin for a couple seconds when applying. Staphylococcus aureus (SA) cultures, photography, and objective SCORAD severity index (O-SSI) were done at baseline and after 4 weeks.	Of the 20 patients whose SA cultures were positive and were randomized so that they used VCO only 1 patient was still positive. Of 12 patients whose cultures were positive and were using VOO 6 patients were still positive. Relative risk of nontreatments for VCO was 0.10. Risk of nontreatment with VOO was 10 times that. Absolute risk was calculated and is -0.45. There was no significant difference at baseline between the O-SSI scores of the two treated arms. However, the difference between post-intervention scores between the 2 treatment arms was a significant value of p = 0.004.	No adverse side effects were reported.	2008	4 weeks	Humans	Yes	Yes
Effect of olive and sunflower seed oil on the adult skin barrier: implications for neonatal skin care [32]	Epidermal Barrier Function	Olive oil	Sunflower seed oil	19	Two randomized forearm -controlled mechanistic studies	First cohort- topically applied 6 drops of olive oil twice daily for 5 weeks Second cohort- applied six drops of olive oil to one forearm and six drops of s unflower seed oil to the other twice daily for 4 weeks	no significant difference in TEWL between the treated and untreated sites. Olive oil caused a significant reduction in stratum corneum (SC) thickness and integrity, Total SC thickness calculated based on Fick's first law show decreased thickness of the stratum corneum ($p<0.05$), determined using a paired t test. Induced mild erythema in volunteers with and without out a history of AD.	Mild erythema observed at the sites treated using olive oil in this study.	2012	4 weeks/ 5 weeks 2 cohorts had different lengths of study	Humans	No	Yes

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
The effect of daily treatment with an olive oil/lanolin emollient on skin integrity in preterm infants: a randomized controlled trial [33]	Emollient Potential	olive oil cream (70% lanolin, 30% olive oil)	water-in-oil emollient cream (Bepanthen)	173	Randomized controlled trial	Skin therapy was applied twice a day (10 g total/day) in the body, except for face and scalp, for a maximum of 4 weeks.	Infants receiving olive oil cream from day 4 to 28 exhibited significantly lower rates of dermatitis in comparison to those treated with emollient cream. Noticeable treatment benefits were observed as early as 1 to 2 weeks into the regimen, with the most pronounced effects evident during weeks 3 and 4. Olive oil cream demonstrated superiority over water-in-oil emollient cream in mitigating dermatitis.	No adverse effects reported	2008	4 Weeks	Human neonates	No	Yes
Application of Extra Virgin Olive Oil to Prevent Nipple Cracking in Lactating Women [34]	Nipple Fissures	Extra virgin olive oil	Breast milk	300	Randomized, experimental, prospective study	Topical application of extra virgin olive oil to the skin of the nipple	Patients showed significantimprovement in the occurrence of nipple cracking. Mothers treated with EVOO suffered much lower occurrence (2.7%) than untreated mothers (44%).	No adverse effects reported	2020	1 Month	Huamns	No	Yes
The safety and efficacy of a mixture of honey, olive oil, and beeswax for the management of hemorrhoids and anal fissure: a pilot study [35]	Anal Fissure/ Hemorrhoids	1:1:1 mixture of honey, olive oil, and beeswax	None	15	Comparative Study	Topical application of a spoon size of the mixture around the skin BID for 4 weeks (max)	Following treatment, patients with anal fissures experienced a notable decrease in pain, bleeding, and itching. Signs of healing, including the regression of posterior ulcers and epithelialization, were observed in all patients within four weeks of treatment initiation. Furthermore, erythema and edema, which were present in two patients initially, completely resolved within two weeks.	No adverse effects reported	2006	4 Weeks	Humans	No	No

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
Efficacy of Aloe vera/olive oil cream versus betamethasone cream for chronic skin lesions following sulfur mustard exposure: a randomized double-blind clinical trial [36]	Pruritis	Olive oil with aloe vera	Betamethasone 0.1%	67	Randomized double-blind clinical trial	Test agent was applied topically twice daily	Both treatments led to significant reductions in pruritus frequency ($p < 0.05$), burning sensation ($p < 0.01$ and $p < 0.001$ in the Aloe vera/olive oil and betamethasone groups, respectively), scaling ($p < 0.01$ and $p < 0.05$), and dry skin ($p < 0.001$) at the trial's conclusion. Fissures and excoriations were only diminished in the Aloe vera group ($p < 0.05$). However, changes in the frequency of hyper- and hypopigmentation lesions, blisters, erythema, and lichenification did not reach statistical significance in any group ($p > 0.05$). Mean pruritus ($p < 0.05$) and Visual Analog Scale (VAS) scores ($p < 0.01$ and $p < 0.05$) were significantly decreased by the trial's end in both groups. The rate of improvement in pruritus severity, defined as being classified in a less severe category (mild, moderate, and severe), was comparable between the groups ($p > 0.05$).	No adverse effects	2011	6 Weeks	Human	No	Yes
Wax-oil lubricants to reduce the shear between skin and PPE [37]	Friction Reduction	Olive oil	Neat light mineral oil	7	Basic Science/ Experiment	Topical lubricant	Combination beeswax-olive oil-mineral oil lubricant mixture significantly showed the greatest reduction in coefficient of friction both immediately	No adverse side effects reported	2021	4 Hours	Human	Yes	Yes

(Contd...)

Table 2: *(Continued).*

Article Title	Disease Type	Test Agent	Comparison Agent	N	Study Design	Treatment protocol	Results	Safety (N)*	Year	Study Duration	Species	Blinding	Randomized
							after application and 4 hours later compared to unlubricated skin. It comprises a blend of 20 wt% beeswax, 40 wt% olive oil, and 40 wt% mineral oil. Compared to unlubricated skin, this mixture yields a significant 87% reduction in instantaneous coefficient of friction (P = 0.0006) and a 59% reduction in 4-hour coefficient of friction (P = 0.0015).						

The maximum sample size was 571 patients using olive oil as a preventative method for pressure ulcers. All the studies, but one, reported no adverse effects; the one reported study found erythema at the sites treated using olive oil. Only one study found that the skin condition did not improve upon usage of olive oil (Table 2).

Ulcers, Including Pressure Ulcers and Skin Ulcers

One publication describes a randomized, multicenter, double-blind clinical trial that compared the efficacy of olive oil and hyperoxygenated fatty acids (HOFAs) for preventing pressure ulcers in at-risk populations, specifically among nursing home residents [17]. The trial lasted 30 days or until the onset of a pressure ulcer, and neither group received a vehicle-based placebo. The products were packaged identically by a pharmaceutical company and coded to conceal their identity. Of the 29 patients who developed PUs during follow-up, 18 were in the HOFA group, and 11 were in the olive group. The incidence of PUs was 6.7% in the HOFA group and 4.18% in the Olive group, with no adverse effects reported in the olive group and only one case of skin rash and itching reported in the HOFA group (Table 2).

Miraj et al. describe a randomized single-blind controlled trial that investigates the effect of the topical application of olive oil on preventing the development of pressure ulcer grade [18]. Seventy-two patients with stage one bedsores and no history of skin disease or allergy were divided into two groups: control and intervention (receiving olive oil). In the intervention group, olive oil was applied once daily for seven days to the wounded area, while in the control group, no intervention was made. The pressure ulcer scale for healing (PUSH) tool was used to assess ulcer healing status on the first, fourth, and seventh days. On the fourth and seventh days, the olive oil group showed a lower PUSH score and statistically significant improvement in ulcer healing status ($p < 0.001$) compared to the control group. No change was observed in the control group (Table 2).

Dermatitis, Including Radiation-Induced Dermatitis, Atopic Dermatitis, Contact Dermatitis, Psoriasiform Dermatitis, and Diaper Dermatitis

Koukourakis et al. describe a prospective open-label clinical trial evaluating the efficacy of a natural herbal formulation in preventing radiation-induced dermatitis in individuals undergoing radiation therapy of the head,

neck, or breast [19]. The formulation included a cream, ointment, and shower gel, all containing a combination of olive oil, beeswax, calendula and hypericum oils, and aloe gel. No placebo was used. Of the 59 subjects in the trial, 24 remained in grade 1 toxicity throughout the study, with a statistically significant prophylactic effect observed for breast and head/neck radiation therapy ($P<0.0001$ and $P=0.015$, respectively). Quality of life was also assessed through a survey, with 94.9% of subjects reporting no effect in week 1. This number was reduced to 66.1% by the end of the study, with 15.2% noting a small effect. The products scored well in relieving itching, burning, and irritation (Table 2).

Cooke et al. describe an assessor-blinded, randomized, controlled trial examining the effect of topical oils on infant skin in the development of atopic dermatitis [20]. One hundred and fifteen full-term neonates were randomly assigned to receive olive oil, sunflower oil, or no oil application twice a day for four weeks. No placebo group was used. Parents applied four drops of oil to the left arm, left thigh, and abdomen of their infant, while the control group received no application. Both oil groups showed statistically significant improvement in hydration, and lipid lamellae structure showed less improvement than the control group. No significant changes were observed in the scores of TEWL, pH, or erythema/skin. More research is required to recommend the use of oils on neonatal skin confidently (Table 2).

Panahi et al. describe a randomized, double-blind clinical trial comparing the efficacy of Olivederma, a combination of virgin olive oil and aloe vera, to betamethasone on quality of life, serum IgE levels, eosinophil count, and disease severity in patients with atopic dermatitis (AD) [21]. 36 patients with AD were treated for 6 weeks with either Olivederma or betamethasone, without the use of placebos. Both treatments resulted in a statistically significant decrease in AD severity, with Olivederma showing a greater improvement (64.5% vs. 13.5%, $p < 0.001$). AD patients treated with Olivederma also had a significant improvement in quality of life (60.7%, $p < 0.001$), compared to betamethasone (22.3%, $p < 0.001$). After 6 weeks, Olivederma led to a significant decrease in serum IgE and eosinophil count.

Sharifi-Heris et al. report a triple-blind randomized clinical trial investigating the impact of topically applied olive and calendula ointments on children with diaper dermatitis (DD) [22]. 73 healthy children under the age of 2 with non-infected and non-severe diaper dermatitis (DD) were assigned to receive either 1.5% olive ointment or 1.5% calendula ointment using a random block method with a 2:2 ratio over 7 days. No placebos were used. Results showed no statistically significant difference between the groups in any demographic or baseline characteristic and no statistically significant difference in the improvement of DD on days 0, 3, 5, and 7 of the intervention ($p > 0.05$) (Table 2).

Cui et al. describe a randomized, controlled, double-blind trial evaluating the efficacy of topical olive oil in preventing acute radiodermatitis in patients with nasopharyngeal carcinoma (NPC) undergoing concurrent chemoradiotherapy [23]. Forty-seven patients were divided into two groups: prophylactic and control. The prophylactic group received thrice-daily olive oil treatment for nine weeks, while the control group received a general skin care regimen and water as a placebo. Radiodermatitis severity was assessed using the graded scale from the Radiation Therapy Oncology Group (RTOG) and the Visual Analog Scale (VAS). Results showed that olive oil statistically significantly reduced dermatitis severity and skin injuries compared to placebo treatment ($p< 0.01$). Mild reactions to radiation were observed in 44/47 patients in the prophylactic group compared to 34 patients in the control group, while severe reactions were observed in 3/47 and 13/47 patients in those same groups, respectively. Improvement of symptoms upon radiotherapy termination was observed in 35/47 patients in the prophylactic group compared to 22/47 patients in the control group (Table 2).

Treating Striae gravidarum

Taavoni et al. describe a randomized controlled clinical trial conducted to evaluate the effectiveness of olive oil in reducing the occurrence of striae gravidarum (SG) during the second trimester of pregnancy [24]. Human subjects were divided into an experimental and control group, with women in the experimental group applying olive oil to their abdominal skin twice daily. Women in the control group did not use any oil. After 8 weeks, results showed SG occurred in 40% of the women in the experimental group and 50% of women in the control group. The use of olive oil did not yield any statistical significance in the occurrence of SG compared to the control (Table 2).

Soltanipour et al. describe a parallel randomized controlled clinical trial comparing the efficacy of olive

oil and Saj(®) cream (Iranian cream made of lanolin, stearin, triethanolamine, almond oil, and bizovax glycerin amidine) in preventing and reducing striae gravidarum [25]. The study included 150 nulliparous women in their second trimester of pregnancy who were randomly assigned to either an olive oil, Saj (®) cream, or a control group. Striae gravidarum occurred in 72% of the participants in the olive oil group, with 32%, 26%, and 6% of them being mild, moderate, and severe, respectively. For those who used Saj (®) cream, striae occurred in 64% of the cases, with 16%, 34%, and 14% being mild, moderate, and severe, respectively. In the control group, striae occurred in 60% of the participants, with 22%, 24%, and 14% being mild, moderate, and severe, respectively. The incidence and severity of striae did not show any statistically significant differences among the three groups (Table 2).

Soltanipoor et al. describe a randomized control trial evaluating the effectiveness of olive oil in preventing striae gravidarum (SG) in pregnant women [26]. A hundred nulliparous pregnant women were allocated into two groups, with one receiving topical olive oil twice daily on the abdomen until delivery (approximately 22 weeks) and the other serving as a control group (no treatment). Results found no statistical significance between the two group's incidence and severity, with SG appearing in 64% of the olive oil-treated group and 60% of the control group (Table 2).

Bielfeldt et al. report a randomized controlled trial evaluating the effectiveness of plant-based body oil, enriched with oleic and linoleic acids, in improving the appearance of scars and striae [27]. In this 8-week randomized controlled trial, 80 human test subjects with non-hypertrophic scars (40) or stretch marks (40) not older than 3 years applied a plant body oil rich in oleic and linoleic acids. Treated areas showed a statistically significant mean reduction of 5% on the Observer Scar Assessment Scale (OSAS) (P=0.0006), while the untreated areas remained unchanged. The Patient Scar Assessment Scale (PSAS) gave a 20% reduction for the treated area and 6% for the control area. The overall product effect was 14% (p=0.0001), and most volunteers reported beneficial effects of the test agent, while only 17% reported no effect (Table 2).

Treating Inflammation

Currò et al. describe an observational study investigating the effects of OZOILE®, a formulation of ozonated olive oil with vitamin E acetate, on the inflammatory status and tissue remodeling in 30 male children with Balanitis xerotica obliterans (BXO) [28]. Fifteen patients with BXO were treated with OZOILE® cream once a day for 7 days before circumcision and compared to a control group of fifteen age-matched patients with BXO without treatment. After 7 days of treatment, a significant reduction in mRNA levels of pro-inflammatory cytokines (IL-1B, TNF-a, INF-y, transglutaminase 2, and NOS2) was observed in foreskin tissues treated with OZOILE compared to untreated ones ($p<0.001$). No statistically significant differences were observed in NF-κB activation. OZOILE treatment up-regulated HIF-1alpha, VEGF, and E-cadherin gene expression ($p < 0.001$) (Table 2).

Palacios et al. describe a quasi-experiment evaluating the topical efficacy of an oily fluid enriched with oleocanthal (OC) extract from extra virgin olive oil (EVOO) to a conventional oily fluid in reducing inflammation following conventional photodynamic therapy (PDT) of actinic keratosis [29]. The study included 47 patients, with 23 receiving the oleocanthal-enriched fluid and 24 receiving the conventional fluid. After 48 hours, patients in the oleocanthal group had significantly reduced inflammation and a higher likelihood of complete response at three months (60.9% vs. 29.2%). Both groups reported similar levels of pain and had no statistically significant differences in baseline characteristics (Table 2).

Akarsu et al. describe a single-blind vehicle-controlled study evaluating the impact of topical petrolatum, basis cream, glycerine, and olive oil on the minimal phototoxic dose (MPD) of psoralen plus ultraviolet A (PUVA) in 29 volunteers diagnosed with psoriasis, lichen planus, parapsoriasis, mycosis fungoides, and vitiligo prior to their PUVA therapy [30]. The study found a statistically significant increase in the mean MPD values with the application of white petrolatum compared to pure PUVA ($p = 0.011$). There was no significant change in the mean MPD values after the application of basis cream ($p = 0.326$), glycerine ($p = 0.611$), or olive oil ($p = 0.799$). No placebo was used in the study (Table 2).

Verallo-Rowell et al. describe a double-blind controlled trial aimed at comparing the effectiveness of virgin coconut oil (VCO) and virgin olive oil (VOO) in moisturizing dry skin and removing *Staphylococcus aureus* (SA) from the colonized skin of individuals with atopic dermatitis (AD) [31]. In this trial, 52

subjects from two outpatient dermatology clinics received either VCO or VOO topically for 4 weeks. Of the 20 patients whose SA cultures were positive and randomized to use VCO, only one patient remained positive, compared to 6 patients who remained positive among the 12 patients using VOO. The relative risk of nontreatment for VCO was 0.10, while that of VOO was 10 times higher. The calculated absolute risk was -0.45. There was no significant difference in objective-SCORAD severity index (O-SSI) scores between the two groups at baseline, but the post-intervention scores showed a statistically significant difference ($p = 0.004$). The reduction in O-SSI score and *in vitro* broad-spectrum activity against SA, fungi, and viruses by VCO and monolaurin suggest potential use as a treatment for AD colonization (Table 2).

Danby et al. describe a randomized control trial exploring the effect of sunflower oil and olive oil on the biophysical characteristics of the skin in 19 adult volunteers with and without atopic dermatitis [32]. The first cohort applied olive oil to one forearm twice daily for 5 weeks, while the second cohort applied olive oil to one forearm and sunflower seed oil to the other twice daily for 4 weeks. The findings of this study revealed that topical application of olive oil resulted in a significant reduction in stratum corneum (SC) thickness and integrity and induced mild erythema in volunteers with and without a history of AD, without any notable improvement in SC hydration. The most statistically significant difference was seen in volunteers with AD, where olive oil exacerbated the defective skin barrier, likely due to the excess of monounsaturated fatty acids (OA). These findings challenge the common recommendation of olive oil for skin care (Table 2).

Use as a Moisturizing Agent

Kiechl-Kohlendorfer et al. describe a randomized controlled trial aimed at comparing the effects of two different topical ointment therapies on infant skin [33]. One hundred and seventy-three neonates between 25- and 35-weeks' gestation were randomly assigned to group A (Bepanthen® [water-in-oil emollient cream]), group B (olive oil), or group C (control). Skin therapy was applied twice a day for a maximum of 4 weeks, and measurements were taken at baseline, day 7, day 14, day 21, and day 28. Results showed that neonates treated with olive oil cream had statistically less dermatitis than those treated with emollient cream. Moreover, both the emollient cream and the olive oil showed better outcomes than the control group ($p<0.001$) in weeks 2-4 (Table 2).

Treating Fissures, Burns, and Pruritus

Cordero et al. describe a randomized, prospective experimental study evaluating the efficacy of extra virgin olive oil (EVOO) in preventing nipple cracking among lactating women [34]. 300 women were randomly assigned to either group 1 (n=150), in which EVOO was topically applied to the nipple after breastfeeding, or to the control group 2 (n=150), in which drops of breast milk were applied. The occurrence of nipple cracking was statistically significantly lower in the EVOO group (2.7%) than in the control group (44.0%), with a quantitative efficacy of 97.3%. The application of EVOO was found to be safe for both mothers and newborns and was effective even when breastfeeding posture was inadequate (Table 2).

Al-Waili et al. describe a comparative study evaluating the therapeutic effect of a mixture of honey, olive oil, and beeswax in a 1:1:1 ratio for the treatment of anal fissures or hemorrhoids [35]. 15 patients with anal fissures or hemorrhoids topically applied the mixture to the affected skin twice daily. Results showed that in patients with hemorrhoids, the mixture provided effective pain relief within a week, with complete pain relief achieved in three weeks. Additionally, the mixture significantly reduced bleeding in all patients except for two with mild bleeding, reduction in itchiness, and resolution of erythema and edema ($p <0.05$). Notably, two patients with third-degree hemorrhoids experienced improvement without surgery. Patients with anal fissures also had statistically significantly reduced pain, bleeding, and itching, with signs of healing in four weeks. No side effects or complications were reported (Table 2).

Panahi et al. present a randomized, double-blind clinical trial conducted with the aim of determining if a combination cream of olive oil and aloe vera was more effective than betamethasone 0.1% cream for treating chronic pruritus lesions caused by sulfur mustard toxic exposure [36]. Sixty-seven Iranian chemical warfare-injured veterans exposed to mustard gas were included in the study. Thirty-four were randomly assigned to the olive oil/aloe vera group, while thirty-three were assigned to the betamethasone group. Both groups applied the cream twice daily for six weeks. A pruritic score questionnaire and visual analog scale (VAS) were used to evaluate the results. Both treatment groups

showed a significant decrease in mean pruritus score and mean VAS score ($p < 0.01$ in the olive oil/aloe vera group and $p < 0.005$ in the betamethasone group), with no significant difference between the two groups. However, the olive oil/aloe vera group showed an additional statistically significant reduction in fissure and excoriation ($p < 0.05$) (Table 2).

Use for Friction Reduction

Yap et al. describe a randomized controlled trial aimed at identifying the optimal wax-oil combination for developing a lubricant that reduces friction (shear) between the skin and personal protective equipment (PPE) for a duration of up to 4 hours [37]. Four wax-oil lubricant mixtures, namely paraffin wax-olive oil, paraffin wax-mineral oil, beeswax-olive oil, and beeswax-mineral oil, were tested on seven participants between the ages of 23-28. Results indicated that the beeswax-olive oil lubricant resulted in a 44% reduction in the CoF after 4 hours compared to unlubricated skin ($p=0.003$) while the beeswax-mineral oil lubricant had the lowest coefficient of friction (CoF) (85% lower than unlubricated skin) immediately after application ($p <0.0001$). Among all the tested combinations, the beeswax-olive oil-mineral oil mixture exhibited the lowest friction, resulting in an 87% reduction in coefficient of friction immediately after application ($p = 0.0006$) and a 59% reduction after 4 hours ($p = 0.0015$) when compared to the unlubricated skin (Table 2).

DISCUSSION

This review synthesized the current literature on the topical effects of *O. europaea* derivatives, encompassing only human studies. We addressed the human studies, summarized the limitations, highlighted the most substantiated uses of olive, and discussed future directions. Among the included papers, a total of 21 studies met our inclusion criteria. These encompassed a range of study designs, from clinical trials to basic science experiments, animal trials, and more. Notably, many of these studies reported positive outcomes, with only a few exceptions. Several limitations were identified across the reviewed studies. These included limited sample sizes in some cases, a lack of control groups in certain trials, and variability in the quality of evidence. In addition, there were seven studies that tested products that consisted of olive oil derivatives in addition to other ingredients that were not derived from olive oil [19,21,27,28,33,35,36]. The most common ingredients that were present in these mixtures include aloe vera and other oily substances, such as lanolin and vitamin E acetate. Aloe vera has been implicated in treating multiple dermatological conditions, including enhanced skin permeation, anti-inflammatory effects, wound healing, moisture retention, and burn healing [38,39]. Similarly, beeswax, honey, and calendula also promote skin barrier protection [40-42], and even serve as prevention for many skin conditions such as radiation dermatitis [43], skin aging [44], and wound care [45]. Lanolin and vitamin E acetate also have skin protective, skin softening, and moisturizing properties [46,47], however they are both highly allergenic especially topically in inducing allergic contact dermatitis [48-50]. Other plant-derived ingredients such as safflower oil are also found to be useful in enhancing cosmetic effects on the skin [51]. These ingredients might add to the beneficial properties of the treatment solution with its supplementation thus potentially skewing the results shown in these studies. Additional research is needed to separate the effects of olive oil compared to the compounds added. These limitations should be considered when interpreting the results.

Our review identified a wide array of potential therapeutic uses for olive derivatives. These include wound healing, particularly in cases of ulcers, burns, and skin injuries, dermatitis management, including radiation-induced dermatitis, atopic dermatitis, contact dermatitis, psoriasiform dermatitis, and diaper dermatitis, prevention and treatment of pressure ulcers and skin cancers, improvement of epidermal barrier function in some cases, relief from pruritus and chronic pruritus lesions, reduction of friction between the skin and personal protective equipment.

With its wide set of uses and high prevalence especially in lower socioeconomic countries, it can serve as an accessible treatment for multiple skin ailments that has a low risk of side effects and a high efficacy rate. Lack of training needed to administer this as a skin treatment adds to its versatility and can allow widespread administration of treatment without a licensed professional, adding to its use as a home remedy.

Given the promising findings in many studies, there is ample room for further research and exploration in the field of olive derivatives. Future investigations should strive to conduct larger-scale human trials to

strengthen the evidence base, address the limitations of previous studies, explore additional applications of olive derivatives in skincare and dermatology, investigate the potential for olive-based formulations to serve as safe and effective alternatives to traditional treatments, and assess the long-term effects and safety profiles of these treatments.

CONCLUSION

O. europaea and its derivatives are effective in treating a multitude of skin conditions. This systematic review found that *O. europaea* derivatives can successfully reduce, prevent, or treat various conditions ranging from ulcers to pruritus. The use of *O. europaea* extracts is noted to be safe as the studies reviewed found almost no adverse effects, except for one. Additional research should be done to ensure that the use of *O. europaea* as a therapeutic agent will be beneficial to patients before being implemented for use to treat a multitude of conditions. The use of O. *europaea* has the potential to improve the outcomes and experiences of numerous dermatological patients soon.

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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Our Dermatology Online

Original Article

The role of phytotherapy in the management of dermatological conditions: The case of the northern region in Morocco

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ABSTRACT

Background: Phytotherapy is currently gaining significant popularity among the North African and Moroccan population, particularly in the treatment of common dermatological conditions. **Material and Methods:** This prospective, cross-sectional descriptive study, conducted over six months from June 2022 to December 2022, involved patients seen at the dermatology department of the University Hospital Center in Tangier. The study aimed to investigate the use of phytotherapy among Moroccans, particularly in the northern context. A questionnaire in Moroccan Arabic (Darija), comprising three parts related to the study's objectives, socio-cultural profiles, and selected diseases, was administered to collect data. Data entry and analysis were performed using IBM SPSS software, version 25. The survey identified a significant number of plant species from versatile botanical families being used in aqueous maceration, infusion, and decoction. Common ailments treated with phytotherapy include alopecia, acne, and eczema, primarily among female patients. **Results:** We recruited 215 patients suffering from various dermatoses, who had used phytotherapy for the past five years. There was a predominance of females, with a sex ratio of 3, and the average age was 32 years. Our survey identified 50 species of plants belonging to 26 botanical families used in the form of aqueous maceration (54.6%), infusion (37.4%), and decoction (11.8%). The level of satisfaction varied among the patients, with the majority (76%) reporting satisfaction with results ranging from a partial regression of lesions to complete whitening and complete hair regrowth for patients with alopecia. However, 24% of the patients were dissatisfied due to the lack of improvement or worsening of their dermatoses. Side effects encountered were infrequent to rare. **Conclusion:** The findings of the study were consistent with previous research in Morocco, highlighting the growing popularity of phytotherapy as a medical alternative. Accordingly, the study concluded that phytotherapy is widely embraced in Morocco, offering a wide range of benefits due to the active biochemical and organic components in medicinal plants.

Key words: Dermatological pathologies, Phytotherapy, North of Morocco, Diversity and multiparity of medicinal plants

INTRODUCTION

Data from the World Health Organization (WHO) indicates that more than 80% of the global population relies on traditional medicines for their essential primary healthcare needs. The utilization of traditional medicines in Africa reflects a well-established history of human interactions with nature and the environment. Botanicals, employed in traditional medicine, encompass a wide range of compounds that may be utilized to address various skin-related conditions [1].

Practices in traditional medicine vary widely from country to country and region to region [2]. They are influenced by known factors such as culture, history, and personal philosophies. Natural products are highly

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valued as raw materials for various sectors, including cosmetics, pharmacy, agri-food, phytosanitary, and industry [1,2]. Consequently, there has been a recent and unprecedented surge in the interest in the use of herbal remedies. An increasing number of people are in search of "natural" medicines, and it seems that herbal-based cosmetics and household products are becoming more and more prevalent [1,2].

Similarly, within the Moroccan population, considering the diverse range of medicinal plants with potent therapeutic properties in Morocco, the use of herbal remedies is embraced for various health conditions [2]. Notably, there is a substantial focus on addressing dermatological issues. Dermatological diseases, which are numerous and prevalent, are regarded as a group of pathologies with their most visible symptoms manifested in target organs, particularly the skin, mucous membranes, and appendages. In the northern region, the reliance on traditional medicine is widely ubiquitous, with numerous herbal remedies, either used individually or in combination, being recommended for the treatment of dermatological conditions [2].

MATERIALS AND METHODS

The study is conducted in the region of Tangier, situated in northern Morocco. Tangier is a strategically located port city at the Strait of Gibraltar, facing Spain. This region is known for its cultural diversity, rich historical background, and significant geographical importance. Tangier serves as a major economic hub due to its bustling port. It is also recognized for its distinctive cultural influence, shaped by centuries of interactions between various civilizations. The northern region of Morocco, where Tangier is positioned, has a reputation for traditional medical practices, including the widespread use of traditional medicine and herbal remedies to address various health issues, including dermatological conditions. The study was conducted within this context, with the aim of exploring the utilization of phytotherapy in treating common dermatoses among the local population. This was a prospective, cross-sectional, descriptive study conducted over a six-month period from June 2022 to December 2022. The study included patients who attended consultations at the dermatology department of the University Hospital Center in Tangier. The survey utilized a questionnaire translated into Moroccan Arabic (Darija), comprising three parts: the first part provided information about the study's objectives, the second part focused on socio-cultural profiles, and the third addressed specific diseases. Data collection, entry, and analysis were performed using the IBM SPSS software, version 25.

RESULTS

Patients Population

The 215 recruited patients suffered from various dermatoses and had used phytotherapy for the previous five years. Among those surveyed, women were the primary users of plants, accounting for 70%, compared to 30% in the case of men.

The age range of individuals varied between 13 and 70 years old. The age group between 19–30 years represented the highest percentage (44.8%) of individuals engaging in the use of medicinal plants. Additionally, 38.6% of individuals using plants fell within the age range of 31–50 years, and 7.6% of users were below 18 years of age.

Regarding the level of education, 67% of the individuals surveyed were not educated. The remaining 33% of the surveyed individuals were distributed between primary education (15.2%) and secondary education (18.6%) (Fig. 1).

As regards the most frequently reported pathologies by the respondents, alopecia topped the list with a percentage of 34.6%, followed by atopic dermatitis (eczema) with a percentage of 26.4%, acne with a percentage of 20%, and superficial mycoses with a percentage of 10% (Fig. 2).

The majority of the population (50%) accessed information from social media and the Google search engine. On the other hand, 45% of the population

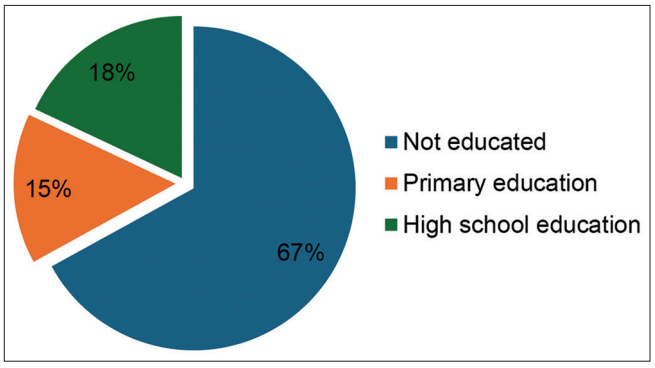

Figure 1: Distribution of the population by level of educational attainment.

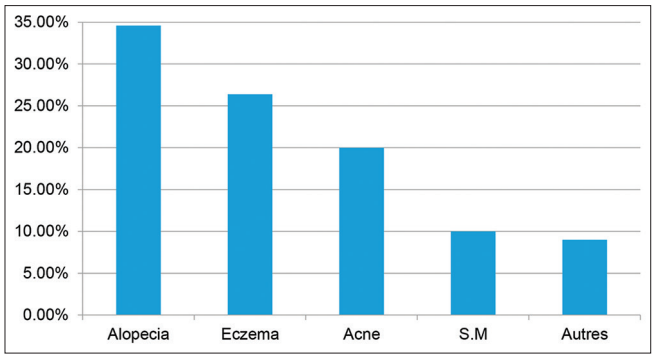

Figure 2: Most prevalent pathology among the population using traditional medicine.

obtained information through personal experiences and those of others, while 5% of the patients utilized other sources. Our survey identified 50 species of plants belonging to 26 botanical families used in the form of aqueous maceration (54.6%), infusion (37.4%), and decoction (11.8%).

The most commonly treated conditions with phytotherapy were alopecia (34.6%), where *Allium sativum* (garlic) was the most frequently used plant (40%). Garlic was also frequently applied in the treatment of superficial mycoses (13.1% of the population). For acne (20.7%), the most frequently utilized plants were apple cider vinegar, green tea, and basil with percentages of 26.9%, 23.8%, and 21.7%, respectively. Eczema was the third most commonly treated condition with phytotherapy, accounting for 17% of the cases, with *Lawsonia inermis* being used in 36.1% of the treated cases.

We identified three plant species belonging to three families used against eczema. The most mentioned species are *Lawsonia inermis*, cited by 36% of the individuals, *Trigonella foenum-graecum*, *Matricaria chamomilla*, tar, and ground sulfur, reported respectively by 14.4%, 15,9%, 18.7%, and 22.2% of the patients (Tables 1 – 4).

The degree of satisfaction varied from patient to patient, with the majority (76%) reporting satisfaction, with results ranging from partial regression of lesions to complete whitening, and complete hair regrowth for patients with alopecia. However, 24% of the patients were dissatisfied due to the lack of improvement or worsening of their dermatoses (Fig. 3).

Side effects encountered were infrequent to rare, with eczematization reported by 13 patients, 8 of whom used henna (*Lawsonia inermis*), and 5 used garlic (*Allium sativum*). Irritation was reported by 5 patients who used garlic (*Allium sativum*) and by 3 patients who applied tar, all of whom had associated superinfection. Additionally, two-thirds of the patients who used garlic (*Allium sativum*) reported tingling sensations during use. Six patients who made use of curcuma (*Curcuma longa*) to treat their melasma reported digestive symptoms such as bloating and nausea.

Table 1: List of medicinal plants used against acne, documented in the Northern region of Morocco.

English Name	Scientific Name	Frequency
Apple cider vinegar	*Acetum malorum.*	26.9%
Green tea	*Camellia sinensis*	23.8%
Basil	*Ocimum basilicum*	21.7%
Aloe vera	*Aloe barbadensis miller*	11%
Others		16.6%

Table 2: List of medicinal plants utilized for addressing alopecia, documented in the region of Tangier, Morocco.

English Name	Scientific Name	Frequency
Garlic	*Allium sativum*	39.7%
Rosemary	*Rosmarinus officinalis*	15.3%
Henna	*Lawsonia inermis*	13.7%
Green tea	*Camellia sinensis*	11.7%
Castor bean	*Ricinus communis*	6.9%
Others		12.7

Table 3: List of medicinal plants employed against Melasma, documented in Tangier region, Morocco.

English name	Scientific name	Frequency
Turmeric	*Curcuma longa*	24.8%
Aloe vera	*Aloe vera*	17.8%
Inules	*Inula genus*	15.8%
Frankincense trees	*Boswellia*	15%
Henna	*Lawsonia inermis*	12.4%
Others		14.2%

Table 4: The list of medicinal plants used against superficial fungal infections.

English name	Scientific name	Frequency
Garlic	*Allium sativum*	43.5%
Strong-scented geranium	*Pelargonium graveolens*	20.1%
Green tea	*Camellia sinensis*	11.4%
Common pomegranate	*Punica granatum*	6.9%
Ginger	*Zingiber officinale*	4%
Sea buckthorn	*Hippophae rhamnoides*	3.5%
Henna	*Lawsonia inermis*	1.85
Others		8.8%

DISCUSSION

In Morocco, medicinal plants play a crucial role in traditional medicine and contribute significantly to the national economy (Bellakhdar, 1997). According to Scherrer et al., Morocco stands out among

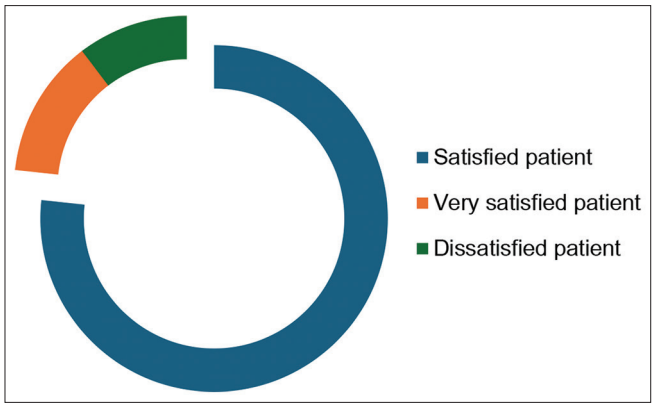

Figure 3: Satisfaction of the survey respondents with treatment outcomes.

Mediterranean countries for its extensive medical tradition and traditional knowledge related to medicinal plants [3]. Nevertheless, although the sector of aromatic and medicinal plants is more advanced in Morocco when compared to other Maghreb countries, phytotherapy involves the use of medicinal plants for therapeutic purposes [1,3]. This practice dates back to antiquity, and throughout human history, various cultures have developed recipes based on their intelligence, ingenuity, cultural understanding of health and illness, and their relationship with the environment [4].

Phytotherapy in Acne

Reminder on acne

Acne is a chronic condition of the pilosebaceous follicle that typically develops during puberty. It affects 80% of individuals between the ages of 12 and 20, with severe forms representing only 15%. The comedones, in the form of a microcyst, are consistently present in "true" acne. Juvenile polymorphic acne is the most common form, yet there are numerous clinical variations [5].

Phytotherapy and acne

Green tea

The antibacterial and anti-inflammatory potential of natural compounds derived from plants has been reported in numerous studies. *In vitro* and *in vivo* studies have revealed that essential oil blends, oleoresin, flavonoids, alkaloids, phenolic compounds, tannins, xanthones and their derivatives, diterpene acids, phenylpropanoid glycosides, acteoside, and bisnaphthoquinone derivatives are effective in acne treatment thanks to their antimicrobial and anti-inflammatory activities [6,7]. Many plant-derived procedures involve the use of different plant extracts; for example, *C. sinensis* or green tea extracts have been associated with health benefits since antiquity [8]. The primary mediators of these biological effects are polyphenolic catechins and terpenes, which promote a reduction in the expression of genes associated with inflammation, an increase in the expression of antioxidant genes, and antimicrobial activity.

Basil (Ocimum basilicum L.)

Belonging to the *Lamiaceae* family, basil (*Ocsimum basilicum L.*) is a medicinal and aromatic plant cultivated worldwide. It has numerous oil glands that store essential oils. The basil essential oils (OBEO) extracted from the leaves and flowers of *O. basilicum* contain various biologically active compounds characterized by their antioxidant and antimicrobial activities [9].

In addition to the OBEO, basil also contains substantial amounts of phenolic compounds, including flavonoids, phenolic acids (such as caffeic, rosmarinic, and chicoric acids), and anthocyanins, which possess strong antioxidant effects [9].

Phytotherapy in Alopecia

Generalities

At birth, each individual has a genetically determined capital of hair follicles. This capital gradually diminishes over time due to two main factors: age and the influence of seasons. The seasonal hair loss is explained by the hormonal influence on the hair follicle cycle. Beyond physiological variations, there are numerous non-physiological causes, including psycho-affective shocks, pregnancy and postpartum, surgical interventions, strict dietary regimes, anemia, thyroid disorders, medication use, chemotherapy, radiotherapy, intoxication, certain diseases (alopecia, ringworm, acute systemic diseases), aggressive hair care practices, and the most common, hormonal influence responsible for androgenetic alopecia [10].

Phytotherapy and alopecia

Garlic

Allium sativum (Garlic) is used and recommended by the traditional Iranian medicine reference in the treatment of alopecia [11]. Known for its effect in promoting cutaneous microcirculation [12], a study showed that the use of *Allium sativum* gel in combination with topical betamethasone valerate had a significantly superior therapeutic effect compared to betamethasone valerate alone in the treatment of alopecia. This suggests that it may be an effective complementary topical therapy for alopecia [13].

Green tea (Camellia sinensis)

It is reported that epigallocatechin-3-gallate (EGCG), a major polyphenol in green tea with powerful anti-cancer and antioxidant properties [14,15], stimulates human hair growth through its proliferative and anti-apoptotic effects on dermal papilla cells [16].

Lawsonia inermis

Its extract has significant potential for hair growth development, and this effect may be due to its regulatory effects on cell growth and the expression of the growth factor gene [17].

Phytoterapy in Melasma

Overview of Melasma

The term *melasma* is derived from the Greek word "melas" and refers to an acquired hypermelanosis of the face that develops slowly and symmetrically, with shades ranging from light brown to dark brown. Melasma most commonly appears in women using oral contraception or during pregnancy. However, melasma may be observed outside of any hormonal influence in both women and men. Clinical examination allows for the identification of 4 clinical forms on the face based on the topography of hyperpigmentation [18-20]: centrofacial type: 63% of cases (involving the cheeks, forehead, chin, upper lip); malar type: 21% of cases (symmetrical involvement of the cheeks and nose); maxillary type: 8% of cases (involvement of the ascending branch of the maxilla); and labio-mentonnier type: 8% of cases (involvement of the upper lip and chin) [21-23].

Phytotherapy and melasma

Turmeric

Ponders have investigated the potential focal points of turmeric, curcumin (dynamic component in turmeric), and fragrant (ar)-turmerone (a normally happening turmeric oil) in overseeing hyperpigmentation clutters. Turmeric, deductively alluded to as *Curcuma longa*, capacities as both a flavor and a broadly recognized home-grown supplement known for its antioxidant, anti-inflammatory, antimicrobial, and antineoplastic properties. Swanson et al. conducted a double-blind, split-face study on non-melasma patients and found that a topical cream containing turmeric extricate viably decreased hyperpigmented spots. An examination by Stop et al. inspected the anti-melanogenic impact of ar -turmerone, uncovering its capacity to decrease the quality expression of tyrosinase-related proteins 1 and 2 and smother the tyrosinase action. In spite of the fact that ar-turmerone showed more prominent viability, curcumin essentially ruined the melanin union and tyrosinase action [24].

Boswellia (BAs)

These are pentacyclic triterpenes known for their potent anti-inflammatory properties. These compounds are extracted from the gum resins of the tropical tree *Boswellia serrata*, which is native to India and Africa. Traditionally, research on Boswellia has primarily focused on the immunomodulatory characteristics of the resin. Multiple clinical trials and studies conducted *in vitro* and *in vivo* have demonstrated that boswellic acids exhibit significant anti-inflammatory and pro-apoptotic effects [25]. While the precise mechanism of action in hyperpigmentation remains unclear, *Boswellia* is commonly incorporated into various cosmetic products.

Aloe vera extract

Research conducted on animals revealed that the leaf extract of *Aloe vera* and its active component, aloin, demonstrated potent, dose-dependent melanin aggregating effects with physiological significance, resulting in skin lightening through adrenergic receptor stimulation [26]. Aloe vera extract is utilized as an ingredient in various commercially available formulations.

Phytotherapy in Eczema

Generalities

Dermatitis, also known as eczema, is an itchy, inflammatory skin reaction that may present with a variety of histologic and clinical features. One dermatitis associated with the atopic state is atopic dermatitis. The patient has a history of dermatitis that is extremely itchy, especially on the flexures, and either a family or personal history of atopy (asthma, hay fever, urticaria, etc.).

Phytotherapy in eczema

Chamomile

Herbal remedies have long been utilized, either topically or orally, to treat skin conditions because of their anti-inflammatory and antipruritic properties. An overview of the principles of phytotherapy in dermatology has been provided by Bedi [27]. Regarding topical application, two randomized controlled trials that analyzed the safety and efficacy of a chamomile preparation and a St. John's wort preparation, respectively, have been identified [28,29]. In a comparative trial involving 69 patients with

atopic eczema, the commercial chamomile extract preparation (Kamillosan-Creme) was compared to a 0.5% hydrocortisone cream or a base cream without an active agent.

Regarding the most important clinical criteria such as itching, erythema, and desquamation, the chamomile preparation was slightly superior to the hydrocortisone preparation after two weeks. However, there was no difference between the chamomile preparation and the base cream. Unfortunately, the publication does not provide information on the results of statistical tests.

Fenugreek (Trigonella feonum-graecum L.)

It is a dicotyledon, annual, fodder crop frequently used as a herb and spice. Although it originated in an area that stretched from Iran to Northern India, it is currently grown in China, North and East Africa, Greece, and Ukraine. Fenugreek is referred to as "an old world" crop for the "new world" because it is one of the oldest known medicinal plants. When applied topically, fenugreek seed's gelatinous texture may help calm sensitive skin caused by eczema or other ailments [30].

Phytotherapy in Superficial Mycoses

Overview of superficial mycoses

Cutaneous mycoses encompass infections that affect the skin on a superficial, semi-deep, or deep level, caused by microscopic fungi. Approximately ten classes of fungi contribute to most cutaneous mycoses. These microorganisms are categorized into three primary groups: filamentous fungi (dermatophytes), yeasts from the *Candida* and *Malassezia sp.* genera, and in exceptional cases, molds. This classification is crucial both from an epidemiological standpoint and therapeutic considerations, as antifungal agents exhibit varying degrees of efficacy against these three fungal groups [31]. Dermatophytoses include conditions such as ringworm, epidermophytosis (dermatophytic intertrigo affecting large and small folds, as well as circinate dermatophytosis), and onychomycosis caused by dermatophytes [32]. Candidiasis is a widespread condition caused by yeasts belonging to the *Candida* genus. These yeasts are responsible for superficial infections (mucosal and cutaneous) as well as deep or disseminated mycoses. Akin to dermatophytes, these yeasts cause cutaneous issues, including intertrigo in large or small folds, digital intertrigo (with digitoplantar intertrigo more commonly attributed to dermatophytes), and nail infections [32].

Pityriasis versicolor is a prevalent superficial mycosis that occurs in areas of the skin with high concentrations of sebaceous glands. The proliferation of *Malassezia furfur* is the underlying cause of this mycosis [32].

Phytotherapy for dermatomycoses

Allium sativum

Fungal infections, which are hard to eliminate using topical treatments, may require an extended course of systemic therapy. Additionally, the use of synthetic antifungals is associated with the risk of significant adverse effects. This often leads patients to explore alternative treatments, including phytotherapy. Consequently, numerous clinical trials are conducted to assess the antifungal efficacy of plant extracts. An *in vitro* study specifically examined the antifungal activity of aqueous extracts derived from *Allium sativum* (garlic) against *Malassezia furfur* (25 strains), *Candida albicans* (18 strains), and other *Candida* species (12 strains). The results indicate that garlic (*Allium sativum*) could be promising in the treatment of diseases associated with fungi from important pathogenic genera such as *Candida*, *Malassezia*, and dermatophytes [33].

Pelargonium graveolens

An investigation into the chemical composition, antifungal capabilities, and antioxidant properties of *Pelargonium graveolens* essential oil was presented in this study. The essential oil profile was identified through GC and GC-MS analysis, highlighting key compounds such as citronellol (24.54%), geraniol (15.33%), citronellyl formate (10.66%), and linalool (9.80%). Minimal inhibitory concentrations (MIC) and minimal fungicidal concentrations (MFC) were determined using microdilution and macrodilution methods, with the commercial antimycotic bifonazole used as a reference. Concentrations within the range of 0.25 to 2.5 mg/mL exhibited fungicidal effects [34].

Zingiber officinale

It is a perennial herbaceous plant belonging to the *Zingiberaceae* family, which has been utilized for over two centuries due to its medicinal and nutritional properties. It is regarded as a safe plant with negligible adverse effects. Numerous studies, both *in vitro* and *in vivo*, have substantiated the beneficial effects of *Zingiber officinale*, encompassing its roles as an anti-nausea, anti-inflammatory, antioxidant, antimicrobial, anticancer, antidiabetic, cardiovascular, and respiratory agent [35]. The aim of this study was to assess the specific biological activities of ginger essential oil, obtained through

hydrodistillation from dried rhizomes. Notably, the study evaluated antibacterial and antifungal activities. The essential oil's antibacterial and antifungal efficacy was tested against six bacterial strains: *Escherichia coli*, *Salmonella typhi*, *Micrococcus luteus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and a yeast (*Candida albicans*), utilizing the agar diffusion method. The resultant essential oil displayed a yellow to brown color with a yield of 0.25%. Findings from the antibacterial and antifungal assessments revealed a notable inhibitory activity on nearly all tested strains, with growth inhibition varying across species [36].

CONCLUSION

Traditional herbal medicine remains widely practiced in Morocco, enjoying strong popular demand due to its perceived effectiveness. With the advent of communication tools, there has been an exchange of traditional medicines from other regions of the world, continually enriching this practice. A significant component of this medicine is dedicated to the treatment of dermatological conditions.

Medicinal plants offer extensive solutions to the complex problems of common dermatological diseases, serving as complementary therapeutic options to conventional treatments. Although the list of plants used for dermatological and cosmetic purposes is extensive, their use persists despite the absence of scientific studies justifying many of them. However, confirming the effects of certain plants and understanding their mode of action are hindered by various obstacles, including the lack of clinical trials evaluating their effectiveness and safety. Therefore, the implementation of a comprehensive research program is necessary to better understand these modulations.

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.

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Our Dermatology Online

Original Article

Hidden behind the mask: An observational study of mask-induced acne during the COVID-19 pandemic in south India

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ABSTRACT

Background: During the COVID-19 pandemic, masks were used to prevent and interrupt the transmission of the infection. However, wearing masks for prolonged periods of time is associated with a local rise in temperature and humidity around the masked area. Consequently, this resulted in acute flares of acne, especially in healthcare workers who used masks for 8–12 hours a day. **Materials and Methods:** In this questionnaire-based study, we present patient-reported observations regarding acne severity. **Results:** Overall, 104 responses were collected (males: 64.4%; age: 13–46 yrs.). Following the use of a mask, 28.8% of the patients experienced flaring of acne, while 71.2% did not report any significant change. Among the participants who experienced flaring of acne, 30% had mild acne, 60% had moderate acne, and 10% had severe acne. **Conclusion:** N95 masks and a duration of mask use above six hours were related to the development of maskne.

Key words: COVID, Acne, Maskne, Masks

INTRODUCTION

Sars-CoV-2 infection resulted in a global pandemic of corona virus disease (COVID-19). During the pandemic, wearing a mask was encouraged for the prevention of the dispersal of droplets during talking, coughing, and sneezing, thus reducing the transmission of the virus.

Acne vulgaris is a chronic recurrent inflammatory disease of the pilosebaceous unit. It is one of the most common skin diseases globally and affects all ethnicities and races. The cutaneous findings in acne may include open or closed comedones, papules, pustules, abscesses, and nodules. The most common anatomical sites affected include the face, back, and chest. While wearing a mask may help prevent aerosol infections, wearing it for prolonged durations may result in flaring of acne due to a localised increase in temperature and humidity on the facial skin secondary to respiration and perspiration. Such acne has also been termed *maskne* or *mask-acne*.

Mask-acne is a variant of *acne mechanica* that arises due to the friction between textile/mask and the facial skin, thus leading to the disruption of the skin microbiome [1]. Furthermore, increased virulence of *Cutibacterium acnes* due to the disturbances in the cutaneous microbiome has been hypothesized to be the primary factor that results in inflammation in mask-

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acne [1]. Additionally, hair follicles may be occluded by the mask along with increased sebum production and sweating, which also contribute to mask-acne [2]. Hu et al. reported that surgical masks and personal protective equipment modified the levels of hydration, transepidermal water loss, pH, erythema, and sebum production [3,4]. Generally, in such cases, dressings and moisturizers must be used to prevent dehydration and pressure ulcers; however, topical agents may also worsen facial dermatoses, especially acne [5]. Increased sebum production may work in favor of *Demodex folliculorum* as well, thus intensifying the inflammatory component of acne and resulting in pustules and erythema [6].

The objective of this study was to investigate the effects of face masks on acne.

MATERIALS AND METHODS

In this cross-sectional, web-based survey, an online questionnaire was employed to collect responses from various geographical regions and populations of people. The preformed questionnaire included questions regarding the type of mask, duration of its use, changes in the severity of acne, and symptoms of COVID-19, if applicable. The sample size was chosen for convenient sampling. The participants included students at a government medical college who received the questionnaire via email and text messages. A pilot study was conducted with five participants to evaluate the questionnaire; consequently, the necessary changes were incorporated into the questionnaire. Three dermatologists with a combined experience of 30 years designed and evaluated the questionnaire.

The inclusion criteria included students and faculty members at a government medical college who used masks regularly. The exclusion criteria included only a participant's refusal to participate in the study. In view of the questionnaire-based study design, the requirement for ethic committee approval was waived. Informed consent was obtained from the participants before presenting the questionnaire to them.

Statistical Analysis

Data was initially recorded in Excel (Microsoft® for Mac, 2023, Redmond, WA, USA). The data was exported to SPSS v23 (Armonk, NY, USA) for further analysis. Numbers and proportions were calculated for the overall study population and subgroups.

RESULTS

Overall, 104 responses were collected, which included 67 (64.4%) males and 37 (35.6%) females (Table 1). The participants were aged 18–46 years, with the most common age being 24 years. Regarding the educational status, most had completed bachelor's level of education (data not shown).

Overall, 39.4% of the patients reported acne before using a mask, while 60.6% did not report pre-existing acne. In those with pre-existing acne, the severity of the acne was mild in 75.6%, moderate in 22.0%, and severe in 2.4% of the participants. The overall type of mask used included N95 masks (67.3%), surgical masks (16.3%), cloth masks (12.5%), and respirators (3.8%). The average daily duration of use was 6–8 hours in 29.8%, > 8 hours in 26.9%, 4–6 hours in 17.3%, 2–4 hours in 15.4%, and < 2 hours in 10.6% of the participants (Table 2).

Following the use of masks, 28.8% of the participants experienced flaring of acne, while 71.2% did not report any significant change in the severity of acne. Among the participants who experienced flaring of acne, 30% had mild acne, 60% had moderate acne, and 10% had severe acne. Additionally, among those with the flaring of acne, 43.3% had pre-existing acne, while 56.7% had not have acne before.

The analysis was furthered according to the type and duration of mask use (Table 3). Among 30 patients who experienced worsening of acne, a majority (56.7%) did not have pre-existing acne. Furthermore, 76.7% had used N95 masks, and 56.7% had used masks for > 8 hours daily; interestingly, 76.7% of the patients had worn their masks for a minimum of 6 hours. Lastly, moderate acne was the most common severity grade (60%), while N95 masks were the most common type of masks used by these participants (Table 3).

Table 1: Demographic data and status of acne in the respondents

Parameter	Males	Females	Total
Number (*n*)	67 (64.4%)	37 (35.6%)	104
Age (yrs.)	26.5±5.9	27.5±6.6	27.1±6.3
Pre-existing acne			
Yes	24 (35.8%)	17 (45.9%)	41 (39.4%)
No	43 (64.2%)	20 (54.1%)	63 (60.6%)
Severity of pre-existing acne			
Mild	19 (28.4%)	12 (32.4%)	31 (75.6%)
Moderate	5 (7.5%)	4 (10.8%)	9 (22.0%)
Severe	0 (0%)	1 (2.7%)	1 (2.4%%)

Table 2: Type and duration of mask use and the changes in acne

Parameter	Males	Females	Total
Duration of mask use			
< 2 h	5 (7.5%)	6 (16.2%)	11 (10.6%)
2–4 h	10 (14.9%)	6 (16.2%)	16 (15.4%)
4–6 h	14 (20.9%)	4 (10.8%)	18 (17.3%)
6–8 h	18 (26.9%)	13 (35.1%)	31 (29.8%)
> 8 h	20 (29.9%)	8 (21.6%)	28 (26.9%)
Type of mask			
Cloth	7 (10.4%)	6 (9%)	13 (12.5%)
Surgical	9 (13.4%)	8 (11.9%)	17 (16.3%)
N95	49 (73.1%)	21 (31.3%)	70 (67.3%)
Respirator	2 (3%)	2 (3%)	4 (3.8%)
Change in acne post-mask			
No change	51 (76.1%)	23 (34.3%)	74 (71.2%)
Worsened	16 (23.9%)	14 (20.9%)	30 (28.8%)
Pre-existing acne (n = 30)	6 (37.5%)	7 (50%)	13 (43.3%)
No pre-existing acne (n = 30)	10 (62.5%)	7 (50%)	17 (56.7%)
Masks used by those with worsening acne post-mask			
Cloth	0 (0%)	2 (5.4%)	2 (6.7%)
Surgical	1 (1.5%)	0 (0%)	1 (3.3%)
N95	13 (19.4%)	10 (27%)	23 (76.7%)
Respirator	2 (3%)	2 (5.4%)	4 (13.3%)
Severity of maskne			
Mild	8 (11.9%)	1 (2.7%)	9 (30%)
Moderate	8 (11.9%)	10 (27%)	18 (60%)
Severe	0 (0%)	3 (8.1%)	3 (10%)

Table 3: Mask type, duration, and severity of acne flare-up

Mask	Duration of mask	Male	Female	Grand Total
Cloth mask	< 2 hours	0 (0%)	1 (7.1%)	1 (3.3%)
	> 8 hours	0 (0%)	1 (7.1%)	1 (3.3%)
Total		0 (0%)	2 (14.3%)	2 (6.7%)
Surgical mask	< 2 hours	1 (6.3%)	0 (0%)	1 (3.3%)
N95 mask	2–4 hours	1 (6.3%)	1 (7.1%)	2 (6.7%)
	4–6 hours	1 (6.3%)	1 (7.1%)	2 (6.7%)
	6–8 hours	2 (12.5%)	4 (28.6%)	6 (20%)
	> 8 hours	9 (56.3%)	4 (28.6%)	13 (43.3%)
Total		13 (81.3%)	10 (71.4%)	23 (76.7%)
Respirator	4–6 hours	1 (6.3%)	0 (0%)	1 (3.3%)
	> 8 hours	1 (6.3%)	2 (14.3%)	3 (10%)
Total		2 (12.5%)	2 (14.3%)	4 (13.3%)

DISCUSSION

In this questionnaire-based study, we evaluated the effects of wearing masks for prolonged periods of time on the severity of acne in young adults aged 18–25 years. We found that 28.8% of the participants experienced the flaring of acne. Furthermore, patients with both mild and moderate acne reported flare-ups.

Teo summarized the diagnostic criteria for maskne as follows: a) *de novo* acne that develops 6 weeks after regular mask wear or b) worsening of pre-existing acne in mask-covered areas, along with c) the exclusion of the main differential diagnoses, such as seborrheic dermatitis [7]. However, 6 weeks may be too long for a threshold since acne may develop into nodulocystic forms much faster during a flare-up.

Kurt studied the prevalence of mask-acne in physicians who had a history of acne and reported that the exacerbation of acne was reported by 45.3% of the responders, while one-third reported relapses as well [8]. Similarly, another study reported mask-acne in 56.0% of healthcare workers [9]. In a larger study, Techasatian et al. evaluated 833 individuals, which included 42.9% of healthcare workers; the authors reported that the most common reported mask-related facial adverse event was acne (39.9%) [10]. Furthermore, the prevalence of mask-acne was higher in healthcare workers than in non-healthcare workers (59.0% vs. 51.0%, respectively). In our study, 28.8% of the respondents reported worsening of acne. We believe that the differences in the prevalence rates are dependent on the type of mask as well as the use of other protective measures such as an occlusive face screen and double masks [11].

Interestingly, a majority of the responders (60%) in our study reported moderate acne during flare-ups, which was in contrast to other studies that reported mild severity of mask-acne [2,12]. We believe that the reason may be the differences in the prevalence of pre-existing acne. Furthermore, only 10% of our patients reported severe acne, most of whom had a history of acne. Therefore, mask-acne tends to be mild or moderate at presentation. Berjawi et al. evaluated 201 responses and concluded that mild acne was the most common severity at presentation [13]. Additionally, they identified several risk factors that contributed to mask-acne, such as age < 30 years, the female sex, and wearing masks for > 8 hours daily [14]. In our study, we found that maskne was predominantly seen in males and with > 6 hours of mask use. The differences in the geographic environments and skin types may have contributed to the differences in our findings.

Regarding the type of masks, studies have reported a correlation between N95 mask use and an increased risk of mask-acne [12,15]. However, Berjawi et al. did not note such an association in their study. Additionally, they reported no significant associations of mask-acne with the reuse of masks and taking breaks from wearing these masks [13]. In our study, a majority of the patients (67.3%) used N95 masks. Additionally, among those with the worsening of acne following the use of masks, 13 (81.3%) and 10 (71.4%) men and women had used N95 masks regularly, respectively. Furthermore, a majority (76.7%)

used their masks for at least 6 hours daily, thus implying that this threshold may be used as the maximum duration of single mask use before changing the masks.

Limitations

The main limitation of this study was the use of a web-based and self-designed questionnaire. Consequently, the severity of acne was assessed by the participants, which impacts the quality of evidence. Additionally, the materials used in the masks were not evaluated, which could have helped in the use of appropriate materials to prevent maskne.

CONCLUSIONS

Maskne, or mask-induced acne, is a common occurrence in healthcare workers who wear occlusive masks for prolonged periods of time; such maskne is predominantly of mild or moderate severity, while some may develop severe acne and require systemic therapies. The effects of occlusive masks and changes in the microenvironment of the masks require further research. The materials used to manufacture masks, the duration of contact, and the educational awareness of the user are important factors to consider in maskne. The major risk factors for maskne include N95 masks and mask use longer than six hours.

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.

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Our Dermatology Online

Original Article

Characteristics of lupus erythematosus in dermatology: Analysis of a series of 72 hospital cases in Abidjan, Côte d'Ivoire

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ABSTRACT

Background: Several African studies have focused on the clinical features of lupus in black skin, yet the immunological, biological, and imaging profile of the disease remains poorly described in Côte d'Ivoire. **Objective:** The aim of this study was to investigate the epidemiological, clinical, paraclinical and evolutionary aspects of lupus patients followed at the Dermatology Department of a University Hospital. **Methods:** This was a cross-sectional, retrospective study of patients received at the dermatology and venereology department of a university hospital over a six-year period. The diagnosis was based on the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria. **Results:** We included 72 lupus patients. The sex ratio was 9/1 (female-to-male) and the mean age was 37.9 **years**. Mucocutaneous manifestations were noted in 66% of the patients and were dominated by discoid lupus (88.9%). Rheumatological involvement was the most common extra-dermatological manifestation (21.8%). The main antibodies found were AAN (73.19%), anti-DNAn (45.8%), and anti-Sm Ac (27.8%). The main treatments used were hydroxychloroquine (98%), corticosteroids (37.5%), immunosuppressants (47.2%), and sun protection. Progression was favorable in 37.5%, and 51.2% of the patients were lost to follow-up. **Conclusion:** Lupus erythematosus is a rare pathology at the dermatology department, with a female predominance. Its main treatment is hydroxychloroquine, and many patients are lost to follow-up.

Key words: Lupus erythematosus, epidemiology, clinical aspect, biology, sub-Saharan Africa

INTRODUCTION

Lupus erythematosus (LE) is a non-organ-specific autoimmune disease belonging to the connectivitis group. It is a protean, chronic, and spontaneously severe systemic disease characterized by the presence of autoantibodies directed against nuclear antigens, the deposition of immune complexes and chronic inflammation in target organs such as the skin, joints, and kidneys [1]. It is a rare condition, preferentially affecting young women of childbearing age. The black race is said to be more predisposed to developing this condition [2].

Several African studies have examined the clinical features of lupus in black skin, yet the immunological and biological profile of the disease remains poorly described in sub-Saharan Africa.

The aim of our study was to update our knowledge of lupus erythematosus in dermatology in order to improve

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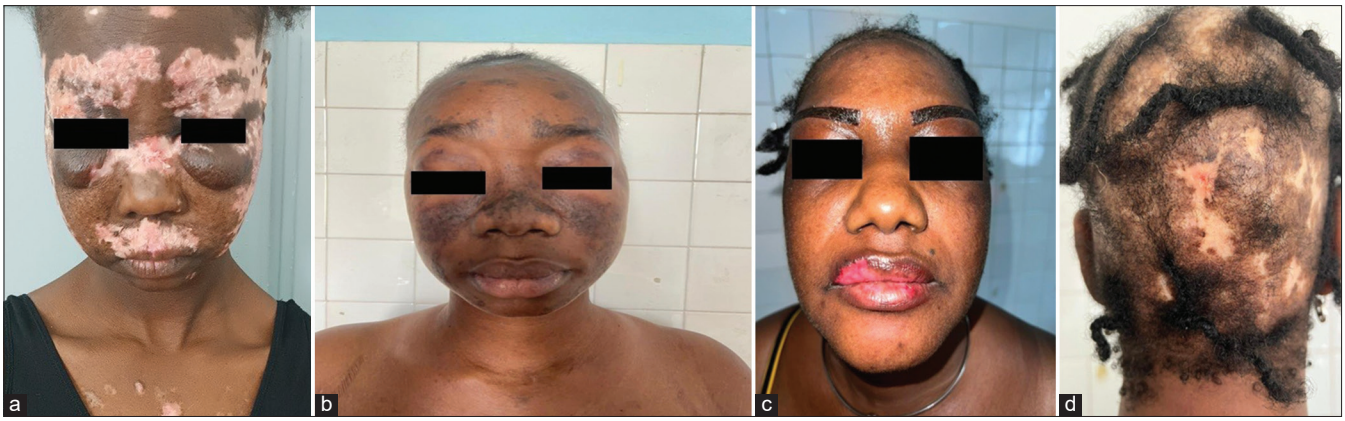

Figure 1: (a) Discoid plaques of the face in a 32-year-old adult woman. (b) Butterfly rash in a 34-year-old woman. Figure 1c: (c) Oral lip erosions in a 35-year-old woman. (d) Cicatricial alopecia in a 36-year-old woman.

its management and to study the epidemiological, clinical, paraclinical, and therapeutic aspects of lupus patients followed at the dermatology department of a university hospital.

METHODS

This was a cross-sectional, retrospective study of patients received at the dermatology and venereology department of a university hospital over a six-year period.

We included patients of all ages and sexes with LE as described above according to the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria [3]. Pregnant women and patients with incomplete paraclinical examinations and those with lupus in the context of mixed connectivitis were excluded from the study.

Sampling was consecutive and exhaustive.

The data required for the study was obtained from the patients' files. They were collected on a survey form. Quantitative variables were described by means and standard deviations. Qualitative variables were described in terms of numbers (*n*) and proportions (%). 95% confidence intervals (CI) were calculated. Graphs were edited using Office Excel 2013 as well as CSPRO, version 7.3, software, and tables using Office Word 2013, then all exported to SPSS 26 software for statistical analysis.

Ethics Statement

Ethical approval was received from the institutional review boards. Patient consent was not required for the study, as data collection was retrospective. However, the photos used in the study were presented after receiving signed consent from the patients concerned for their scientific use.

Table 1: Sociodemographic data (*n*=72)

	Number (n)	Percentage (%)
Sex		
Female	65	90.3
Male	7	9.7
Age (yrs.)		
10–20	3	4.2
20–30	15	20.8
30–40	24	33.3
40–50	13	18.1
≥ 50	17	23.6
Occupation		
Students and unemployed	25	34.7
Housewife	21	29.1
Liberal and independent professions	13	18.1
Sector employee private	7	9.7
Public sector employee	6	8.3
Marital status		
Married	40	55.6
Bachelor	25	34.7
Widower	7	9.7
Area of residence		
Urban area	68	94
Rural area	4	6
Level instruction		
Uneducated	12	16.7
Level primary	10	13.9
Level secondary	22	30.6
Level superior	28	38.9
Background medical and lifestyle		
Arterial hypertension	2	2.8
Diabetes	1	1.4
Epigastralgia	4	5.6
HIV infection	3	4.2
Smoking	2	2.28
Alcoholic drinks	5	6.94
Exposure to industry products agricultural	1	1.4
Sun exposure	72	100

RESULTS

Sociodemographic and Clinical Characteristics

Eighty-six (86) cases of lupus erythematosus were diagnosed out of 68,780 patients, representing a hospital prevalence of 0.13%. We were able to include 72 patients in our study. The socio-demographic characteristics of this population, presented in Table 1, reveal a clear female predominance (90.3%) and an average age of 37.9 years, with extremes of 13 and 69 years. The 30-39 age group was the most represented (33.3%). Pupils/students and the unemployed were most concerned (34.7%), followed by housewives (29.1%). Patients living in urban areas (94%) and those with higher education (38.9%) were the most represented. All patients had frequent exposure to the sun. There were 3 HIV-infected patients (4.2%) and one case of familial lupus.

Clinical characteristics

Table 2 shows the clinical characteristics of our population. Cutaneous lupus accounted for 65.9% and systemic lupus for 30.5%. Chronic cutaneous lupus of the discoid type was the most common (90%), followed by acute (6%) and subacute (4%) lupus erythematosus.

Discoid plaques (Fig. 1a) accounted for 88.9% of cutaneous manifestations, followed by butterfly-wing erythema (Fig. 1b) (45.8%). They were mostly located in the cephalic region (72.2%), particularly on the face (31.9%). We also found hyperpigmented plaques close to discoid plaques in all patients. Twenty-five percent (25%) of our patients had mucosal involvement, especially in the mouth (23.6%) (Fig. 1c).

Of the 72 lupus patients, 32 (44.4%) were affected on the skin, including 27 cases of alopecia (84.4%), mainly of the diffuse type (65.6%) (Fig. 1d).

Rheumatological involvement was the primary extra-dermatological manifestation (21.8%), mainly polyarthralgia. Pleuropulmonary manifestations were present in 14 patients (19.44%), with cough, dyspnea revealing pleurisy and interstitial pneumopathy. We noted 7 cases of neurological involvement (9.7%), with headaches and convulsions. Weight loss was reported in 34.72% of patients.

Paraclinical characteristics

Skin biopsy was performed on 39 patients (54.2% completion rate), of whom 35 (48.6%) had abnormalities of the acute, chronic, discoid and systemic type.

Table 2: Clinical features.

	Number (n)	Percentage (%)
Lesions cutaneous		
Erythema in butterfly wing	33	45.8
Discoidal plates	64	88.9
Facial edema	5	6.9
Fixed urticariform lesions	8	11.1
Ulcerations or erosions buccal	17	23.6
Locations of lesions cutaneous		
Faces	46	63.9
Ears	11	15.3
Leather hairy	18	25.0
Thorax	8	11.1
Superior members	5	6.9
Inferior members	7	9.7
Mucosal lesions	18	25.0
Buccal	17	23.6
Genital	1	1.4
Lesions of the appendages	32	44.4
Onycholysis	2	2.8
Trachyonychia	3	4.2
Alopecia	27	37.5
Extracutaneous manifestations		
Renal	38	52.8
Rheumatological	25	34.7
Pleuropulmonary	14	19.4
Cardiac	12	16.7
Neurological	7	9.7
Digestive	3	4.2

Table 3: Therapeutic modalities (*n*=72)

Treatment	Number (n)	Percentage (%)
Hydroxychloroquine	71	98
Prednisone	27	37.5
Cyclophosphamide	16	22.2
Methotrexate	11	15.8
Mycophenolate mofetil	7	9.7
Dermocorticoids	56	77.8
Calcineurin inhibitors	11	15.3
Clothing protection	72	100
Topical photoprotection	72	100

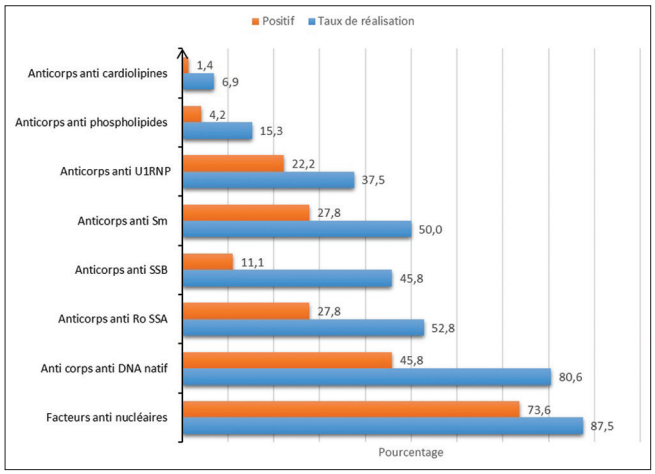

Figure 2: Distribution of patients by antibody type.

In our series, there were 44.4% cases of inflammatory anemia and 38.9% of lymphopenia. The sedimentation rate (SV) was accelerated at 56%.

Immunological data are summarized in Fig. 2, with an average antibody realization rate of over 80%. These examinations revealed the presence of anti-nuclear antibodies (84.1%), anti-native DNA (56.9%), anti-Sm (55.6%), anti-Ro-SSA (52.6%), and antiphospholipids (27.3%).

On imaging, abnormalities were noted on ECG (53.8%) and chest X-ray (21.5%), with cardiomegaly, interstitial syndrome, pleurisy and conduction disorders. High 24-hour proteinuria was reported in 52.4% of patients.

Therapeutic modalities and progression

These are summarized in Table 3. In our series, 98% of patients were treated with hydroxychloroquine, 47.2% with immunosuppressants and 37.5% with corticoids. Local treatment was based on dermocorticoids (77.8%) and calcineurin inhibitors. Protective clothing and sunscreen were recommended for all patients.

Progression under treatment after 6 months was favorable in 37.5% of cases. Patients were lost to follow-up in 51.2% of cases.

DISCUSSION

Sociodemographic characteristics

We identified 86 patients with lupus, representing a hospital prevalence of 0.13%.

LE is a ubiquitous disease affecting all populations and races. It is frequently found in Asian, African American, Hispanic American, and Caribbean populations, compared with Caucasians [2,4,5].

This study of lupus in West Africa highlighted specific characteristics. It is an uncommon disease in the region, with hospital frequencies ranging from 0.02% to 1.9% of cases yearly. The wide disparity in frequencies between countries generally sharing similar socio-demographic and economic contexts could be explained by the large number of under-diagnosed cases, often linked to a lack of awareness of the disease by non-specialist practitioners, sometimes due to clinical complexity or geographical and financial inaccessibility of paraclinical examinations complementary to diagnosis [4,6-14].

The predominance of women in our study was in line with the literature (80%). Lupus disproportionately affects women, with incidence rates 2 to 9 times higher in women than in matched male populations. Women's susceptibility to lupus is the result of a complex interaction between several conditions: a high-risk genetic terrain linked to the double X chromosome carrying genes capable of causing dysfunction of the autoimmune system; a high-risk immunological terrain in which the expression of immune regulation is reduced, while immune reactivity is increased [15]; and finally, the impact of endocrine factors through the role of female sex hormones (estrogen) on the immune response. This influence of hormonal factors is reinforced by the fact that these diseases occur more frequently in women during the genital period, and by the sometimes-aggravating role of pregnancy and hormonal contraception [16].

The average age of our study population was 37.9 years. This was in line with data from various studies in sub-Saharan Africa. Usually, the literature describes systemic diseases in young adults, and more specifically in young women at the time of genital activity [2,4,5].

Clinical characteristics

Regarding symptoms, facial erythema dominated the reasons for consultation, accounting for 84.7% of all cases. These results bear witness to the symptomatology classically described in the literature for lupus erythematosus. Practically the same signs were found in studies carried out at dermatology departments by Sangaré et al. in Côte d'Ivoire [12] and Lèye in Senegal [14].

In our study, renal involvement (52.4%) was the second most frequent extradermatological clinical manifestation, after rheumatological involvement (37.5%). In non-dermatological studies, symptoms were dominated by rheumatological disorders such as polyarthralgia. In Louzir's study in Tunisia [17], rheumatological involvement was the most frequent clinical manifestation (90%), whereas in Saudi Arabia, the most common manifestations of the disease were hematological abnormalities (82.7%), followed by joint involvement (80.4%), with mucocutaneous involvement at the third place (64.3%).

Paraclinical characteristics

Immunologically, we noted a high rate of anti-nuclear factors (73.6%) in our series. We also determined that

most autoantibodies were found. This result was in perfect agreement with the literature, in which they were detected in 90% to 100% of LE cases. Indeed, antinuclear autoantibodies were positive in most cases, in 90% of cases in African studies: 92% in Tunisia [17], 93% in Togo [9], and 97.8% in Senegal [18].

In our study, treatment was based on hydroxychloroquine in 98% of the cases, a value close to that obtained by Arfaj [19] at 98.10% of cases. In Tunisia [17], synthetic antimalarials (SMAs) were used in 48% of cases. The use of cyclophosphamide-type immunosuppressants in our study was found in 22.2% of cases, compared with 26.2% in Senegal [18], and 14% in Tunisia [17]. On the other hand, the use of methotrexate in our study was 9.7%, a higher value than that obtained in the Tunisian series, which was 3% [17]. The use of mycophenolate mofetil was 9.7% in our study, a value superimposed on that of Konan in Côte d'Ivoire, which was 8.9% [20].

Therapeutic modalities and progression

As local treatment, the application of sun cream was the most widely used, followed by topical dermocorticoids, and complementary treatment and/or a hygienic-dietary regimen were recommended, if necessary, which was also found in Tunisia [17]. UV light is the main recognized risk factor for lupus erythematosus. UV rays are capable of inducing skin lesions, as well as progressive flare-ups of the disease, and certain signs are highly photosensitive.

Sun avoidance by wearing protective clothing and the use of a highly protective broad-spectrum sunscreen have a beneficial effect in the management of the lupus subject as demonstrated in this randomized clinical trial [21].

CONCLUSION

Our study reveals that LE remains a rare condition in dermatology, with a clear predominance of young women. Clinically, cutaneous manifestations were dominated by photosensitivity, discoid plaques, alopecia and oral erosions. Paraclinical findings included inflammatory anemia and anti-nuclear antibodies. The most commonly used treatment for skin lesions was hydroxychloroquine and sun protection. Most patients were lost to follow-up treatment, hence the need for therapeutic education to improve patient compliance in Abidjan dermatology.

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.

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Brief Report

Severe cutaneous adverse drug reactions: A search for the culprit in a retrospective study of 107 patients

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ABSTRACT

Background: Severe drug eruptions, posing life-threatening risks, necessitate immediate discontinuation. This study (2014–2023) examined clinical profiles and prognoses in Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, Stevens–Johnson (SJS) syndrome, Toxic Epidermal Necrolysis (Lyell's syndrome), and Acute Generalized Exanthematous Pustulosis (AGEP). **Materials and Methods:** A retrospective analysis included hospitalized patients with severe drug reactions. **Results:** Implicated drugs: allopurinol (44.9%), neuroleptics (20.6%), antibiotics (12.1%), sulfasalazine (5.6%), and NSAIDs (5.6%). Allopurinol dominated in DRESS syndrome (51.4%), SJS (35.3%), Lyell's syndrome (45.5%). Neuroleptics caused SJS (35.3%), Lyell's syndrome (27.3%), and DRESS syndrome (18.1%). Antibiotics linked to AGEP (28.6%), SJS (17.6%), Lyell's syndrome (9.1%), and DRESS syndrome (9.7%). Sulfasalazine was associated with SJS (9.0%) and DRESS syndrome (6.9%), NSAIDs with AGEP (42.9%), and DRESS syndrome (4.2%). Significant correlations included sulfasalazine with hepatic impairment and allopurinol, neuroleptics, and antibiotics with renal failure. Mortality was 9.3%, primarily from allopurinol (60%), antibiotics (20%), and sulfasalazine (20%). **Conclusion**: Allopurinol and neuroleptics pose higher risks with significant correlations to severe complications. Haut du formulaire.

Key words: Drugs, Culprit, Allopurinol, DRESS syndrome, Stevens–Johnson syndrome, Lyell's syndrome

INTRODUCTION

Severe drug-induced skin reactions are acute idiosyncratic reactions, infrequent yet capable of compromising the prognosis and constituting a diagnostic and therapeutic emergency. Hence, there is a legal obligation to report them to pharmacovigilance authorities. Severe drug-induced skin reactions encompass Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, Stevens–Johnson syndrome (SJS), Toxic Epidermal Necrolysis (Lyell's syndrome), and Acute Generalized Exanthematous Pustulosis. Diagnosis relies on a combination of clinical, biological, histological, and chronological evidence. Treatment is not well standardized, yet immediate cessation of the suspected drug is the crucial step in both immediate and subsequent therapeutic management. All drugs may be implicated, with the most common ones being antiepileptics, allopurinol, nonsteroidal anti-inflammatory drugs (NSAIDs), and antibacterial sulfonamides [1,2]. Our study aimed to investigate the drugs most frequently associated with severe drug-induced skin reactions by analyzing the clinical profile and associated prognosis.

MATERIALS AND METHODS

We conducted a retrospective, descriptive, and analytical study at the Dermatology Department of

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CHU HASSAN II in Fez over the period from 2014 to 2023.

All patients hospitalized for severe drug-induced skin reactions (DRESS syndrome, SJS/Lyell's syndrome, AGEP) were included, and the diagnosis was based on clinical, biological, histological, and chronological criteria, referring to data provided by the pharmacovigilance laboratory. The RegiSCAR score was calculated for cases of DRESS syndrome.

Drug-induced vasculitis and angioedema cases were excluded.

Data analysis was performed with SPSS software, version 26, employing the chi-squared test and Fisher's test to investigate various correlations. A p value was considered significant if it was less than 0.05 ($p < 0.05$).

RESULTS

In our study, a total of 107 patients were included, comprising 34.6% of men and 65.4% of women, with an average age of 53.48 years. As for the medical history, 20.6% had diabetes, 6.5% had renal insufficiency, 34% had cardiovascular diseases (heart failure, hypertension, ischemia), and 2.8% had a neoplasm.

Hospitalization involved 72 cases of DRESS syndrome (67.3%), 17 cases of Stevens–Johnson syndrome (SJS) (15.9%), 11 cases of Lyell's syndrome (10.3%), and 7 cases of acute generalized exanthematous pustulosis (AGEP) (6.5%).

The most implicated drugs, in descending order, were allopurinol (44.9%), neuroleptics (20.6%), antibiotics (12.1%), sulfasalazine, and non-steroidal anti-inflammatory drugs (NSAIDs) (5.6% each) (Fig. 1).

Allopurinol caused 51.4% of DRESS syndrome cases, 45.5% of Lyell's syndrome cases, and 35.3% of SJS cases, with no cases of AGEP. Neuroleptics resulted in 35.3% of SJS cases, 27.3% of Lyell's syndrome cases, and 18.1% of DRESS cases, with no cases of AGEP. Antibiotics were responsible for 28.6% of AGEP cases, 17.6% of SJS cases, 9.1% of Lyell's syndrome cases, and 9.7% of DRESS syndrome cases. Sulfasalazine caused 9.1% of SJS cases and 6.9% of DRESS syndrome cases, with no cases of SJS or AGEP. NSAIDs led to 42.9% of AGEP cases, 4.2% of DRESS syndrome cases, with no cases of Lyell's syndrome or SJS. Fig. 2 summarizes the different forms of severe cutaneous adverse drug reactions based on each medication. No statistically significant correlation was found between the type of drug eruption and the implicated medication.

Systemic involvement included 39.3% of hepatic, 47.7% of renal, and 64.5% of eosinophilia cases. Allopurinol, neuroleptics, antibiotics, sulfasalazine, and NSAIDs caused hepatic involvement in 50%, 16.7%, 9.5%, 11.9%, and 2.4%, respectively. Similarly, they caused renal involvement in 70.6%, 11.8%, 3.9%, 3.9%, and 3.9%, respectively. A statistically significant association was found between renal involvement and allopurinol, neuroleptics, and antibiotics. Another significant correlation was noted between sulfasalazine and hepatic involvement. Regarding eosinophilia, allopurinol had the highest contribution (57%), followed by neuroleptics (21%), antibiotics (14%), sulfasalazine (5%), and NSAIDs (3%), yet no significant correlation was established. Table 1 summarizes all systemic involvements correlated with the implicated drugs.

Out of the total sample, there were 10 deaths (9.3%), with 6 cases in DRESS syndrome (8.3%) and 4 in Lyell's syndrome (6.4%), and none in AGEP or SJS. Allopurinol was responsible for 60% of deaths, while sulfasalazine and antibiotics each led to 20% of mortalities.

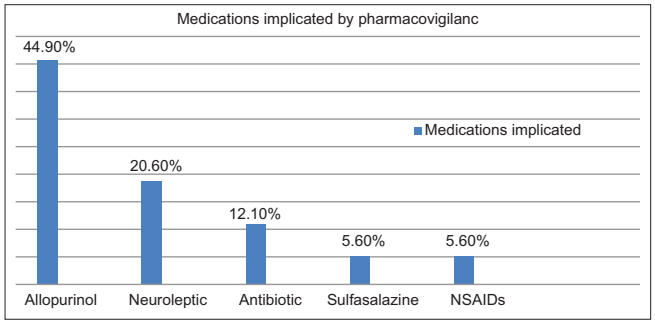

Figure 1: Various implicated medications.

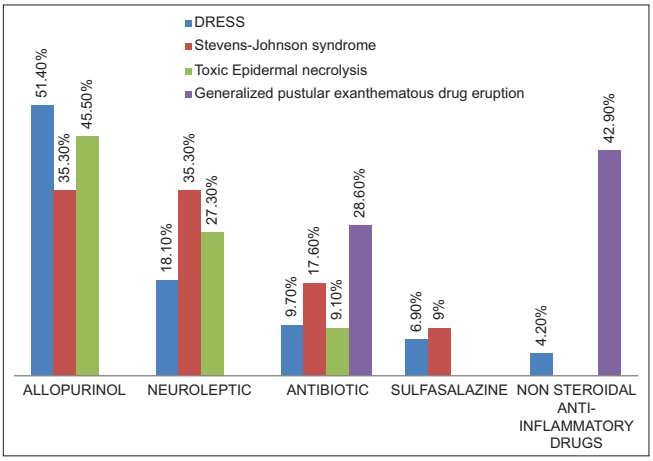

Figure 2: Type of drug eruption and associated medication.

Table 1: Systemic involvements and implicated medications

Culprit	Liver involvement	*p* value	Kidney involvement	*p* value	Eosinophilia	*p* value
Allopurinol	21 (50%)	0.39	36 (70.6%)	0.001*	35 (50.7%)	0.1
Neuroleptic	7 (16.7%)	0.423	6 (11.8%)	0.032*	13 (18.8%)	0.553
Antibiotic	4 (9.5%)	0.504	2 (3.9%)	0.013*	9 (13%)	0.768
Sulfasalazine	5 (11.9%)	0.033*	2 (3.9%)	0.681	3 (4.3%)	0.664
NSAIDs (non-steroidal anti-inflammatory drugs)	1 (2.4%)	0.4	2 (3.9%)	0.681	2 (2.9%)	0.183

*: $p < 0.05$ = significant

Follow-up revealed 3.7% of systemic sequelae, all dysthyroidies, and 30.8% of cutaneous-mucous sequelae, predominantly post-inflammatory hyperpigmentation (72.7%) (Fig. 3a), nail abnormalities (9%) (Fig. 3b), cutaneous xerosis (40.4%), genital synechiae (12%) (Fig. 3c), and ocular synechiae (9%) (Fig. 3d). Allopurinol was accountable for all systemic sequelae and 50% of cutaneous-mucous sequelae, while neuroleptics, NSAIDs, and sulfasalazine caused 27.27%, 6%, and 3% of cutaneous-mucous sequelae, respectively. No significant correlation was established between mortality or sequelae and the various implicated drugs.

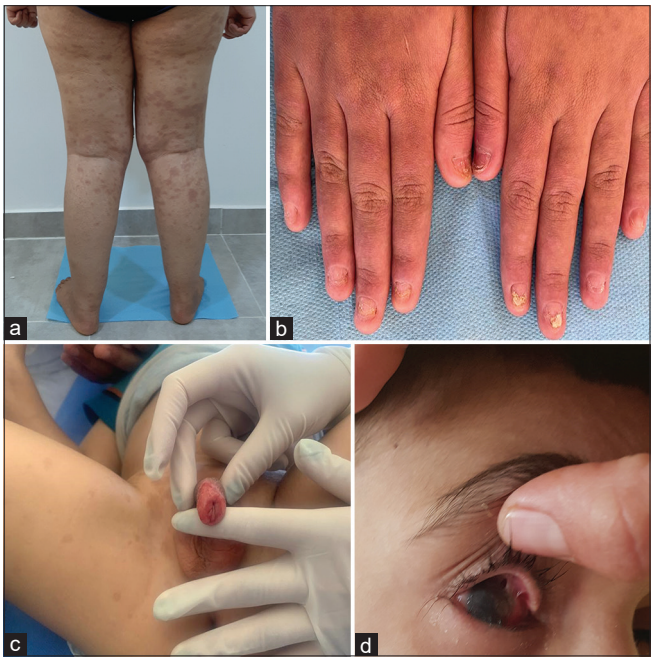

Figure 3: Clinical images of cutaneous and mucosal sequelae: a) post-inflammatory hyperpigmentation following DRESS syndrome, b) anonychia following Lyell's syndrome, c) genital synechia following Stevens–Johnson syndrome, d) ocular synechiae following Lyell's syndrome.

DISCUSSION

The term *toxidermia* encompasses all cutaneous and mucosal adverse effects following the administration of a drug internally [3]. These are unpredictable skin reactions that are not dose-dependent; they do not depend on the conventional dose of the drug yet rather on the individual and their personal constitution and the drug itself [4]. Thus, they are defined as hypersensitivity reactions, whether immunologic or not, ranging from a simple benign rash to more severe conditions such as DRESS syndrome, Stevens–Johnson syndrome, Lyell's syndrome, and finally PEAG. Although rare, severe toxidermias occur in 2% of hospitalized patients [4], the severity of systemic involvement necessitates the physician to, firstly, diagnose them rapidly, secondly, identify the causative drug for immediate cessation to improve the patient's prognosis; and finally, know how to direct the patient to the appropriate department, either to intensive care for extensive toxic epidermal necrolysis or to a dermatology service [5]. Early discontinuation of the suspected drug and reporting to pharmacovigilance units not only aids in diagnosis yet also improves immediate and long-term prognosis, as demonstrated, at least for SJS and Lyell's syndrome [6].

A multitude of drugs may be implicated, with most studies agreeing that antiepileptic drugs, especially carbamazepine, phenytoin, antibiotics, anti-inflammatories, and allopurinol, are the leading culprits [1,4]. Our findings align with the literature, identifying the same implicated molecules, although allopurinol is at the forefront. This may be explained by our predominantly elderly population with cardiovascular and renal histories, leading to more frequent allopurinol prescriptions by cardiologists, nephrologists, and family physicians for such patients.

However, each type of toxidermia is associated with a specific drug. In our study, we found that neuroleptics were mainly responsible for SJS and Lyell's syndrome, followed by DRESS syndrome, aligning with work by Yan et al. on severe toxidermias from neuroleptics in the Asian population [7]. They demonstrated that aromatic antiepileptics such as carbamazepine, lamotrigine, and phenytoin were primarily responsible for SJS and Lyell's syndrome and secondarily for DRESS syndrome. The carbamazepine is also identified as the main cause of DRESS syndrome in the European Register of Severe Cutaneous Adverse Reactions (RegiSCAR) [8]. Other antiepileptic drugs responsible for severe

toxidermias are phenytoin, lamotrigine, oxcarbazepine, levetiracetam, and topiramate [9].

The risk of developing such reactions depends on various factors, including genetic predispositions and non-genetic variables. The frequency and nature of these reactions vary significantly among ethnic groups and geographical regions. Several studies have established a close link between HLA (human leukocyte antigen) alleles and drug-induced skin reactions [1]. For instance, in the European and Japanese populations, the HLA-A31.01 allele is specifically associated with carbamazepine-related adverse effects, especially for DRESS syndrome [1,10]. However, the HLA-B15:02 allele is also implicated in toxic epidermal necrolysis reactions (SJS and Lyell's syndrome) for carbamazepine and other aromatic antiepileptics in the Chinese population [1]. This genetic and ethnic variability could explain the difference in results.

In our series, allopurinol caused 51.4% of DRESS syndrome cases, 45.5% of Lyell's syndrome cases, and 35.3% of SJS cases, with no cases of PEAG. This aligned with findings by Park et al. on the clinical characteristics and prognosis of allopurinol-induced toxidermias, where DRESS syndrome, followed by SJS and Lyell's syndrome, were the most reported, with no cases of PEAG [11]. They also showed that allopurinol led to more pronounced eosinophilia compared to other drugs, which was consistent with our results. Although the majority of allopurinol users tolerate it, some may develop hypersensitivity reactions. Approx. 1% to 5% of allopurinol users experience minor side effects [12]. Severe toxidermias related to allopurinol are observed in about 0.4% of new users, with a high mortality rate ranging from 9% to 32% [13-15]. These patients may die due to multi-systemic involvement or infection. The increasing prevalence of gout worldwide, the affordability of the drug, and its widespread prescription by many specialists explain the growing prevalence of allopurinol-induced toxidermias. This aligned with our results; allopurinol was the most frequently reported agent in our study, causing the most hepatic and renal systemic involvement, with the highest mortality rate and systemic and cutaneous/mucosal sequelae.

As for PEAG, long considered a variant of psoriasis, it is mostly caused by several drugs such as antibiotics (beta-lactams, aminopenicillins, sulfonamides, quinolones), as well as terbinafine, fluconazole, diltiazem, and hydroxychloroquine. It may also be secondary to the consumption of certain plants or insect venom [1]. Its prognosis is generally favorable, with reduced mortality [4]. To our knowledge, our study is the first to shed light on the association between the suspected drug and internal organ involvement, with significant results for sulfasalazine and hepatic involvement and for allopurinol, neuroleptics, antibiotics, and renal involvement. The implication of sulfasalazine as a sulfonamide in severe toxidermias has been reported [16,17], as well as the hepatotoxicity it may cause [18]. Finally, our results align with other studies on the Moroccan population, showing that in DRESS syndrome [19] and in the spectrum of SJS and Lyell's syndrome [20], allopurinol was the most incriminated drug, followed by neuroleptics and antibiotics, with the liver and kidney being the two most affected organs.

Regarding prognosis, the mortality rate was higher for Lyell's syndrome, followed by DRESS, which was consistent with the literature [1]. Allopurinol, sulfasalazine, and antibiotics were the leading causes of death, in order of frequency. We attribute this to the fact that allopurinol induced the most severe toxidermias and systemic involvement, while sulfasalazine led to more SJS cases and was significantly associated with hepatic involvement. Finally, there were no deaths from neuroleptics in our series, possibly due to the rapid discontinuation of the drug, which is often easily reported by the family and the patient themselves, a further indication of the importance of promptly seeking and stopping the suspected drug. As for the sequelae, allopurinol was the medication most associated with sequelae, followed by neuroleptics. This is due to the fact that these two medications caused the most cases of SJS and Lyell's syndrome and DRESS syndrome. It is noteworthy that DRESS syndrome is a chronic disease with long-term sequelae, whether cutaneous or systemic, such as thyroid disorders, diabetes, alopecia, and other systemic diseases [21]. Since, in our series, DRESS syndrome was most commonly associated with allopurinol, this explains why all systemic sequelae and the majority of cutaneous and mucosal sequelae are attributed to it. Finally, neuroleptics are mainly responsible for toxic epidermal necrolysis. This serious condition, considered an extensive and severe burn of the skin, explains its involvement in cutaneous and mucosal sequelae, including genital and ocular involvement [22].

CONCLUSION

Allopurinol, neuroleptics, antibiotics, and sulfasalazine were the most implicated drugs in our study. The

clinical profile we observed was as follows: Allopurinol and neuroleptics were mainly associated with DRESS syndrome and SJS/Lyell's syndrome, while antibiotics were responsible for conditions ranging in severity from PEAG to SJS. Allopurinol, neuroleptics, antibiotics, and sulfasalazine were linked to systemic involvement. In terms of prognosis, Allopurinol was associated with systemic and cutaneous-mucosal sequelae and significant mortality. On the other hand, neuroleptics did not result in any deaths due to their rapid identification as the suspected drug and immediate discontinuation.

Given the strong association with Allopurinol, it would be prudent to carefully consider the merits and drawbacks before prescribing it, while raising awareness among cardiologists, nephrologists, rheumatologists, and general practitioners.

According to some authors, initiating treatment with a dose not exceeding 100 mg could be an alternative to mitigate the severity of cutaneous reactions to Allopurinol. Further in-depth studies in this regard are necessary.

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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Our Dermatology Online

Brief Report

Beyond the skin: Unraveling the connection between atopic dermatitis and obsessive-compulsive disorder

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ABSTRACT

Background: Atopic dermatitis (AD) is a chronic skin disorder affecting up to 20% of the population characterized by a compromised skin barrier, elevated immunoglobulin E (IgE), and immune system dysregulation. Various factors, including genetic predisposition and environmental triggers, contribute to AD's pathogenesis. Treatment approaches include topical moisturizers, anti-inflammatory therapies, phototherapy, and systemic medications for severe cases. The condition is associated with allergic and autoimmune diseases, and elevated IgE levels may indicate allergic disorders or be associated with other conditions such as infections or cancer. There is a known link between AD and neuropsychiatric disorders, yet limited data exists on its connection to obsessive-compulsive disorder (OCD). **Materials and Methods**: This case report examines a thirty-year-old patient suffering from severe, persistent pruritus despite two years of topical steroid treatment. The patient had no significant medical history, recent travel, or medication use. Examination revealed scratch marks without primary lesions, and a skin biopsy showed dermal eosinophilia. Blood tests indicated eosinophilia and elevated IgE levels (7280 IU/mL), suggestive of allergic pathology, although allergy testing was negative. Treatment included montelukast, antihistamines, and desensitization, yet with no improvement after six months. Following psychiatric consultation, the patient was diagnosed with OCD, linked to sterilization obsessions exacerbated by the COVID-19 pandemic. **Results**: Treatment with systemic antidepressants and behavioral therapy led to significant symptom improvement. The diagnosis of allergic dermatitis was confirmed, and the OCD treatment improved the patient's quality of life. This case underscored the complex interaction between dermatological and psychiatric disorders. **Conclusions**: This case highlighted the importance of recognizing psychiatric comorbidities such as OCD in patients with atopic dermatitis. Early diagnosis and treatment may lead to better therapeutic outcomes. The bidirectional relationship between dermatological and psychiatric disorders calls for increased awareness and interdisciplinary collaboration in patient care. Further research into shared genetic and environmental pathways is essential for developing targeted interventions.

Key words: Atopic Dermatitis, OCD, Pruritus, Comorbidities

INTRODUCTION

Atopic dermatitis (AD) is a long-standing and chronic inflammatory skin condition that affects nearly 20% of individuals around the world [1]. This disorder is marked by a disruption in the skin's protective barrier, an elevation of immunoglobulin E (IgE) levels, and various immune system imbalances. The onset of AD is influenced by a combination of genetic susceptibility and environmental triggers, resulting in a multifaceted clinical presentation, often involving severe itching and eczematous rashes [2]. The immune system's heightened response in individuals with AD is evidenced by elevated IgE levels, which are frequently associated with allergy [3].

The management of AD is tailored to its severity and may range from basic treatments such as the application of moisturizers and topical anti-inflammatory medications to more potent therapies, including corticosteroids and

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calcineurin inhibitors. In more severe cases, patients may require advanced treatments such as phototherapy or systemic immunomodulators [4,5]. However, despite the availability of these therapies, the treatment of AD is often complicated by the presence of concurrent allergic and autoimmune conditions, including asthma, allergic rhinitis, and various food sensitivities, making the disease challenging to manage [6,7].

Beyond its obvious dermatological symptoms, AD has been increasingly associated with a range of neuropsychiatric disorders. Studies have identified connections between AD and conditions such as attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) [8]. However, research into the link between AD and obsessive-compulsive disorder (OCD), a condition characterized by recurring, intrusive thoughts and compulsive behavior, remains limited. This case study sought to investigate the potential relationship between AD and OCD, highlighting the complex interplay between dermatological and psychiatric disorders [9].

MATERIALS AND METHODS

We present the case of a thirty-year-old female patient who had been suffering from severe, chronic itching (pruritus) for two years, despite the regular application of topical corticosteroids. Her medical history did not reveal any notable contributing factors; there were no reported allergies, no recent travel history, and no recent introduction of new medications. This lack of significant medical background initially made it difficult to pinpoint a specific cause for her persistent symptoms.

Upon clinical examination, multiple excoriations, or scratch marks, were observed on her back, yet no primary lesions were visible, which is uncommon in cases of allergic skin disorders. Given the absence of clearly identifiable skin lesions, a skin biopsy was taken to further investigate the underlying cause. The biopsy revealed dermal eosinophilia, a key indicator often associated with allergic skin conditions. In addition to the biopsy results, blood tests showed pronounced eosinophilia and exceptionally high levels of immunoglobulin E (IgE), which peaked at 7280 IU/mL—strongly suggesting an allergic etiology. However, despite these suggestive findings, multiple allergy evaluations, including skin prick tests and serum-specific IgE assays, yielded negative results, providing no clear allergic triggers.

The patient's initial treatment plan included montelukast, a leukotriene receptor antagonist, along with antihistamines and a desensitization protocol aimed at decreasing her hypersensitivity responses. Despite adherence to this treatment regimen for six months, the patient experienced no significant relief from her symptoms. With the failure of these conventional therapies, a more extensive diagnostic approach was taken. This involved additional skin biopsies and repeated bloodwork, yet all further investigations continued to return inconclusive results, leaving the underlying cause unresolved.

Given the unresponsiveness to standard treatments and the absence of identifiable allergic triggers, a psychiatric evaluation was considered as part of a broader diagnostic framework. The psychiatric assessment led to a diagnosis of obsessive-compulsive disorder (OCD), with the psychiatrist attributing the elevated IgE levels and persistent itching to the patient's compulsive behaviors, particularly her obsession with cleanliness and sterilization, which had intensified due to the COVID-19 pandemic. Her excessive use of alcohol-based hand sanitizers contributed to the breakdown of her skin's barrier function, aggravating the chronic pruritus.

RESULTS

Following the diagnosis of obsessive-compulsive disorder (OCD), the treatment plan for the patient was comprehensively adjusted to include systemic antidepressants, specifically selective serotonin reuptake inhibitors (SSRIs), and was complemented by cognitive-behavioral therapy (CBT) tailored to address her compulsive behaviors and rituals. This combined psychiatric intervention, which integrated both pharmacological and psychotherapeutic approaches, resulted in notable and substantial improvements in both the patient's dermatological and psychiatric symptoms. Over the course of several months, there was a marked reduction in the intensity of her pruritus, a condition that had previously been severe and debilitating. Concurrently, her levels of immunoglobulin E (IgE), while still elevated compared to the general population, began to show a gradual decrease. This outcome underscores the critical importance of employing an integrated treatment strategy that encompasses both dermatological and psychiatric care, demonstrating its effectiveness in managing complex cases.

This case highlights the vital need to assess and address psychiatric comorbidities in individuals suffering from persistent dermatological conditions, particularly when traditional treatments fail to provide adequate relief. The growing body of literature increasingly supports the connection between atopic dermatitis (AD) and OCD. Emerging research suggests that the immune system abnormalities observed in AD patients may play a significant role in the development of OCD. Specifically, immune dysregulation associated with AD could potentially trigger neuroinflammatory responses, which may, in turn, exacerbate psychiatric symptoms [10,11]. This case exemplified the necessity of a holistic treatment approach, emphasizing the need for a multidisciplinary strategy that addresses both the dermatological and psychiatric dimensions of complex patient presentations.

DISCUSSION

The intricate bidirectional relationship between dermatological conditions such as atopic dermatitis (AD) and psychiatric disorders such as obsessive-compulsive disorder (OCD) underscores the critical need for a holistic and multifaceted approach to patient management. Extensive research has documented the impact of AD on mental well-being, revealing that the chronic inflammation and persistent pruritus associated with AD are strongly correlated with heightened incidences of anxiety, depression, and other mood disorders [12-14]. This relationship is thought to be driven by complex neuroimmune interactions, where sustained immune activation in AD leads to the production of pro-inflammatory cytokines. These cytokines have the capacity to cross the blood–brain barrier, thereby influencing neural circuits involved in mood regulation [13,14]. Similarly, psychiatric disorders such as OCD may also be associated with immune dysregulation, as some patients with OCD exhibit elevated levels of inflammatory biomarkers [15].

In the case of our patient, the excessive and prolonged use of alcohol-based sanitizers, driven by obsessions related to cleanliness and sterilization exacerbated her dermatological symptoms. This behavior compromised her skin barrier, creating a vicious cycle of increased pruritus and inflammation. It is evident that her OCD contributed significantly to the persistence of the symptoms, directly impacting her skin condition. This case highlights the crucial importance of integrating psychiatric evaluation and intervention in the management of patients with AD, particularly when conventional dermatological treatments fail to alleviate their symptoms.

Our observations are consistent with the growing body of research exploring the connections between AD and psychiatric disorders. While the precise mechanisms linking AD with OCD remain partially understood, it is likely that shared genetic and environmental factors play a significant role [16]. Further research is needed to elucidate these underlying mechanisms more clearly and to develop targeted therapeutic strategies for individuals grappling with both dermatological and psychiatric conditions. This case study underscores the necessity for a comprehensive and interdisciplinary approach to effectively address and manage complex patient presentations.

The bidirectional relationship between dermatological conditions such as AD and psychiatric disorders such as OCD highlights the necessity for a comprehensive approach to patient management. The effects of AD on mental well-being have been extensively documented, with research indicating that chronic inflammation and persistent pruritus associated with AD are linked to higher incidences of anxiety, depression, and other mood disorders.

CONCLUSION

This case highlights the profound and multifaceted relationship between atopic dermatitis (AD) and obsessive-compulsive disorder (OCD), illustrating the critical need for clinicians to remain vigilant about the potential for psychiatric comorbidities in patients presenting with dermatological conditions. The integration of psychiatric evaluation into dermatological care has been shown to significantly enhance the effectiveness of treatment strategies and improve the overall quality of life for affected individuals.

The bidirectional nature of the relationship between dermatological and psychiatric disorders underscores the necessity for heightened awareness and a comprehensive approach among healthcare providers. Dermatologists, in particular, who often act as the initial point of contact for patients with AD, must be especially attuned to the possibility of underlying psychiatric conditions. Addressing these comorbidities through timely diagnosis and integrated care may lead to more nuanced and effective treatment plans.

Future research is essential to further elucidate the common genetic and environmental factors that contribute to the co-occurrence of AD and OCD. A deeper understanding of these shared determinants will facilitate the development of more targeted therapeutic interventions. Moreover, incorporating psychiatric assessments into routine dermatological evaluations may greatly aid in the early identification of comorbid conditions, allowing for the formulation of personalized and comprehensive treatment strategies.

Recognizing and addressing the psychological dimensions of chronic skin disorders such as AD may lead to a more holistic approach to patient management. By integrating mental health considerations into dermatological care, clinicians can achieve improved outcomes in both dermatological and psychological domains, ultimately enhancing the overall well-being of patients.

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Our Dermatology Online

Case Report

Extensive condyloma acuminata: Complete remission after topical 5% imiquimod in an HIV patient

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ABSTRACT

Condyloma acuminata are genital warts caused by HPV [6,11]. The therapeutic arsenal includes chemical, immunomodulatory, and physical treatments. In seropositive patients, condyloma may be refractory to treatment. Herein, we report the case of extensive anogenital condyloma treated with 5% imiquimod monotherapy. A twenty-year-old, HIV-positive, female patient consulted for venereal vegetations evolving over the past four months. Multiple vegetative lesions with verrucous surfaces were found on the vulva together with cauliflower-shaped lesions on the anus. The dermoscopic and histological appearance was in favor of condyloma acuminata without signs of malignancy. The patient was initially started on trichloroacetic acid with no clear improvement and, then, administered 5% imiquimod at a rate of two applications per week. Complete remission was obtained after only four months. In HIV patients, condylomas present an important risk of extension, therapeutic resistance, and dysplastic lesions. In our case, imiquimod monotherapy was sufficient to achieve complete remission.

Key words: Condyloma, Imiquimod, Sexually transmitted infections

INTRODUCTION

Condyloma acuminata are genital or perianal warts caused primarily by human papillomavirus (HPV) types 6 and 11.

In seropositive patients and in homosexual males, the prevalence of anal HPV infection is particularly high (45% to 95%) [1]. As in HIV-negative individuals, genital warts may be refractory to treatment and tend to be transformed into giant warts (Buschke–Löwenstein tumors), whose main risks are the capacity for invasive growth, with high rates of recurrence after resection (66%) and a high incidence of malignant transformation (56%) into invasive squamous cell carcinoma [2].

The optimal strategy for this disease has not been fully determined. The therapeutic arsenal involves three methods: chemical treatments (podophyllotoxin, 5-fluorouracil, podophyllin, trichloroacetic acid), immunomodulatory treatments (imiquimod), and destructive or ablative physical treatments (cryotherapy, laser, electrosurgery, surgical excision) [2].

Herein, we present a case of extensive anogenital condyloma in an HIV-positive patient treated with 5% imiquimod monotherapy.

CASE REPORT

This was a twenty-year-old, HIV-positive patient with a history of unprotected sexual intercourse and on antiretroviral treatment for the past six months. The patient consulted for venereal vegetations evolving over the past four months with a rapid increase in size causing pruritus and itching with an important alteration in the quality of life.

A clinical examination revealed vegetative vulvar lesions with multiple verrucous surfaces of pinkish color and confluent (Fig. 1a). At the anal level, there were

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cauliflower-like vegetations, with the largest measuring 3 cm (Fig. 1b). There was no involvement of the oral mucosa. Anoscopic and rectoscopic examinations showed no intra-anal involvement. Hepatitis B and C and syphilis serologies were negative.

The dermoscopic pattern revealed a relatively long papillomatous structure in clearly separated fingers and mosaic structures. At the periphery of the lesions, there were scattered pigmentations. The vascular pattern was characterized by a glomerular and dotted appearance surrounded by a whitish halo (Fig. 2).

We completed a histological study in order to eliminate a degeneration, which revealed a polypoid formation covered with a squamous mucosa. The lining was hyperplastic and papillomatous, with hyperthokeratosis and neutrophilic exocytosis. The dermis was the site of a diffuse inflammatory infiltrate consisting of neutrophils, eosinophils, lymphocytes, and plasma cells with numerous congestive vessels. There were no signs of malignancy. This concluded to the appearance of condyloma acuminata.

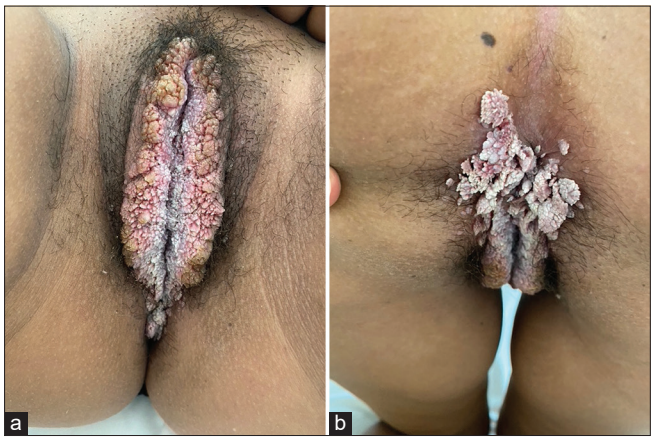

Figure 1: (a) Vegetative vulvar lesions. (b) Cauliflower perianal lesions.

Therapeutically, we put the patient on 50% trichloroacetic acid for two months without any clear improvement; then, we administered 5% imiquimod cream twice a week. After four months, there was a clear regression of the lesions and a significant improvement in the patient's quality of life, with a follow-up of ten months (Fig. 3).

DISCUSSION

The correlation between human papillomavirus (HPV) and HIV infection has been the subject of several studies, and numerous case reports exist in the literature describing a giant form of condyloma acuminata, perianal involvement, extensive lesions, and severe painful ulcerations more frequent in the HIV-positive group.

In an Indian study by Shikha Chugh et al. [3], a quarter of HIV-positive patients (sixty patients) with genital warts were resistant to conventional treatment.

Given the increased risk of dysplasia and squamous neoplasia in HIV-positive patients, the presence of atypical warts or multiple relapses should be grounds for HIV screening [3].

Imiquimod is a nucleoside analogue of the imidazoquinoline family. As an immune response modifier, it activates natural killer cells, macrophages, and other immune cells via toll-like receptors [4].

The topical application of 5% imiquimod stimulates both innate and cell-mediated systems to tumor and viral antigens. Interferon α, IL 1, 6, 8, 10, and 12 are produced by monocytes, keratinocytes, Langerhans cells, and T lymphocytes to inhibit viral activity and promote

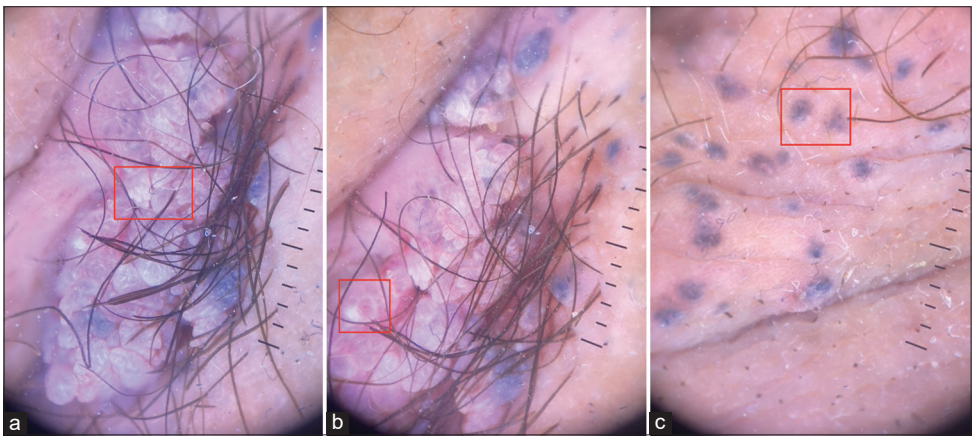

Figure 2: (a-c) Dermoscopy of the lesions: papillomatous structures in fingers and mosaics and dotted vessels with a whitish halo and pigmentation.

Table 1: Previous cases of Buschke–Löwenstein tumors treated with imiquimod reported in the referenced literature

Author	Age and Sex	Duration	Areas	Treatment and Results
Erkek et al. [6]	50 years Male	8 years	Scrotum, base of the penis	Oral acitretin 50 mg/day+5% imiquimod (3 times/week) Imiquimod stopped after four months. At six months, complete regression.
Suarez-Ibarrola et al. [7]	3 years Male	2 years, HIV-positive	Scrotum, base of the penis, foreskin, perineal area, and anal sphincter	Initially, 5% imiquimod (3 times/week) with no visible improvement. Electrosurgical resection. Then, IFN-alpha (2 million units/week)
Dinleyici et al. [8]	2 years Female	1 year and a half	Perianal	Topical cryotherapy: aggravated lesions. 5% imiquimod (3 times/week) for 12 weeks: complete elimination.

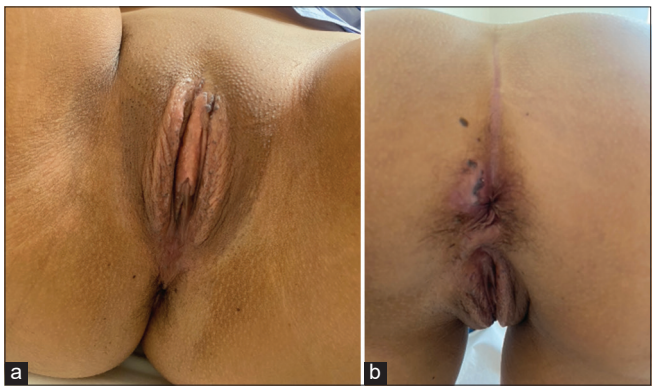

Figure 3: Disappearance of the lesions and a remission after treatment.

cell-mediated immune responses. B lymphocytes also proliferate to produce immunoglobulins. Via stimulated apoptosis, the drug inhibits associated pathological angiogenesis [5]. Therefore, it serves as a potent antiviral and antitumoral agent and provides a protective cytotoxic immune response against HPV.

5% imiquimod cream represents a novel treatment of BLT and is approved by the U.S. FDA [6], which has always been traditionally combined with other modalities; to electrosurgical resection and INF alpha in seropositive subjects [7], to oral acitretin [6], finally to cryotherapy; although, some authors have reported worsening after application, particularly, in perianal locations [8] (Table 1).

Although combination therapy remains the mainstay of treatment for Buschke–Löwenstein tumors, standalone treatment with imiquimod may be attempted in special cases. An Indian team successfully treated a case of a penile localization after sixteen weeks of imiquimod monotherapy resulting in the complete disappearance of the lesion and a relapse-free period of at least five years in a patient who was not a candidate for surgery and oral retinoids [4]. Combaud et al. successfully treated exophytic vulvar cauliflower warts after twelve weeks with 5% imiquimod alone with a marked regression in the lesions accompanied by an improvement in symptoms with no recurrence reported during a follow-up period of three years [9].

In our case, monotherapy with imiquimod was sufficient after a period of sixteen weeks, which saved the patient from an irritant treatment with trichloroacetic acid and potentially damaging surgical means.

A meta-analysis comparing the different local therapeutic modalities in the treatment of genital warts including 6371 patients demonstrated a superior efficacy of 5% podophyllotoxin compared to 5% imiquimod for the elimination of lesions (odds ratio: 194) yet was associated with a higher overall adverse event rate. 15% sinecatechins ointment (odds ratio: 21) was significantly less effective than 5% imiquimod cream in clearing lesions. Idoxuridine, polyhexamethylene biguanide, and cidofovir have shown therapeutic efficacy comparable to conventional therapies [10].

CONCLUSION

Condyloma acuminata is more frequent, more extensive, and often multifocal and resistant to conventional treatment in HIV-positive individuals. They represent a significant risk of dysplastic lesions and malignant transformation, especially in cases of advanced immunosuppression. We emphasize, through this observation, the importance of a well-conducted medical treatment in monotherapy with imiquimod in remission. Our result was similar to some cases reported in the literature.

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. Informed consent was obtained from all individual participants included in the study.

Statement of Informed Consent

Informed consent for participation in this study was obtained from the patient.

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Our Dermatology Online

Case Report

Acute cutaneous disseminated histoplasmosis and secondary syphilis as an initial presentation in an HIV patient

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ABSTRACT

Herein, we report a case of cutaneous disseminated histoplasmosis associated with secondary syphilis in a 32-year-old male with a history of progressive weight loss of 30 kgs and HIV diagnosis for five months. He presented with a generalized dermatosis with a predominance on the face, trunk, and upper limbs, consisting of multiple papules, nodules, and plaques of 1 month of evolution. During the diagnostic approach, viral load above 400,000 copies/ml, CD4 count of only 1 cell/μL, and histopathological features of histoplasmosis along with disseminated disease, in addition to a positive PCR test for syphilis. The treatment for syphilis was penicillin G-benzathine for three weeks and, for histoplasmosis, amphotericin B for twenty-one days and itraconazole for one year. The patient was considered clinically and microbiologically cured of both conditions.

Key words: Acquired immunodeficiency syndrome, Human immunodeficiency virus, *Histoplasma capsulatum*, *Treponema pallidum*, Cutaneous disseminated histoplasmosis, Secondary syphilis

INTRODUCTION

Histoplasmosis is a systemic fungal infection caused by a dimorphic fungi *Histoplasma capsulatum* that occurs primarily in immunocompetent and immunocompromised patients. In patients with acquired immunodeficiency syndrome (AIDS), histoplasmosis is the most common endemic mycosis and is an AIDS-defining disease and a leading cause of death in people living with HIV/AIDS, with mortality rates ranging from 13% to 48% [1,2].

Histoplasmosis may be asymptomatic or may cause self-limiting flu-like symptoms or pneumonia in immunocompetent individuals. Although, under immunosuppressive conditions such as AIDS patients, it occurs as acute progressive disseminated histoplasmosis or severe pneumonia. Most cutaneous disseminated cases do not have obvious pulmonary involvement, yet it is believed that they may spread to the skin from an initial pneumonic focus. It is important to note that there are no pathognomonic lesions due to the polymorphic nature of cutaneous histoplasmosis, which usually occur on the face and neck, yet may occur in any clinical topography, including palms and soles, as well as in all mucous membranes (oral, anal, and genital) [1,3]. The dissemination of the disease to various organs and systems, such as the heart, adrenal glands, eyes, meninges, has been reported. Most cases are fatal, especially those associated with AIDS [3,4].

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Herein, we present a case of cutaneous disseminated histoplasmosis (CDH) and secondary syphilis in an immunocompromised patient with a recent diagnosis of HIV.

CASE REPORT

A 32-year-old male presented with a generalized dermatosis predominantly on the face, trunk, and upper limbs, consisting of multiple papules, nodules, and plaques of 1 month's evolution. On interrogation, the patient reported progressive weight loss of 30 kg and an HIV diagnosis five months previously on antiretroviral therapy (ART) with Triumeq (Dolutegravir, Abacavir, Lamivudine).

A dermatological examination revealed a generalized dermatosis with the involvement of the palms and soles, consisting of multiple papules, nodules, and erythematous plaques with scaling on the surface, some ulcerated or with central umbilication, some with a warty appearance and some with necrotic areas and crusts on the surface (Fig. 1).

The rest of the physical examination revealed whitish plaques compatible with oral candidiasis in the oral cavity adhering to the hard palate and 2 cm of hepatomegaly and splenomegaly in the abdomen, without other relevant findings.

The clinical diagnosis of CDH was suspected based on the cutaneous findings and complementary studies were requested. The hemogram revealed pancytopenia (normocytic anemia, normochromic WHO grade III (Hb: 6.10 g/dL), leukopenia at the expense of lymphopenia (0.3 thousands/µL), and thrombocytopenia (146000/µL). He also had hypoalbuminemia (1.6g/dL), elevated liver enzymes (serum glutamic-oxaloacetic transaminase: 172 units/L, serum glutamic-pyruvic transaminase: 134 units/L), and elevated alkaline phosphatase: 307 units/L. Viral load resulted with 479,063 copies/mL and CD4 T lymphocyte count with only 1 cell/µL. Acute phase reactants were elevated (ESR 73 mm/hr, CRP 12.99 mg/dL). A simple chest CT scan was performed, which highlighted a ground glass nodule in the peripheral field of the right lower lobe and a left basal consolidation.

Multiple cultures and stains were performed in search of fungi and mycobacteria (members of the *Mycobacterium tuberculosis* complex and non-tuberculosis *Mycobacteria*) in different tissues and

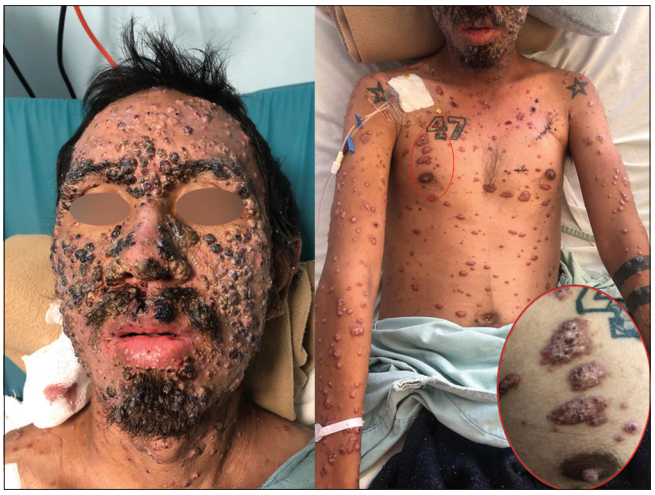

Figure 1: Left: Nodules and papules, some umbilicated and others with crusts and/or necrosis in a patient with CDH & secondary syphilis. Right: Multiple erythematous nodules and plaques, some umbilicated and others with crusts and scales located on the anterior and posterior thorax and arms.

secretions, among which only the urinary antigen for *Histoplasma* was positive (greater than 15 ng/m). Intracellular yeasts were also observed in a smear taken directly from the skin nodule by Wright staining. PCR for *Treponema pallidum* in the blood was also found to be positive.

A skin biopsy report showed that, in the cytoplasm of histiocytes and giant cells, yeast structures with capsule-like reinforcement and peripheral clear spaces were identified (Fig. 2). Therefore, the diagnosis of HCD and secondary syphilis was established.

The patient received initial antifungal treatment with amphotericin B deoxycholate 1.0 mg/kg/day for fourteen days and maintenance with itraconazole 200 mg three times a day for three days and then 200 mg twice a day for one year. Penicillin G benzathine 2,400,000 IU IM was administered weekly for three weeks to treat syphilis. The lesions disappeared completely one year after treatment (Fig. 3). The patient was considered clinically and microbiologically cured of both conditions.

DISCUSSION

With the increasing number of patients with AIDS, a number of unusual clinical manifestations are being observed, and it is important to be aware of them. Immunocompromised patients with disseminated histoplasmosis usually present with other symptoms such as fever, fatigue, anorexia, and weight loss and

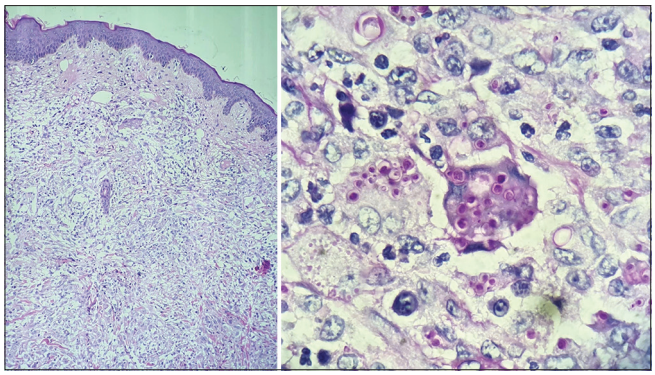

Figure 2: Skin biopsies. Left: Panoramic: Dense granulomatous chronic inflammatory infiltrate consisting of lymphocytes, plasma cells, histiocytes, and giant cells multinucleated (H&E, 10x). In the granulomatous process with histiocytes and giant cells, yeast cells with capsule-like reinforcement (PAS, 80x).

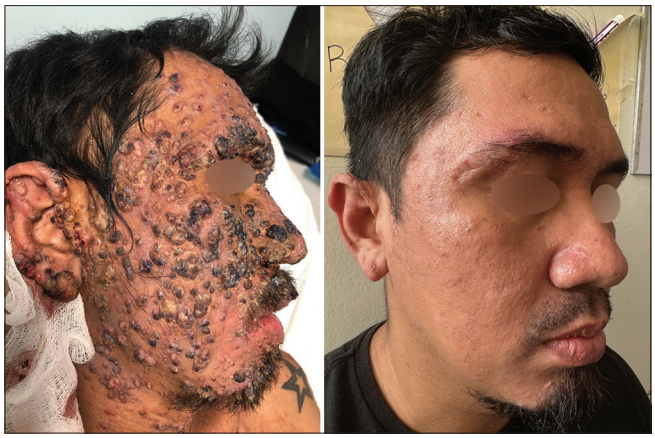

Figure 3: Left: Basal process with nodular and papular lesions on the face. Right: Resolution of lesions after one year of treatment.

even with such an overwhelming infection manifested by shock and multiple organ failure [1]. Physical examination demonstrates hepatosplenomegaly and diffuse lymphadenopathy in half of the patients [5].

The cutaneous lesions of histoplasmosis are non-specific and highly polymorphic, making diagnosis by physical examination virtually impossible. Immunosuppressed patients, including HIV-infected patients, may present with mucocutaneous ulcers or erosions, as well as multiple erythematous papules or nodules with desquamation or crusting, or some may even present with a mollusk-like appearance or necrotic areas. Other manifestations may include abscesses, ulcers, cellulitis, purpuric lesions, and panniculitis, including palmo-plantar lesions (also common in secondary syphilis) [3,6,7].

On the other hand, malignant syphilis is an uncommon form of secondary syphilis associated with HIV infection. The clinical presentation is characterized by necrotic nodules and generalized ulcerated lesions similar to those of histoplasmosis [8]. Thus, although the biopsy diagnosis is compatible with histoplasmosis, it cannot be excluded that some of the dermatologic lesions present in the patient were also due to syphilis [9]. Therefore, in our patient, the lesions of both diseases could coexist.

According to a study on patients living with HIV in Europe, 38.5% of the patients with histoplasmosis had a concomitant opportunistic infection, the most common being invasive candidiasis, *Pneumocystis jirovecii* pneumonia, and mycobacterial infection, and only one patient was found with syphilis [4].

General laboratory studies may reveal pancytopenia and elevated liver enzymes and markers of inflammation, including ESR, C-reactive protein, and ferritin [5]. Adequate diagnosis for histoplasmosis includes culture, biopsy, tissue histochemical stains, body fluid aspiration cytology smears, and antigen and antibody testing (serology). Culture is the gold standard for diagnosis, yet it takes days or even weeks to test positive and is, therefore, impractical as a criterion for initiating treatment [2,3,10].

However, in acute or progressive CDH in AIDS, because of the high fungal burden, blood culture and antigen testing are highly positive (95% and 86%, respectively) and serology is low (83% in immunosuppressed patients compared to 100% in non-immunosuppressed patients) [2,3].

Antigen detection tests have higher performance in diagnosing disseminated histoplasmosis in people living with HIV, with a sensitivity of 95% and a specificity of 97%. Antibody testing had a specificity of 100% and a sensitivity of 58%, probably because these individuals are highly immunosuppressed. Molecular testing by DNA detection has shown high diagnostic accuracy (sensitivity of 95%, specificity of 99%), yet the limitation is the lack of cost-effectiveness [10].

In patients with HIV/AIDS, it may be clinically simulated by deep fungal infections (Cryptococosis, *Talaromycosis-marneffei*, coccidioidomycosis, leishmaniasis and pneumocystosis), so it is important to differentiate it early to initiate targeted treatment. It is usually associated with advanced immunosuppression in AIDS, with CD4 counts less than 150 cells/µL [2]. It is important to highlight that our case had a viral load

of almost 480 thousand copies and one CD4, which implies a state of severe immunosuppression, and that explains the reason for the widespread development of both diseases.

In terms of treatment, severe disease should be treated with 1–2 weeks of induction therapy with liposomal amphotericin B, followed by itraconazole monotherapy for 12 months [10]. The liposomal amphotericin B is preferred to deoxycholate because it has been shown to have higher response rates (88% vs. 64%) and to be associated with fewer side effects. The standard dose of liposomal amphotericin B is 3 mg/kg/day, with a range of 3–5 mg/kg/day, for two weeks, and upon completion of the initial amphotericin B therapy, patients should be placed on oral itraconazole (200 mg three times daily for three days and then 200 mg twice daily) for a total of at least twelve months [11-13]. The patient was treated according to the latest treatment guidelines and showed adequate clinical evolution.

Relapse rates may be as high as 90% in those who do not receive maintenance therapy. Relapse most commonly occurs 6 to 18 months after the discontinuation of induction therapy [12,14].

Conditions for discontinuing itraconazole therapy in AIDS patients with disseminated histoplasmosis on antiretroviral therapy include the following: patient has completed at least 12 months of itraconazole, fungal blood cultures are negative, serum and urine antigen levels are less than 4 U/mL (less than 2 ng/mL in recent studies), CD4 count is greater than 150 cells/mm [5,11-13].

CONCLUSION

The cutaneous manifestations of CDH are highly variable and even more so when they are associated with syphilitic secondary symptoms. In this case, we emphasize dermatological lesions that may not be characteristic of the disease. However, we must analyze the clinical context of the patient and suspect it early, since there are multiple differential diagnoses to which patients with HIV and a low CD4 count are susceptible. This case was an excellent example of the first manifestations in the debut of HIV-AIDS. They may be associated with various infections such as histoplasmosis (common in tropical areas), syphilis, and other sexually transmitted infections.

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.

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Our Dermatology Online

Case Report

Nervous leprosy revealed after treating atopic eczema

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ABSTRACT

Herein, we report a case of pure nerve leprosy revealed after the treatment of pyoderma in the context of atopic dermatitis. Questioning revealed a history of treated leprosy in the grandfather and asthma in the mother. On examination, he presented with multiple, ulcerative, crusted lesions on the backs of his hands, armholes, and on either side of the popliteal creases. Antibiotic therapy combined with an antiseptic, 5% urea Vaseline and betamethasone ointment led to a marked improvement in the lesions. Three weeks later, he returned with pain and paresthesia in his wrists and knees. There was hypertrophy of the peripheral nerves and palmar-plantar hypoesthesia. The condition was reactive. The patient was treated with OMS MB polychemotherapy and oral corticosteroids. He healed without sequelae.

Key words: Nervous leprosy, Atopic dermatitis, Impetigo

INTRODUCTION

The isolated involvement of peripheral nerves by *Mycobacterium leprae* without cutaneous manifestations defines pure nervous leprosy. Ulcerations and thermal burns of the hands and feet are often indicative. This entity remains a mystery due to the absence of cutaneous lesions. In daily practice, pure nervous leprosy is often overlooked due to the absence of skin lesions. Late diagnosis exposes to complications of the disease. Herein, we report a case presenting with an infected eczema.

CASE REPORT

A 55-year-old farmer from Bougouni, 180 kilometers from Bamako, consulted in August 2015 for ulcerative, crusted lesions on the limbs. The patient reported a history of treated leprosy in his grandfather and asthma in his mother. The symptoms began with diffuse itching two weeks before the dermatological consultation, associated with vesicular lesions on the folds of the limbs, evolving into ulcerative, crusted lesions. He received unspecified medications and traditional products without success. An examination revealed a poorly hygienic individual with dry skin. Multiple ulcerative, crusted lesions were present on the back of the hands, armpits, and on both sides of the popliteal creases (Fig. 1). The rest of the clinical examination was unremarkable. The diagnosis of infected atopic dermatitis was established. Antibiotic therapy, antiseptic, 5% urea Vaseline, and betamethasone ointment led to a clear improvement of the lesions. Three weeks later, he returned with pain and paresthesias affecting the wrists and knees. Joint examination was unremarkable, yet neurological examination revealed hypertrophy of the ulnar, radial, and common peroneal nerves. Palmo-plantar hypoesthesia was present. Acid-fast bacilli were not identified in the skin smear (Fig. 2). A biopsy of a branch of the radial nerve showed hypertrophied and dissociated nerve fibers infiltrated by lymphocytes and histiocytes. Acid-fast bacilli were not identified in the biopsy. A diagnosis of reactive leprosy was established. General corticosteroid therapy with oral prednisone 1 mg/kg/day, tapering over three months,

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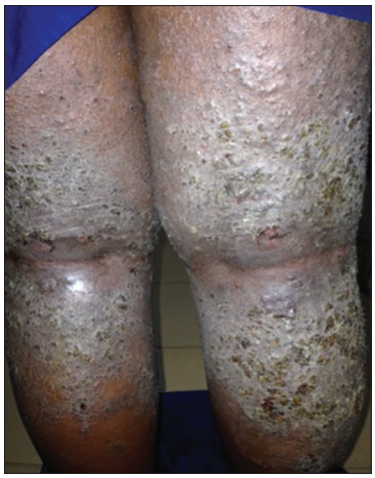

Figure 1: Multiple bilateral and symmetrical crusted vesicular lesion on either side of the hollow of the knees.

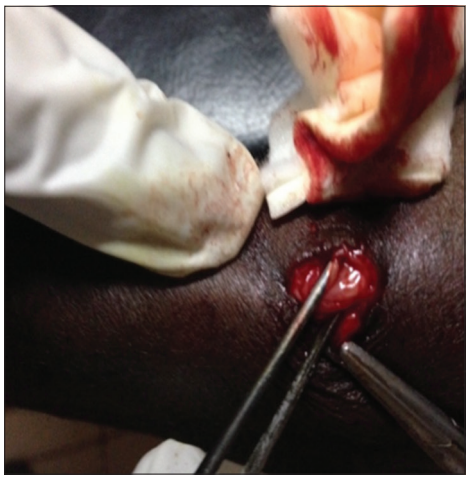

Figure 2: Inserted after a biopsy of a branch of the radial nerve.

resulted in significant pain improvement, combined with WHO multi-bacillary polychemotherapy (MDT) with rifampicin, clofazimine, and dapsone. The patient showed favorable progress after twelve months. No sequelae of leprosy were observed, and the patient resumed normal activities.

DISCUSSION

Herein, we reported a case of pure nervous leprosy revealed after the treatment of secondary pyoderma in atopic eczema lesions. The diagnosis relied on hypoesthesia and nerve hypertrophy. Other diagnostic tests such as nerve conduction velocity measurement or nerve ultrasound were not possible in our context [1]. Histology plays an important role in the diagnosis. However, acid-fast bacilli were not isolated in our patient. Nerve biopsy practice is difficult and reserved for qualified personnel. In our country, this examination was not feasible in peripheral centers, as the country has only one cutaneous histopathology center. The absence of acid-fast bacilli in Ziehl–Neelsen staining does not question the leprosy diagnosis. Indeed, the presence of hypoesthesia associated with nerve hypertrophy is sufficient to diagnose leprosy. Pure nervous leprosy remains a rare entity [2]. In Brazil, 144 cases were described between 1997 and 2010 in a specialized center [3]. It is a particular clinical form due to the absence of skin lesions. It remains a diagnostic challenge due to the absence of cardinal signs of leprosy. According to some authors, pure nervous leprosy may not be a stable clinical form. Indeed, 20% of cases will develop skin lesions during the course of the disease. Indian authors estimate its prevalence to be between 4% and 8% of all leprosy cases. In our case, atopic eczema lesions, with pruritus as the main functional sign, could mask paresthesias induced by leprosy-related neuropathy. The treatment of eczema lesions and infection eradication eliminated pruritus, revealing pain and paresthesias. This allowed for a neurological examination and consideration of leprosy. It is worth noting that pruritus and pain, two functional signs, may attenuate, and in the presence of intense pruritus, pain may be diminished [4]. For atopic dermatitis specifically, studies have shown that stimuli normally triggering pain may also induce itching when applied to the injured skin of patients with this condition [5]. This hypothesis may explain the exacerbation of pruritus compared to paresthesias in the presence of eczema lesions masking the neurological manifestations of leprosy. Neuroimaging studies have also shown altered activity in certain regions of the brain in patients with atopic dermatitis in contrast with healthy controls [6]. Therefore, after treating skin symptoms (pruritus and inflammation), paresthesias and pain may emerge. In this case, what would have been the outcome if the patient had not been detected at this stage? Nervous disease would have spread with infirmities in the extremities. The general corticosteroid therapy's role in managing leprosy neuropathy has been described by authors [7,8]. Skin lesions could have appeared during the evolution, as revealed in the literature, with 20% of pure nervous leprosy cases developing skin lesions [3].

CONCLUSION

Pure nervous leprosy is a rare clinical form. Our case is unique due to the association with atopic eczema, with pruritus as its functional sign that may mask paresthesia. In leprosy-endemic areas, palpation of

peripheral nerves should be systematic in the presence of unexplained polyarthralgia.

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.

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Our Dermatology Online

Case Report

High-frequency ultrasonographic pattern of cutaneous sarcoidosis: A case report

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ABSTRACT

Sarcoidosis is characterized by the presence of non-caseating epithelioid granulomas. Its etiology is not fully understood. A range of predisposing factors for the development of sarcoidosis has been documented, yet it remains a diagnostic and therapeutic challenge for contemporary medicine. The literature documents cases of cutaneous sarcoidosis induced by laser therapy. Herein, we present the case of a 38-year-old female who was diagnosed with cutaneous sarcoidosis following a fractional CO_2 laser procedure. The patient's diagnosis procedures were supported by high-frequency ultrasonography (HFUS). The gold standard to diagnose sarcoidosis is histological examination, while HFUS, an easy-to-use and non-invasive diagnostic tool, allows for precise monitoring of the disease course and serves as an additional instrument to confirm the diagnosis.

Key words: Skin pathology, Sarcoidosis, Diagnostic imaging

INTRODUCTION

Sarcoidosis is a systemic disease characterized by the formation of non-caseating epithelioid granulomas in various organs. The development of sarcoidosis is caused by an enhanced immune response triggered by interacting genetic and environmental factors [1]. Also, local exposure to certain substances such as silica or silica dust [2], microorganisms such as *Mycobacterium tuberculosis* [3] *Propionibacterium acnes* [4] and medications used in highly active antiretroviral therapy [5] are considered triggering factors for cutaneous sarcoidosis. In the available literature, there are cases described in which laser therapy induced cutaneous sarcoidosis [6,7]. The most common sites of sarcoidosis are the lungs and thoracic lymph nodes, which are affected in over 90% of cases, although the disease may involve any organ [8]. In Europe, most cases are reported in the northern regions, with an estimated prevalence of around 60 cases per 100,000 [9]. Cutaneous sarcoidosis is more common in young people, females, non-smokers, and those living in rural areas [10].

CASE REPORT

A female patient aged 38 without chronic diseases and genetic predisposition was admitted to the University Department of Dermatology, Venereology, and Allergology in Wrocław because of the appearance of erythematous and infiltrative skin lesions on her face, one month after laser therapy (Fig. 1). The procedure was performed by a non-medical aesthetician, utilized a 125 mm handpiece with an 8 mm spot size, a density of 25%, and an energy output of 12 watts. The laser therapy comprised a single session.

The first medical consultation was at the outpatient department after one month of laser treatment, herpes virus infection was initially suspected, and acyclovir

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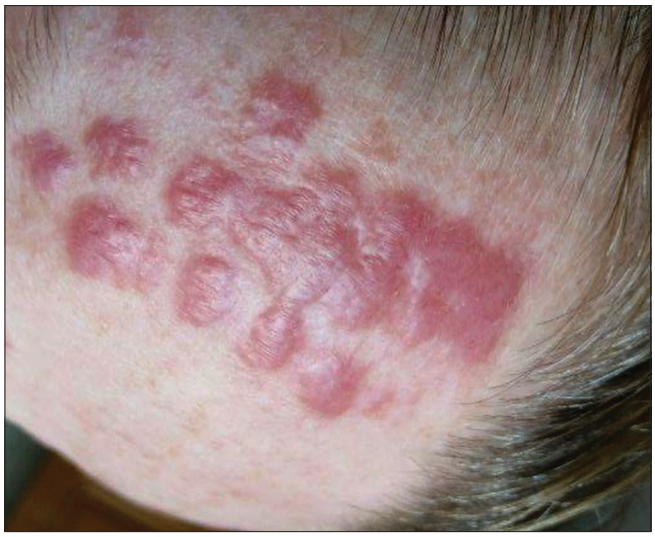

Figure 1: The patient's forehead with numerous erythematous, infiltrated skin changes. Characteristic iatrogenic pattern as the lesions were induced by laser.

was administered, yet this did not yield positive results. Subsequently, a treatment regimen involving topical clobetasol propionate at a concentration of 0.5 mg/g twice a day and oral chloroquine at a dose of 250 mg b.i.d. for two months were implemented. This treatment resulted in a reduction of erythema and infiltration, yet the skin lesions recurred after the discontinuation of the medication.

Consequently, the patient was admitted to the University Department of Dermatology, Venereology, and Allergology for further diagnostics. A skin biopsy was performed, and histological examination revealed granulomatous inflammation mainly in the superficial dermis, without the involvement of the subcutaneous tissue. The confluent granulomas consisted of epithelioid histiocytes with abundant eosinophilic cytoplasm and oval vesicular nuclei. Several multinucleated giant cells were present. The granulomas were surrounded by several adjacent lymphocytes ("naked granulomas") and a fibrotic border in the dermis. Discrete, small, central foci of fibrinoid necrosis were present. The epidermis showed mild acanthosis. The histological picture confirmed cutaneous sarcoidosis (Fig. 2). A high-frequency ultrasonographic image of a skin lesion revealed the broad-band hypoechogenic zone (0.2 mm) interpreted as infiltration in the granulomatous pattern located under the epidermis (Fig. 3).

A chest X-ray, including the lung hilum, an abdominal and peripheral lymph nodes sonography was performed,

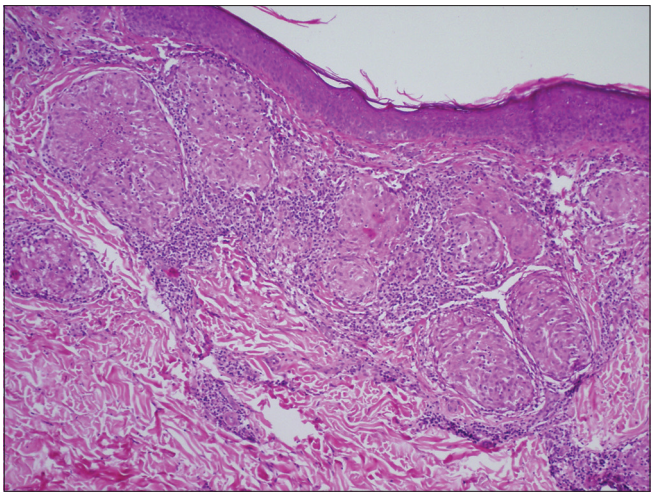

Figure 2: The histological features confirmed cutaneous sarcoidosis (H&E; 100x).

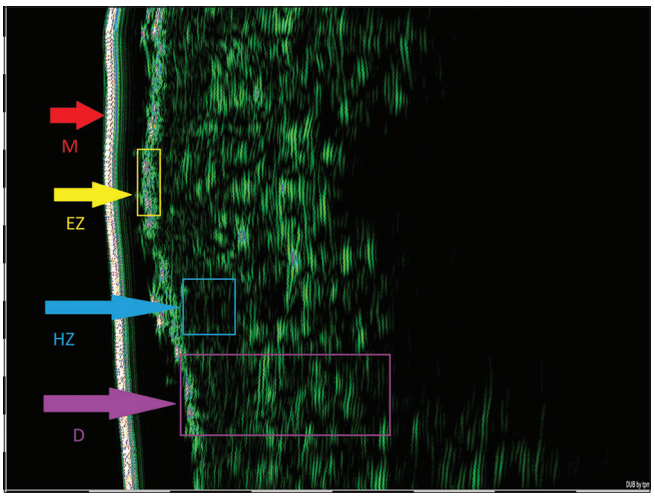

Figure 3: Infiltration in the dermis. Characteristic pattern of the hypoechogenic shadow (hypoechogenic zone, HZ) (sonographic imagine, 22.5 MHz); M–membrane, E–entry zone, HZ–hypoechogenic zone, D–dermis.

revealing no pathological changes. The patient was discharged from the hospital with recommendations to continue treatment with tacrolimus 0.1% ointment b.i.d. and clobetasol 0.05% cream b.i.d., which resulted in a slight improvement.

After two months, the patient was hospitalized again. The erythematous, infiltrated skin lesions had slightly decreased in intensity since the previous hospitalization and were mainly located on the forehead, cheeks, and nose. Laboratory tests, which were performed at that time, were within normal limits, and the Quantiferon test was negative. The treatment was changed to subcutaneous methotrexate at a dose of 15 mg p.w., yet due to dissatisfaction with the treatment results, methotrexate was replaced with prednisone. In the

subsequent phase of treatment, the prednisone dose was gradually reduced (20–10–5 mg daily), which resulted in positive effects and the reduction of skin lesions. After three months, an HFUS examination was performed, which showed a smaller hypoechogenic zone (0.1 mm).

DISCUSSION

High-frequency ultrasound (HFUS) is a non-invasive and inexpensive diagnostic tool in dermatology. The range that it operates on goes from 20 MHz up to 50 MHz [11]. In our case, we used the tpm (taberna pro medicum) GmbH device with a head of a 22.5 MHz frequency, 100 μm width, and a length of 12.8 mm. Because of its small cost and availability, it may dramatically expedite diagnosis during wait time for methods such as MRI and TK [12]. It is also non-invasive compared to histopathology, in which a patient might not give his permission for a biopsy. Although the cost and invasion of this method is minimal, its diagnostic capabilities are on par with other less available tools [13].

It is important to note that, in the literature, we found only two studies describing the use of HFUS in monitoring cutaneous sarcoidosis [14,15]. In a study by López-Llunell et. al [14], sarcoidosis lesions were described as nodules with reduced echogenicity in the skin or subcutaneous tissue, or as pseudonodules, which exhibit increased echogenicity in the surrounding subcutaneous tissue. Furthermore, the longer evolution of sarcoidosis seems to correspond to septal involvement rather than only the lobular pattern in subcutaneous sarcoidosis. Also, a clear correlation was demonstrated between the mean brightness of HFUS images and the results of CSAMI (Cutaneous Sarcoidosis Activity and Morphology Instrument), as well as the histological involvement of the dermis with granulomas [15].

CONCLUSION

Overall, the findings underscore the importance of vigilant monitoring and comprehensive diagnostic approaches in managing cutaneous sarcoidosis. Additionally, HFUS seems to be an especially helpful, non-invasive diagnostic tool for cutaneous sarcoidosis, and further research is needed to cement HFUS in everyday medical use.

Consent

Clinical research is based on the Declaration of Helsinki. All personal details of the patients are kept confidential.

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Our Dermatology Online

Case Report

Huge pigmented Bowen's disease: A rare case report

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ABSTRACT

Bowen's disease is an *in situ* squamous cell carcinoma with the potential to turn into invasive carcinoma. Giant Bowen's disease is its unusual variant with fewer reports, which poses a problem in the differential diagnosis with other pigmented lesions, especially when seen in sun-unexposed areas. It requires a joint effort of the dermatologist and surgeon to plan the line of management. Herein, we report a case of a seventy-year-old female patient with a large, multi-colored, asymmetric plaque with surface erosion in the left upper and outer gluteal region extending onto to the lateral thigh. Wide excision was done with a one-year follow-up showing no recurrence.

Key words: Bowen's disease, Squamous cell carcinoma, Rare variant, Wide excision

INTRODUCTION

Bowen's disease is one of the major histological types of non-melanoma skin cancer. In 1912, Professor John T. Bowen from Boston described this slow-growing premalignant cutaneous neoplasm as a form of *in situ* SCC with the potential to progress to invasive carcinoma [1]. Most studies have revealed a slight female preponderance [2]. Lesions are usually solitary, rarely multiple, mostly noticed in the head and neck region. However, the cheeks and lower legs are more likely to be affected in females [3]. They are usually asymptomatic, yet larger lesions may be pruritic and reach several centimeters in diameter. The giant form typically presents as a large, asymptomatic, reddish-brown plaque, scaly, with well-defined borders, and slowly growing. It affects any site, most frequently in sun-exposed areas. This intra-epidermal carcinoma is more common in the elderly. The pigmented/giant variant is relatively rare, with few reports in the literature. It poses difficulties in diagnosis and treatment. Histopathology is the gold standard diagnostic modality. Herein, we report a case of giant pigmented BD in a seventy-year-old female patient in a photo-protected site due to its rarity.

CASE REPORT

A seventy-year-old elderly female patient with no systemic diseases/immunosuppression presented with asymptomatic, reddish-brown discoloration of the skin with irregular borders with a variety of colors, approximately 7.5 cm in diameter, on the left upper and lateral buttocks extending onto lateral thighs for the past 11/2 years (Fig. 1). There was enlargement and darkening of the skin lesions for the past five months, which caused panic in the patient and relatives, who prompted her to seek treatment. There was no history of previous pre-existing skin diseases, cutaneous carcinomas, or arsenic exposure. Preoperative elliptical skin biopsy was taken and the H&E stained histopathology report revealed remarkable keratinocytes atypia with loss of cell polarity and the presence of some dyskeratotic cells, as well as an irregular and pronounced increase in melanin pigmentation in keratinocytes, both in the basal and in the scaly layer, characterizing pigmented giant BD (Figs. 2a and 2b). Owing to the mega-sized lesion, a wide excision was done (Figs. 3a and 3b). The margins were free of invasion by histopathology. The patient is regularly followed up (Fig. 4).

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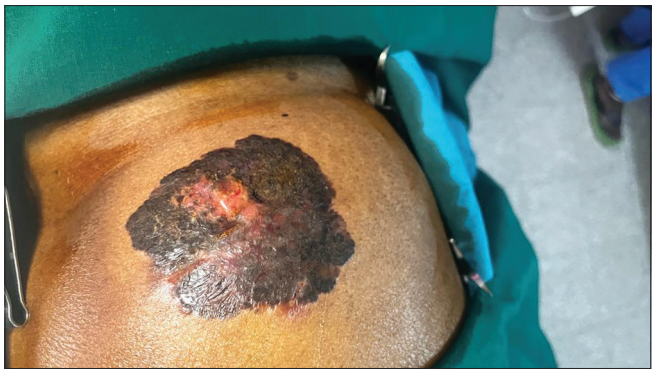

Figure 1: Giant Bowen's disease: A single, large, well-defined, multi-colored plaque.

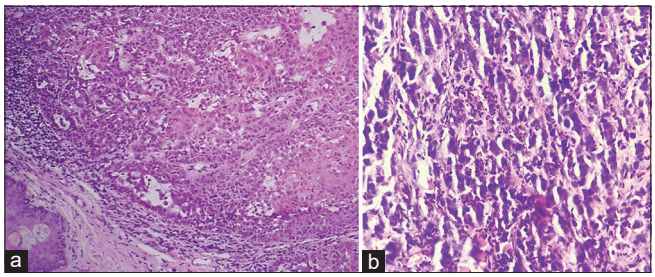

Figure 2: (a) Staining showing full thickness atypia (H&E; 10x). (b) Staining showing areas of hyperchromasia, pleomorphism, and atypical mitosis (H&E; 40x).

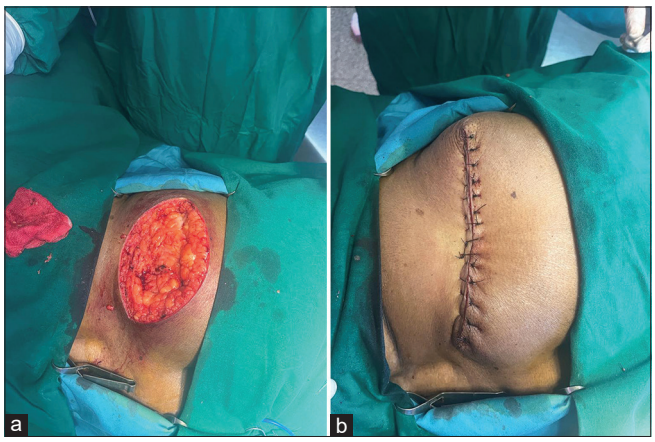

Figure 3: (a) Per-operative image. (b) The defect repaired by suturing.

DISCUSSION

BD typically occurs in persons above sixty years of age [4]. The giant pigmented BD is a rare variant that accounts for even fewer cases and is considered difficult to manage, necessitating tissue-sparing surgeries. Morton et al. defined "large Bowen's Disease" when the lesion dimension exceeds more than 2 cm [5]. Lopez et al. termed lesions with dimensions more than 3 cm as "extensive Bowen's Disease" [6]. It is characterized by the typical clinical picture of BD: full-thickness epidermal dysplasia/melanin increase in the epidermis

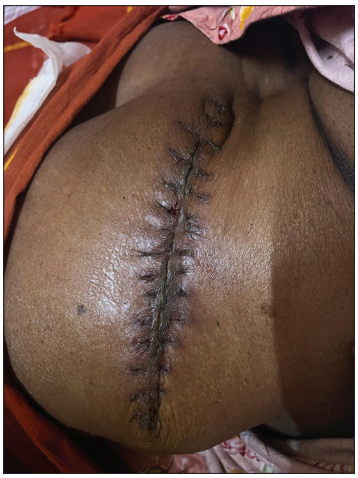

Figure 4: Healed skin site.

and dermis. It is clinically characterized by being large, multi-colored, hyperpigmented, well-defined, and with an uneven surface. Desquamation, erosion, and ulceration may be present, as well as itching or burning, although most lesions are asymptomatic. Risk factors are ultraviolet light exposure (solar light or phototherapy with UVA), organ transplantation, radiotherapy, immunosuppressive drugs, arsenic, thermal trauma, pre-existing skin diseases such as seborrheic keratosis, chronic lupus erythematosus, and lupus vulgaris and human papillomavirus (HPV) infection. Giant BD should be considered in the differential diagnosis (DD) of a huge, asymptomatic, pigmented plaque along with pigmented basal cell carcinoma, pigmented actinic keratosis, plaque psoriasis, and seborrheic keratosis.

Dermatoscopy assists in diagnosis, to exclude other causes. Findings noted are brownish, amorphous pigment (if any epidermal melanin) or grayish (if any dermal melanin), while brownish spots in a regular arrangement on the periphery of the lesion and dotted or glomerular vessels in a linear arrangement. These are not present in all cases. Our case had crops of rounded and coiled blood vessels apart from pigments. Histopathology is the gold standard for diagnosis. We found an acanthotic hyperpigmented epidermis with keratinocytes, showing atypia and loss of the usual pattern of maturation, an abundance of melanin in the cytoplasm of atypical keratinocytes, and a slight rise in the number of melanocytes, which confirmed our diagnosis. Although under- or late-diagnosed, the giant pigmented variant of BD may not be so rare. Challenges are in establishing the diagnosis early, and surgical treatment is the best option due to the large size, sometimes necessitating flaps. Risk-adapted follow-up is done regularly to look for local recurrences

and other keratinocyte cancers such as basal cell or squamous cell carcinoma elsewhere in the body [7,8].

CONCLUSION

The giant pigmented form is a rare variant of Bowen's disease, which may be seen in any keratinized skin. It carries an excellent prognosis if diagnosed early as it is a slow-growing pre-malignant condition. It requires a unified effort of a dermatosurgeon, one surgeon, and a plastic surgeon to plan and devise effective treatment options due to its varied presentation.

ACKNOWLEDGMENTS

We would like to acknowledge the patient for allowing me to use her images in the publication of this case report.

IEC approved the case report for publication.

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.

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Our Dermatology Online

Case Report

Infectious endocarditis revealed by dermatological manifestations originating from basal cell carcinoma

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ABSTRACT

The diagnosis of infectious endocarditis may be difficult. Dermatological examination in patients with suspected infective endocarditis may prove very useful, as it might reveal suggestive abnormalities of this disease, such as Osler's nodes and Janeway lesions. Osler's nodes are painful, purple nodular lesions, usually found on the tips of the fingers and toes. Herein, we report the case of a 57-year-old man who was diagnosed with infectious endocarditis, and basal cell carcinoma was the gateway. This case was of particular interest because of the rarity of the gateway and because it highlighted the importance of skin examination as an essential element in the presumptive diagnosis of infective endocarditis.

Key words: Endocarditis, Basal cell carcinoma, Dermatological

INTRODUCTION

The diagnosis of infectious endocarditis may be difficult. Dermatological examination in patients with suspected infective endocarditis may prove very useful as it might reveal suggestive abnormalities of this disease. This case was of particular interest because of the rarity of the gateway and because it highlighted the importance of skin examination as an essential element in the presumptive diagnosis of infective endocarditis.

CASE REPORT

A 57-year-old male came to the emergency room for a fever that had been evolving for the previous four days. His history included high blood pressure for seven years and dyslipidemia. On clinical examination, fever was confirmed at 38°C. At the cardiac auscultation, a discreet systolic breath at the mitral focus was found. The patient was in good hemodynamic condition. The general review showed an ulcerated and purulent nodular tumor of the scalp (Fig. 1). Biological analysis revealed an inflammatory syndrome: hyperleucocytosis neutrophil polynuclear and negative hemocultures. A histological study of the scalp mass concluded to basal cell carcinoma. The patient was put on intravenous antibiotic treatment with penicillin G at a dose of 16 million units per day. The evolution was marked by the persistence of fever on the third day of antibiotic therapy with the appearance of necrotic pulpitis associated with hemorrhages in subungual flames of the hands (Fig. 2) and purpuric macules (Figs. 3a – 3c). Faced with the strong suspicion of the diagnosis of infectious endocarditis, transthoracic echography was conducted objectifying a large vegetation at the level of the atrial side of the highly mobile 1.8 cm high axis machine valve (Fig. 4). The diagnosis of infectious endocarditis was established. The location of this vegetation represented a significant embolic risk and could compromise the proper mobility of the mitral valve leaflet. Antibiotic therapy was adapted by targeting staphylococcus aureus with good evolution (apyrexia after 48 hours), a regression of biological inflammatory syndrome with a marked decrease in vegetation size. Six weeks later, the patient's progress was excellent, and he returned home.

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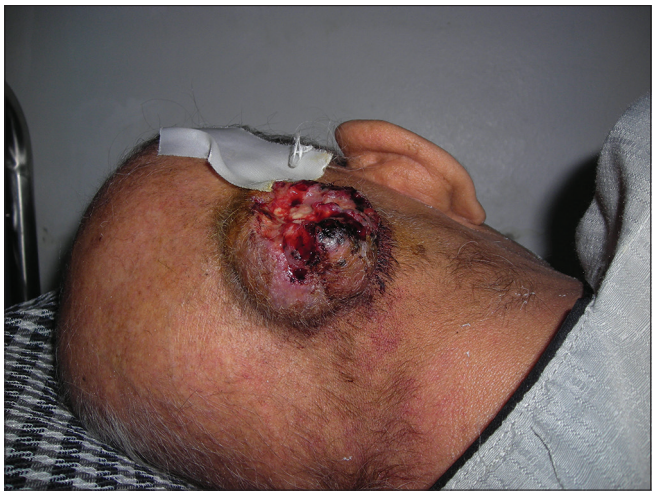
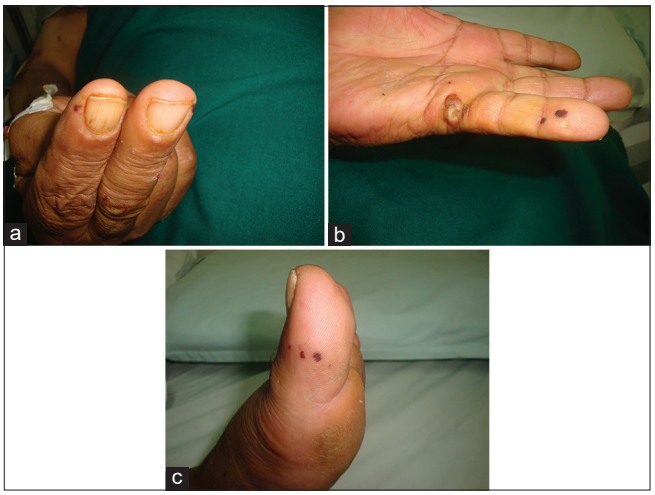


Figure 1: An ulcerated and purulent nodular tumor of the scalp.



Figures 3: (a-c) Purpuric macules.

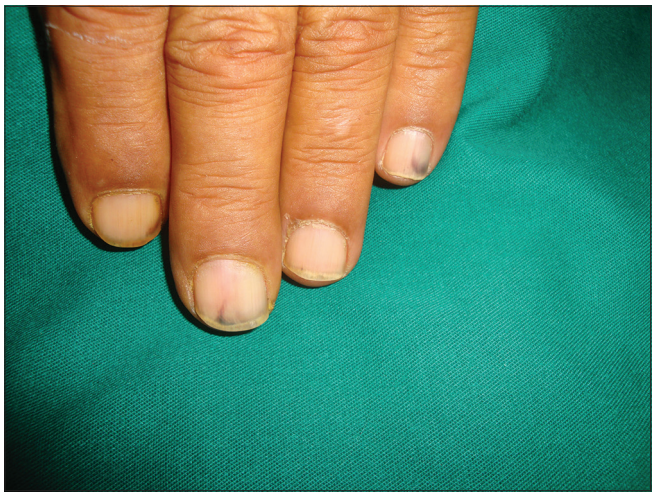


Figure 2: Necrotic pulpitis associated with hemorrhages in subungual flames of the hands.

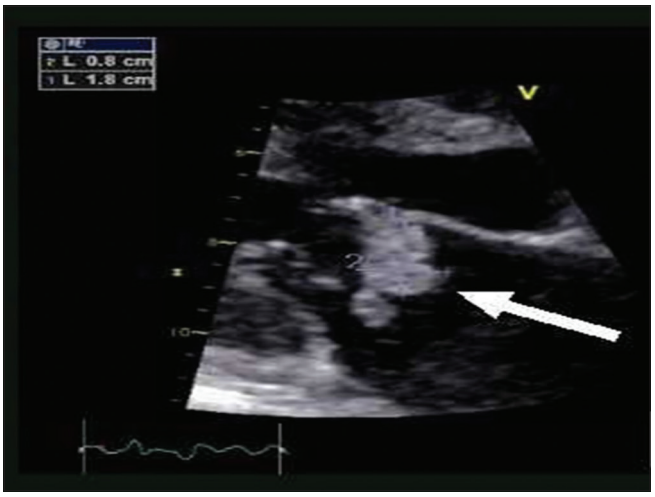


Figure 4: Large vegetation at the level of the atrial side of the highly mobile 1.8 cm high axis machine valve.

DISCUSSION

Our observation emphasizes that the diagnosis of infectious endocarditis may be difficult. The secondary appearance of purpura helped guide the diagnosis of our patient. Infectious endocarditis is a systemic, serious bacterial infection that may affect all heart valves and cause serious and even irreversible damage, sometimes evolving into life-threatening complications. Some factors favor the occurrence of infectious endocarditis, namely risky heart disease associated with an infectious gateway that may be oral (most common), whose germ is *Streptococcus* transmitted most often during dental care with bleeding. It may be urinary (ureteral surgery, prostatectomy) or digestive disease, common in the elderly, caused by *Streptococcus bovis* or *Enterococcus*. Infection through the skin is rarer (sores, boils) and, in general, involves *Staphylococcus aureus* [1]. Overinfected chronic dermatoses may be a gateway to underlying heart disease. In the case of our patient, basal cell carcinoma was the gateway. Iatrogenic entrance doors are not exceptional and more and more frequent: catheters, pacemakers, and post-cardiac surgery. Clinical signs include general signs: fever, splenomegaly, and an alteration in general condition. Cardiac manifestations may occur by the onset or modification of a breath or signs of heart failure. Extracardiac manifestations with skin signs in (5–15%): purpura petechial, false Osler panaris, or Janeway palmo-plantar erythema [2]. Eye signs may be seen (at the back of the eye: Roth spots) conjunctival purpura or even kidney signs (proteinuria, hematuria). The diagnosis of infectious endocarditis follows well-codified diagnostic criteria, called DUKE criteria, based on a set of clinical, ultrasound, and biological criteria. These criteria are useful in assessing the likelihood of infectious endocarditis yet will always

be subject to flaws; indeed, sensitivity and specificity are about 80% [3], which motivates the search for improvements to these criteria [4].

CONCLUSION

Infectious endocarditis remains a serious disease requiring multidisciplinary management medical, surgical, and microbiological management. Although treatment is well codified, mortality remains high. This diagnosis should always be considered in the presence of any prolonged fever and persistent, suggestive skin lesions in a patient at risk. Prophylaxis and education of at-risk patients are essential.

Consent

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

Written informed consent was obtained from the patient for the publication of this case report and its accompanying images.

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Our Dermatology Online

Case Report

Pegylated interferon α-2a in the management of cutaneous T-cell lymphoma

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ABSTRACT

Advanced primary cutaneous T-cell lymphomas often represent a therapeutic challenge regarding the uncertain efficiency of therapies and their poor tolerance. Interferon alpha in combination with phototherapy is part of the therapeutic arsenal of this heterogeneous group of lymphoproliferative diseases, which is mainly dominated by mycosis fungoides. However, its short half-life and poor tolerance by patients often lead us to reconsider this therapeutic option. Herein, we report four cases of our experience with pegylated interferon alpha 2a, its better tolerance profile, and longer half-life.

Key words: Cutaneous T-cell lymphoma, Mycosis fungoides, Pegylated interferon α-2a, Interferon α-2a

INTRODUCTION

Cutaneous T-cell lymphomas (CTCL) are due to the proliferation of activated T-cells in the skin. They form a heterogeneous group of malignant lymphoproliferative disorders (LPD), among which mycosis fungoides (MF), known for its slow and indolent progression, is by far the most common subtype.

Recombinant human interferon-alpha 2A (IFNα-2a), usually combined with PUVA therapy, is among the standard therapeutics for cutaneous T-cell lymphomas. However, its quite short plasma half-life requires administration at least three times a week, with poor tolerance by patients. Pegylated IFNα-2a (PEG-IFNα-2a) is a modified form of IFNα-2a resulting from the non-covalent binding of a methoxy polyethylene moiety. PEG-IFNα-2a has a longer half-life and lower clearance, providing the same or even greater efficacy with fewer side effects. In this paper, we report four cases of cutaneous T-cell lymphoma treated with PEG-IFNα-2a.

CASE REPORT

Case 1

A 63-year-old male patient with no medical history presented mycosis fungoides evolving since 2013, initially diagnosed at the plaque stage, which later evolved to the erythroderma stage (T4N0M0B0), successively treated with methotrexate, RePUVA therapy and IFNα-2a, with only transient improvement. Since his progression to the T3N0M0B0 stage in August 2020 (Fig. 1a), the patient was initiated on PEG-IFNα-2a at a weekly dose of 180 µg subcutaneously combined with PUVA therapy. A three-month outcome revealed a satisfactory response with good tolerance. After nineteen months of treatment, all lesions disappeared, and no new lesions appeared (Fig. 1b).

Case 2

A 71-year-old male had a history of non-metastatic gastric adenocarcinoma treated in 2006 by subtotal

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gastrectomy, in complete remission. Since 2019, he had presented CD30-positive cutaneous pleomorphic large T-cell lymphoma (Fig. 2), treated for eleven months with PEG-IFNα-2a at a weekly dose of 180 µg without improvement. The patient died due to tumor lysis syndrome.

Cases 3 and 4

Two male patients, aged 74 and 77 years, respectively, presented with chemotherapy-refractory mycosis fungoides (Figs. 3a and 3b) that has not responded to methotrexate, CHOP (doxorubicin + vincristine + prednisone), gemcitabine, and DHAP (dexamethasone + cytarabine + cisplatin) protocols. In both patients, the histological examination of skin biopsies found mycosis fungoides with CD30-positive large cell lymphoma transformation and mild pilotropism without follicular mucinosis. Staging assessment revealed IIB (T3N0M0B1a) and IB (T2bN0M0B0) stages, respectively.

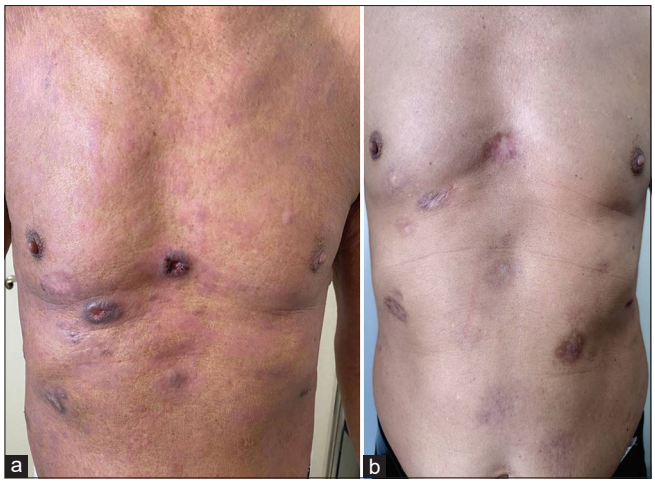

Figure 1: (a) Ulcerated tumor lesions on the trunk. (b) Scar damage after nineteen months of treatment with pegylated Interferon α-2a combined with PUVA therapy.

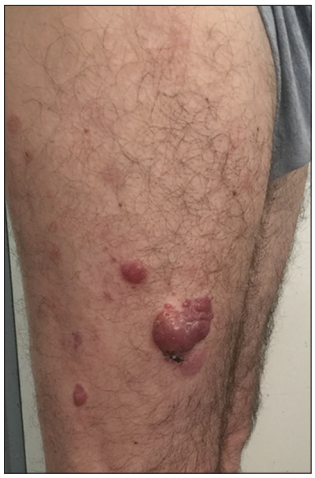

Figure 2: Erythematous tumor lesions of cutaneous pleomorphic CD30+ large cell lymphoma on the thigh.

A treatment with PEG-IFNα-2a was then initiated as follows:

- For the first patient: 135 µg per week for six months, then once every two weeks;
- For the second patient: 180 µg per week for twelve cycles, then one cycle every two weeks, then one every three weeks.

Follow-up showed good clinical and biological tolerance and a satisfactory clinical response in four cycles (Figs. 3c and 3d).

DISCUSSION

Cutaneous T-cell lymphoma is characterized by clonal accumulation T cells in the skin microenvironment. Malignant T-cell populations are made of highly differentiated mature cells that still have the ability to regulate their immune functions. These are memory T-helper cells that mainly present TH2 cytokines, such as interleukin 10, resulting in a local and, then, systemic imbalance of the TH1/TH2 system [1].

Most of these lymphomas are indolent neoplasias with a widely varying clinical presentation. In the early stages, they mainly affect the quality of life through pruritus and clinically visible skin lesions. In the advanced stages, the skin lesions are associated with systemic disorders of the immune response, which lead to an increased risk of infections and secondary malignancies that may be life-threatening [2,3].

Lymphomas usually occur in patients of advanced age, most often with multiple comorbidities. Since there is still no cure, the realistic goal for the management of cutaneous T-cell lymphoma is to achieve long-term remissions with therapies that may be employed safely with no long-term toxicity [4].

Based on this concept, new therapies are being constantly investigated, in particular, pegylated interferon α-2a which has both immunomodulatory and antiproliferative actions. It would be an interesting option in the advanced stages of the disease failing to respond to standard treatments [5]. In addition, its long half-life allows a weekly administration, which is more convenient than a three-weekly dose of INF α-2a [6].

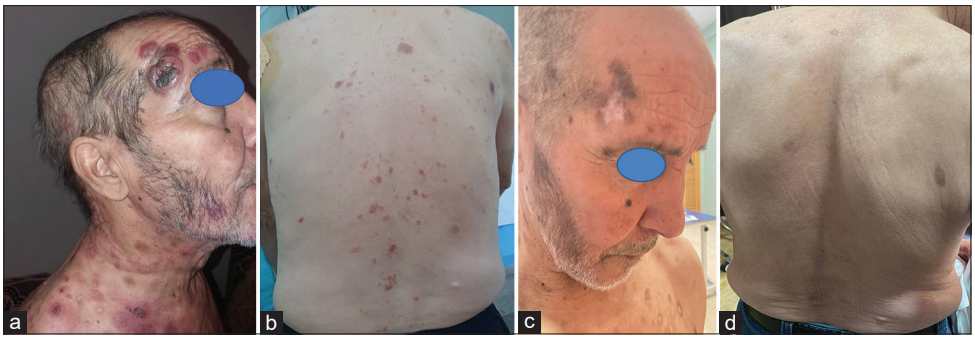

Figure 3: (a) Papulous nodules and erythematous tumors on the cephalic extremity in the first patient. (b) Infiltrated and spread erythematous macules on the back of the second patient. (c) Evolution of the lesions 4 cycles after the beginning of treatment in the first patient.(d) Evolution of the lesions 4 cycles after the beginning of treatment in the second patient.

Schiller et al. reported that PEG-IFNα-2a was generally well tolerated in a series of fourteen patients with mycosis fungoides. The most common side effects were fatigue, acute flu-like symptoms, and hepatic cytolysis. The latter, occurring in one patient receiving a weekly dose of 270 μg, was the only adverse event warranting dose limitation. A response rate after twelve weeks of treatment was 50% in the 180 μg group (OR: 50%; PR: 0%), 83% in the 270 μg group (OR: 67%; PR:17%), and 66% in the 360 μg group (OR: 33%; PR: 33%) [7].

Lype conducted a study on a group of twelve patients with cutaneous T-cell lymphoma treated with PEG-IFN α-2a. All patients were initially treated with a weekly dose of 135 μg with a good clinical response, except for two patients, in whom the weekly dose was escalated to 180 μg. The median response time was 42 days. The duration of treatment ranged from 1 to 17 months, with six patients still undergoing treatment. Pegylated interferon was well tolerated, and no patients interrupted treatment because of toxicity [8].

In four of our patients, PEG-IFNα-2a was also well tolerated, with no side effects. The weekly dose prescribed was 180 μg in three patients and 135μg in one. A good clinical response was noted in three of our patients with mycosis fungoides or transformed MF (T-MF) after twelve, sixteen, and twenty-four weeks of treatment. The patient with CD30-positive large cell pleomorphic lymphoma was in therapeutic failure despite weekly treatment for eleven months.

The duration of PEG-IFNα-2a treatment is not well established in the literature. In fact, the therapeutic protocol of PEG-IFNα-2a in cutaneous T-cell lymphomas is not well defined. In addition, there is insufficient evidence of long-term tolerance.

CONCLUSION

In view of its safety and efficacy, even at high doses reaching up to 360 μg per week, PEG-IFNα-2a could be an advantageous option for patients with progressive cutaneous T-cell lymphomas unable to tolerate standard IFN-α. Nevertheless, in order to assess the comparability between standard IFN-α and PEG-IFN, larger clinical trials are required, studying IFNs alone and in combination with oral photochemotherapy (PUVA).

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.

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Our Dermatology Online

Case Report

Reticular erythematous mucinosis developed in an atypical body part associated with thyroid disease and menstrual cycle: A rare case report

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ABSTRACT

Reticular erythematous mucinosis (REM) is a rare form of diffuse cutaneous mucinosis characterized by a diffuse dermal mucin deposit. It most often involves the midline of the upper chest or back in middle-aged women; however, other atypical places have been observed in the literature. The clinical picture involves erythematous macules and papules that coalesce into a reticulated pattern. The pathophysiology has been poorly identified; nonetheless, correlations have been observed with other autoimmune disorders and various types of cancers. The triggering factors include smoking, hormonal disturbances, menstrual cycle, sunlight, and UV radiation. To date, the antimalarial medications have remained the mainstay of treatment of REM. Herein, we report a case of reticular erythematous mucinosis that exclusively affected the left upper extremity, which interestingly, was associated with the menstrual cycle, sunlight, and thyroid disease. We describe its clinical and histological aspects and management in relation to previously reported cases of REM.

Key words: REM (reticular erythematous mucinosis), Lupus, Atypical rash, Pruritus, Cutaneous mucinosis

INTRODUCTION

Reticular erythematous mucinosis (REM) is an idiopathic disorder of primary dermal mucin accumulation, a rare form of cutaneous mucinosis [1-3]. It most often involves the midline of the upper chest or back in middle-aged women. Other atypical parts involve the face, abdomen, neck, and limbs. It typically presents with erythematous macules and papules that coalesce into a reticulated pattern [4]. The etiology and pathophysiology have been poorly identified; nonetheless, correlations have been observed with other autoimmune disorders such as systemic lupus erythematosus (SLE), scleroderma, thyroid disease, and various types of cancers. The triggering factors include smoking, hormonal disturbances, menstrual cycle, sunlight, and UV radiation [5,6]. There is still an exciting ongoing scientific debate regarding the relation to cutaneous lupus erythematosus (CLE) as they share a clinical and histopathologic resemblance. However, there were identified some histological differences in our case report [7]. Early recognition and diagnosis of REM is important as it will differentiate it from other autoimmune dermatoses such as CLE and will, therefore, offer a different prognosis, systemic involvement, and disease progression [5-7]. Herein, we report the case of a 48-year-old female patient with an atypical variant of REM on the upper extremity that was found to be correlated with her thyroid disease and was exacerbated during her premenstrual period. She mentions a similar clinical presentation twenty-four years ago where no diagnosis was established and was partially improved with topical corticosteroids. The history of autoimmune thyroid disease in our case lent

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further credence to immune function dysregulation as a potential etiology of REM. In our case, we confirm that the antimalarial treatment remains the mainstay of treatment of REM. Ultimately, a close correlation of dermatologic and histologic findings was required to produce a diagnosis in this case and highlights the need for clinical and pathologic correlation in dermatology, especially in cases with atypical and recalcitrant presentations.

CASE REPORT

This is a case of a 48-year-old female patient presenting in September 2023 at our hospital with a long-standing undiagnosed exanthema in her left forearm. Clinically, there were unilateral reticulated and indurated erythro-violaceous papules in the anterior lower part of the left forearm, which were itchy, photosensitive, and deteriorating with light and during the premenstrual period (Figs. 1a and 1b). During history taking, she mentioned there were two to three erythematous plaques initially in the same area over the last four years, which were previously managed as either neurodermatitis with topical corticosteroids with no satisfactory resolution or fungal infection that was unsuccessfully treated as such. She also mentioned that the erythematous plaques first appeared twenty-four years ago, which were managed with minimal improvement as dermatitis with topical corticosteroid. Regarding her medical history, she had iron-deficiency anemia due to menorrhagia, for which she was receiving iron supplements, and a history of thyroid CA, for which she had a total thyroidectomy in 2008 and treatment with iodine. After that, she developed hypothyroidism for which she was receiving T4 *per os*. Fungal cultures from direct examination and cultivation were negative. From the serological investigations microscopic-microcytic anemia was revealed, as expected from the history given and immunological investigations, including anti-dsDNA, anti-Ro, anti-LA, ANA, anti-Centromere, anti-Sm and anti-CCP, which were normal. We took a punch biopsy from the left forearm with a wide range of differential diagnosis, including lichen nitidus, granulomatous disease (granuloma annulare, cutaneous sarcoidosis), cutaneous lupus, lupus tumidus, Jessner's lymphocytic infiltrate, polymorphic light eruption, malignant atrophic papulosis, plaque stage mycosis fungoides and reticular erythematous mucinosis. Histology with H&E stain revealed predominantly tense perivascular infiltration by small lymphocytes at the level of the reticular dermis (Figs. 2a and 2b). There was focal mucus deposition in the dermis (Alcian blue) and a normal epidermis. Immunohistochemistry revealed T lymphocytes with $CD2^+$, $CD3^+$, $CD4^+$, $CD5^+$, $CD7^+$ more than $CD8^+$, TCRδ- and a low Ki67/MiB1 cell proliferation index around 5%. The above findings were consistent with the diagnosis of reticular erythematous mucinosis [6-8]. Therefore, we initiated treatment with photoprotection, topical clobetasol propionate 0.05% cream twice daily for a month followed by Tacrolimus 0.1% ointment twice daily for three months (Fig. 3). Following the concurrent opinion of her hematologist and ophthalmologist as per initiation protocol, we started hydroxychloroquine 200 mg twice daily [9,10]. We noticed complete clearance of all lesions within two months with the above treatment. Following a trial

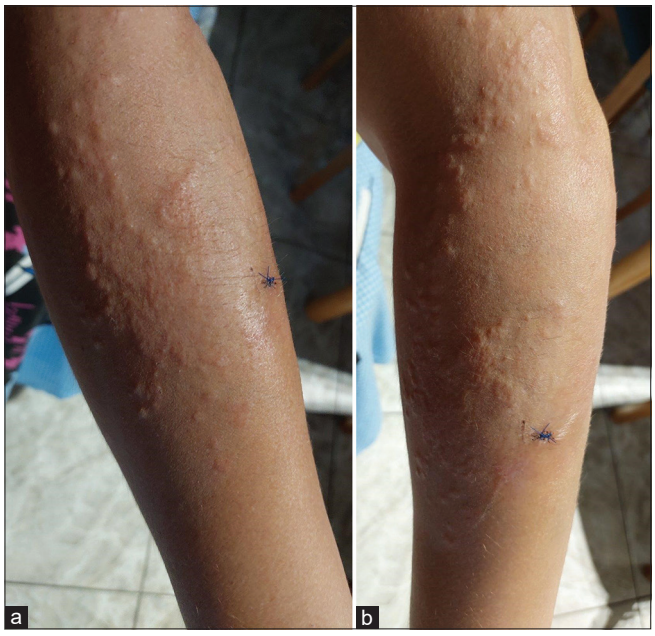

Figure 1: (a) Clinical picture at first review. Unilateral reticulated and indurated erythro-violaceous papules in the anterior lower part of the left forearm, biopsy site. (b) Indurated erythematous papules and plaques on the left forearm at first review.

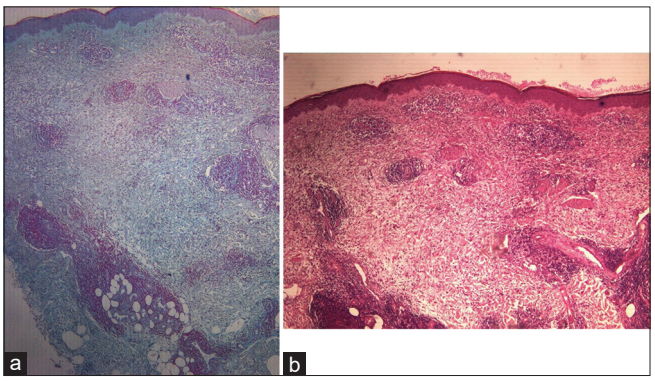

Figure 2: (a) Histopathology. Focal mucus deposition in the dermis (Alcian blue). (b) Histopathology. Tense perivascular infiltration by small lymphocytes at the level of the reticular dermis (H&E stain).

to reduce hydroxychloroquine to once daily at three months, she mentioned minor irritation in the area during her premenstrual period, thus we maintained the dosage twice daily, and on the six- and eight-month follow-ups, she remained free of any exanthema (Fig. 4).

DISCUSSION

REM is a rare form of diffuse cutaneous mucinosis with a poorly identified pathophysiology [1,2]. It usually affects patients in early adulthood and commonly women. Clinically, it is characterized by an asymptomatic, or occasionally pruritic, macular, and reticulated erythematous exanthem typically on the central chest and upper back [3]. Occasionally, however, it may occur on the abdomen, face, and the proximal upper extremities [4]. Exposure to sunlight typically increases the burning sensation on the affected site in most patients. The suggested etiology includes UV radiation, autoimmune diseases, viral infections, and Borrelia infection. It has been associated with withdrawal syndrome from alcohol, SSRIs, or TCAs. The factors that aggravate the disease could be menstruation, pregnancy, hormonal disturbances, hyperhidrosis, and exposure to heat or radiation. The main diagnostic challenge is its differentiation from cutaneous lupus erythematosus since they share similar clinical picture responses to antimalarials, both including photosensitivity and female predominance. Distinguishing them, we should take into consideration that REM lacks antinuclear antibodies and histologically shows mainly lymphocytic infiltration of the dermis and mucin deposition limited to the dermis as opposed to CLE, where there is infiltration of the dermis with a variety of inflammatory cells and extension of the mucin deposition to the subcutaneous tissue, respectively, and additionally, one may observe epidermal atrophy and follicular hyperkeratosis. As mentioned before, the histology in our case was characteristic of REM. Typically, there is perivascular and perifollicular infiltrate, composed primarily of lymphocytes throughout the upper dermis. Fibroblasts are normal in number and appearance, and fibroblasts are normal in number and appearance. Collagen fibers appear similarly unchanged despite diffuse upper dermal edema and mucin deposition. The rapid response to hydroxychloroquine in our case mirrors the up-to-date evidence we have that antimalarial drugs remain the mainstay of treatment from REM [8,9]. Various other treatments that have been mentioned in the literature are corticosteroids, calcineurin inhibitors, tetracycline, antihistamines, UVA-UVB phototherapy, cyclosporine, and dapsone; nevertheless, limited response has been seen in the past [8-12]. According to previous case reports, and as seen in our case, a trial to reduce antimalarials or stop the treatment might trigger a relapse of the disease. Automatic regression of lesions may be seen even fifteen years after the onset of the condition.

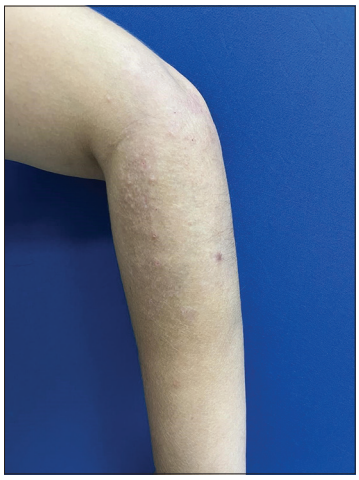

Figure 3: Three weeks follow-up following the use of photoprotection and topical clobetasol propionate 0.05% twice daily.

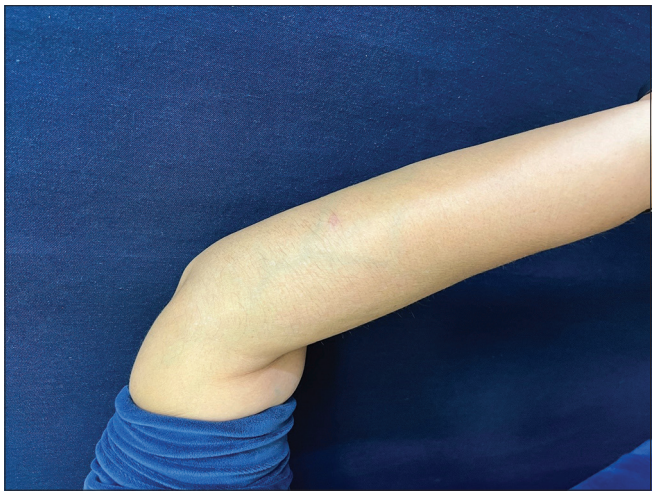

Figure 4: Complete clinical resolution at six months follow-up following treatment with hydroxychloroquine.

CONCLUSION

To summarize, we presented a rare case of a middle-aged woman with REM observed in an atypical body part, more specifically the arms, which was previously unsuccessfully treated as dermatitis. The histology revealed the diagnosis, and treating the patient with hydroxychloroquine, we noticed complete resolution of

the exanthema. Most importantly, this case highlights the need for a biopsy where there is diagnostic doubt and resistance to treatment in patients with dermatological rashes. Additionally, in this case, there seemed to be an association with hypothyroidism as previously described in the literature. We enhance this association and urge the scientific community to investigate the conjunction of REM to thyroid autoantibodies further. A well-controlled thyroid function could improve the symptoms of REM. Moreover, we confirm, to an extent, the connection of REM to menstrual cycle change. Most likely, there is an association with the hormonal changes in the body during the menstrual cycle, and that could be further looked into in the future. In conclusion, the success of antimalarials as a first-line therapy of REM was attested in our case while only limited response to topical corticosteroids was observed.

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Our Dermatology Online

Case Report

Disseminated form of Darier's disease

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ABSTRACT

Darier's disease is a rare genetic skin disorder with two types: type 1, which is unilateral, and type 2, which is bilateral and more common. This article presents the case of a sixty-year-old patient with disseminated Darier's disease successfully treated with acitretin. The patient was diagnosed through clinical examination and a biopsy, which showed typical features such as acantholysis and dyskeratotic keratinocytes. The disease usually begins in childhood due to a mutation in the ATP2A2 gene. It manifests as keratotic lesions on seborrheic areas (chest, neck, trunk, face) that may be itchy and uncomfortable, with possible nail and oral mucosa changes. Darier's disease is chronic and recurrent, and treatment aims to alleviate symptoms and improve quality of life. Understanding its clinical and genetic aspects is crucial for effective management.

Key words: Darier's disease, Genodermatosis, Type 2 Darier's disease, Acitretin

INTRODUCTION

Darier's disease is a rare autosomal dominant genodermatosis. It is associated with a mutation in the ATP2A2 gene resulting in the dysfunction of endoplasmic reticulum calcium ion-dependent ATP-ase, an enzyme responsible for the formation of intercellular bonds and cell adhesion. There are two types of the disease: unilateral and disseminated. The disseminated form is more common. It is characterized by the occurrence of keratotic papules located mainly in the seborrheic areas of the skin involving the truck, scalp, face, and lateral aspects of the neck. Additionally, the clinical picture may include changes in the nail plates and mucous membranes. Histopathological examination shows acantholysis and dyskeratosis. In the treatment of Darier's disease, general therapies and local preparations are used.

CASE REPORT

A sixty-year-old patient came to the Dermatology Department of the Provincial Hospital in Elbląg for the diagnosis and treatment of skin lesions located mainly on the trunk. They were accompanied by slight itching. The patient associated the appearance of skin lesions with exposure to UV radiation and sweating. The family history of dermatological diseases was positive: the patient's brothers were diagnosed with Darier's disease.

During the physical examination, the patient reported additional problems, namely arterial hypertension, chronic kidney disease, osteoarthritis of the spine, a stroke of the brain stem with paralysis of the facial nerve on the right side, and implantation of a DDD stimulator in the past. The patient also reported hypersensitivity to non-steroidal anti-inflammatory drugs. The patient had chronically been taking torasemide, nebivolol, carbamazepine, amlodipine with indapamide, and perindopril.

A physical examination revealed red to brown keratotic papules located on the trunk, with a tendency to merge in the right mammary and deltoid areas and in the presternal area (Figs. 1a – 1d), and longitudinal red and white lines as well as notching of the free edge of the nail plate in the left hand (Fig. 2).

The videodermatoscopic image of the skin lesions revealed a central, yellowish-brown polygonal area surrounded by a white halo (Fig. 3a). Within the

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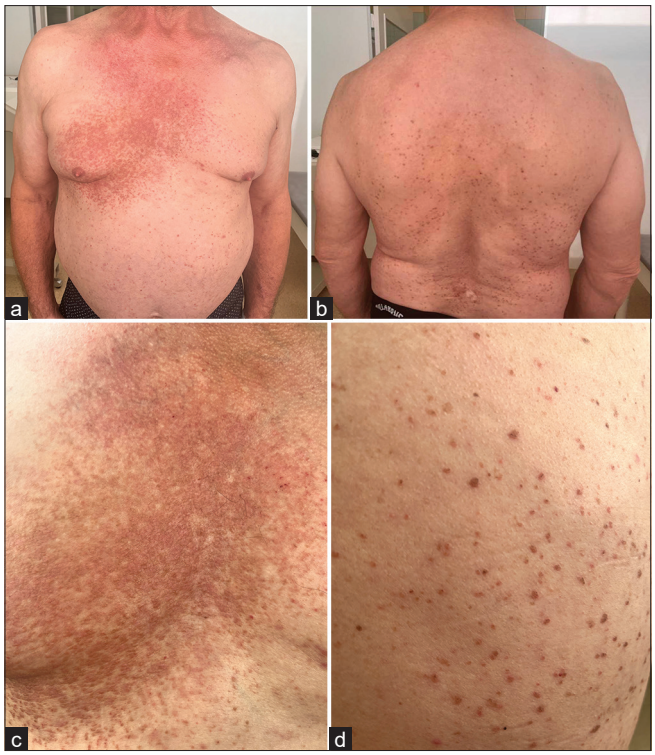

Figure 1: (a-d) Truncal involvement with a predilection for seborrheic areas. The Keratotic papule may vary from red to brown in color and may become confluent.

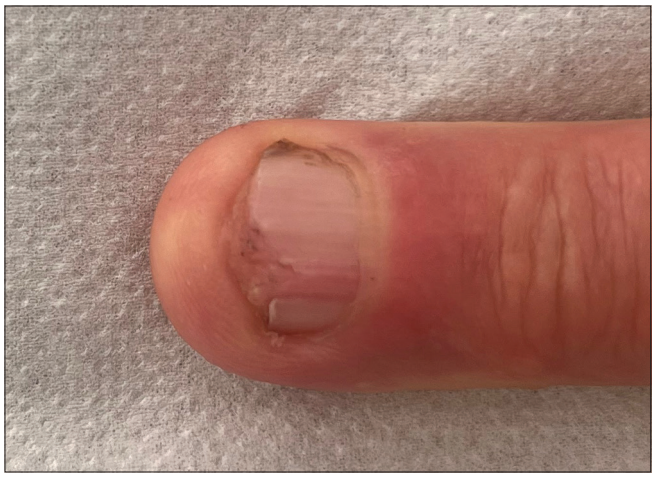

Figure 2: Longitudinal red and white lines as well as notching of the free edge of the nail plate in the left hand.

nail plate, red and white longitudinal stripes with a V-shaped indentation of its free edge were revealed (Fig. 3b).

Laboratory blood tests showed increased levels of total cholesterol, LDL cholesterol, triglycerides, creatinine, urea, and glucose. During hospitalization, a biopsy was taken from the affected skin. A histopathological examination described hyperkeratosis, grains, and *corps ronds* in addition to acantholysis, leading to suprabasilar clefting.

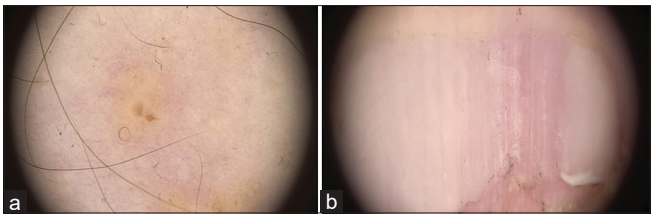

Figure 3a: a) Videodermatoscopic image of the skin lesion on the trunk. b) Videodermatoscopic image of the altered left hand's fingernail plate.

Based on the clinical, videodermatoscopic and histopathological findings, the patient was diagnosed with Darier's disease. During the stay at the Dermatology Department, general treatment with acitretin (20 mg daily) and a local glucocorticosteroid, exfoliation, and moisturizing treatment were administered, resulting in a reduction of skin lesions. Moreover, due to lipid disorders, lipid-lowering treatment was initiated. The patient was discharged home with a recommendation for further care at the Hospital Dermatology Clinic.

DISCUSSION

Darier's disease (DD) or Darier–White disease, also known as keratosis follicularis, is a rare genodermatosis inherited as autosomal dominant (AD), yet not always familial. Approx. 47% of patients do not have a reported family history of the condition [1].

The present patient had a known family history: two of his brothers were diagnosed. Therefore, patients should be provided with genetic counseling that includes information about the likelihood of genetic transmission to their children. DD occurs with the frequency of 1 in 30000–100000 population and has an equal sex and ethnic distribution [2,3]. The onset typically occurs during childhood or adolescence [4]. Approx. 70% of patients experience the disease onset between the ages of 6 and 20 [5].

It was described for the first time in 1889 by Jean Darier and James Clark White [6].

The defect that occurs in this disease is a heterozygous mutation in the ATP2A2 gene, which encodes type 2 of sarcoendoplasmic reticulum Ca2+pump(SERCA2), which transfers calcium ions from the cytosol into the sarcoplasmic or endoplasmic reticulum, facilitating the hydrolysis of adenosine triphosphate (ATP) in conjunction with calcium transport.

ATP2A2 may be expressed in the skin and the brain. Therefore, in some cases, DD presents with neuropsychiatric manifestations [7]. A biopsy of the impacted region is essential for confirming the diagnosis. The characteristic histological features in DD include acantholysis above the basal layer and dyskeratotic keratinocytes referred to as *corps ronds*, and parakeratotic cells, referred to as *corps grains*, are distinctive histological markers of the condition [6,8].

DD belongs to the group of dyskeratotic acantholytic dermatoses, which also includes Hailey–Hailey disease, warty dyskeratoma, and acantholytic dyskeratotic acanthoma. These conditions share common features such as acantholysis and dyskeratosis, which are consequences of abnormal keratinization [9].

Immunofluorescence of a skin biopsy may distinguish between various acantholytic disorders [10]. Patients commonly present with keratotic lesions in seborrheic areas of the upper body, which includes the chest, neck, trunk, and face, which may appear as vesicles or pustules and are frequently associated with itching and discomfort. Furthermore, specific changes may be observed in the nails and oral mucosa [10,11].

Mucous membrane involvement is observed in 15% of patients [12].

The patognomic symptoms of this disease are typical nail changes: V-shaped nick at the free margin of the nail, red and white longitudinal bands, and longitudinal nail ridges [10].

DD follows a chronic course marked by recurrent episodes. The factors that may make the condition worse include lithium carbonate, exposure to UV light, perspiration, heat, and infections [10].

Several other clinical variations have been documented, such as unilateral, linear, segmental, and zosteriform DD [13].

CONCLUSION

The main aim of treating DD is to alleviate symptoms and enhance the patient's quality of life. Systemic retinoids, including isotretinoin and acitretin, which are viewed as providing symptomatic relief rather than being curative, are the initial treatment of choice for all patients and demonstrate efficacy in 90% of cases [14,15]. Numerous dermatological side effects associated with systemic retinoids have been documented, with common occurrences such as dry lips and cheilitis [16].

The duration of treatment should be adjusted based on the patient's clinical response. Recognizing the clinical features and genetic basis of Darier's disease is crucial for precise diagnosis and effective management of affected individuals. With appropriate care, patients with this condition may live rewarding lives.

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.

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Our Dermatology Online

Case Report

Ellis–Van Creveld (EVC) syndrome: A rare case report

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ABSTRACT

Ellis–Van Creveld (EVC) syndrome is a rare autosomal recessive ciliopathic disorder characterized clinically by short stature, bilateral postaxial polydactyly, bone abnormalities, retarded growth, ectodermal, and congenital heart defects. The disorder arises from the mutation of the EVC and EVC 2 genes located on the 4p16 chromosome. More than 300 cases of EVC have been recorded in the literature, with an estimated prevalence of the condition being 7 per 100,000. Herein, we present the rare case of a twelve-year-old male child diagnosed with EVC syndrome, based on oral manifestations, polydactyly, and nail dystrophy.

Key words: Ellis–Van Creveld syndrome, Polydactyly, Chondroectodermal dysplasia, Congenital heart defects

INTRODUCTION

Ellis–Van Creveld syndrome (EVCS), also known as chondroectodermal dysplasia or mesoectodermal dysplasia, was first described by Richard W.B. Ellis and Simon Van Creveld in 1940 [1]. It is a complex and rare autosomal recessive genetic disorder with less than 25 cases reported in India and 300 cases across the world [2].

Mutations in the EVC and EVC 2 genes present in a head-to-head configuration on chromosome 4p16 play an important role in the development of skeletal and endochondral abnormalities of disease [3]. The affected individuals of EVC with mutations in either the EVC or EVC 2 genes have been shown to be phenotypically indistinguishable. Besides, the same mutation is responsible for ciliary dysfunction in EVC syndrome [3]. EVCS has a multisystemic involvement ranging from heart and bone abnormalities to stomatologic ones [4]. The tissues involved in this disorder (particularly nails, long bones of the skeleton and teeth) are covered under the term *chondroectodermal dysplasia* while mesoectodermal dysplasia includes the associated cardiac disorders [4]. Herein, we report a twelve-year-old child presenting at the dermatology outpatient department with characteristic features of EVCS.

CASE REPORT

A twelve-year-old male child of Indian origin, born out of a consanguineous marriage, was brought by the parents to the outpatient department of dermatology with distinctive clinical features, the chief complaints of malformation of the teeth in the upper and lower jaws and deformities of the hands, feet, and nails. There was no history of associated fever, chest pain, or recurrent respiratory tract infections. He was second in birth order, born through normal vaginal delivery at full-term without complications and with a normal birth weight. Her psychosomatic and mental developmental were within normal limits. There was no significant family history, and the other sibling was normal. He was immunized as per the national immunization schedule.

General examination revealed the patient to be of short stature with 117 cm height, with short lower limbs, and a narrow chest (thoracic dysplasia). There was bilateral extra-axial polydactyly of the hands along with hypoplastic and dystrophic nails of both hands and feet. The hair was normal. His hands and feet were broad and square with short fingers and toes. Lower limbs were deformed with outward bending of the knees (*genu valgum*), and there was lateral deviation of the great

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toe with medial deviation of the first metatarsal bone (hallux valgus deformity) (Figs. 1a and 1b).

The examination of intraoral soft tissue revealed a short frenulum and positive labiogingival adherence. Hard tissue examination revealed hypoplasia of the enamel, conical teeth, and hypodontia. Multiple teeth were missing and various malformed teeth existed in the maxillary as well as mandibular arches. The upper lip was normally developed, and the presence of neonatal teeth or any kind of premature eruption was not seen (Figs. 1c – 1e). His neurological, cardiac, opthalmological, and auditory assessments were normal.

Laboratory investigations, including a hemogram, liver function tests, renal function tests, urine analysis, electrocardiogram, echocardiogram, and abdomen ultrasound were normal. Based on the clinical and radiological findings, we diagnosed the case as Ellis–Van Creveld syndrome (Figs. 2a – 2e). Genetic analysis was not conducted as it was unavailable in our hospital.

Parents were counseled about the genetic basis of the disease. The patient was advised to return for regular follow-up with the dentist, orthopedic surgeon, and physiotherapist for further management.

DISCUSSION

In 1933, McIntosh reported the first case of EVC syndrome, yet in 1940, Richard W.B. Ellis of Edinburgh and Simon Van Creveld of Amsterdam first described this condition as EVC syndrome [1]. It is also known as chondroectodermal dysplasia and mesoectodermal dysplasia [2]. EVC syndrome is one of the ciliopathies, and the ciliary dysfunction has been linked to a mutation in two adjacent genes, EVC and EVC2 [3].

There is no sex predilection reported and parental consanguinity has been reported in 30% of cases, which was present in our case. The tetrad of disproportionate dwarfism, bilateral postaxial polydactyly, ectodermal dysplasia, and congenital heart malformation is used to describe the characteristic signs and symptoms [4,5]. The typical syndromic facial characteristics of coarse face, conical anterior teeth, dental agenesis, multiple small extra-labial, non-midline frenula with a high arched palate and a large maxillary labial frenulum were present in our case. Other abnormalities observed comprised short limb dwarfism, a dysplastic genu valgum, an elongated trunk with severe lordosis, pectus excavatum, hypoplastic fingernails and toenails, wide, noticeably malformed hands and feet, and bimanual hexadactyly on the ulnar side of her wrists, bearing resemblance to other studies in the past [5,6]. However, anomalies of other body organs reported in these patients such as strabismus, pulmonary malformations, congenital heart defects, hematologic abnormalities, genitourinary abnormalities, and intellectual disability were absent in our patient [7,8].

EVC syndrome may be diagnosed during pregnancy, prenatally or soon after delivery [4,5]. However, the diagnosis was delayed in our case as the patient belonged to a remote hilly area with no access to

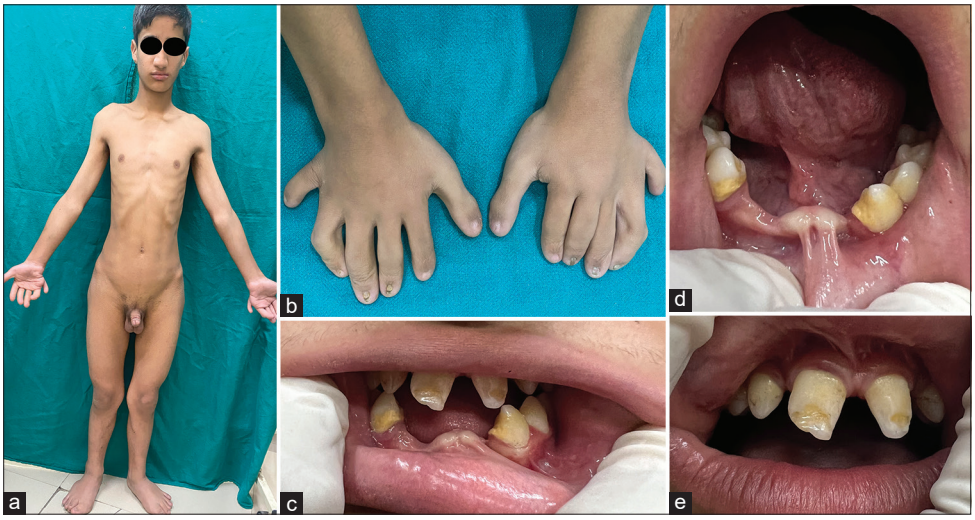

Figure 1: (a) 12-year-old boy showing chondrodysplasia, a narrow chest, deformities of the limbs, short forearms and lower limbs, bent lower limbs, and hallux valgus deformity of the great toes, with normal skin and hair. (b) Showing polydactyly of both hands and shortening of the digits in both hands and feet. Also, nail hypoplasia is seen. (c) Oral cavity showing malocclusion, hypodontia, absent maxillary lateral incisors and mandibular incisors. (d) Oral cavity showing malocclusion, hypodontia, absent maxillary lateral incisors and mandibular incisors. (e) Large maxillary labial frenum, multiple accessory labial frenula, mandibular anterior ridge defect, and crossbite.

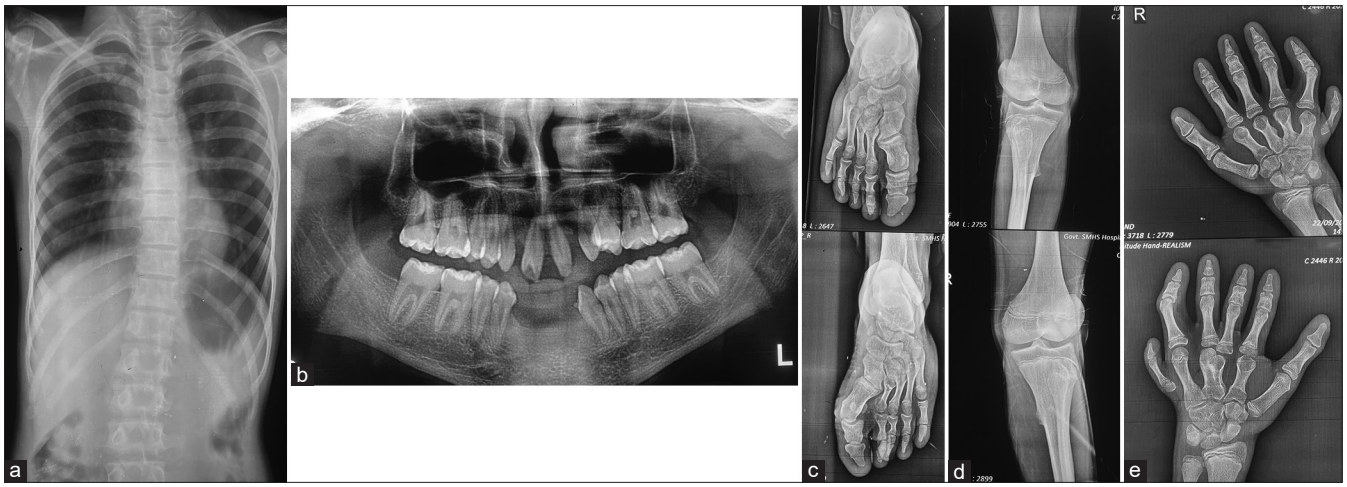

Figure 2: (a) PA view of the chest X-ray showing a narrow chest and short ribs. (b) Panoramic radiograph showing agenesis of the maxillary lateral incisors, mandibular incisors, and all four third molars. (c) X-rays of the hands showing postaxial polydactyly, short middle, and distal phalanges with cone-shaped epiphyses and carpal fusion. (d) X-rays of the feet showing bilateral hallux valgus deformity of the great toes. (e) X-rays of the legs showing lateral tibial metaphysis slanted giving rise to a genu valgum deformity.

healthcare. Ultrasonography after the 18th gestation week is used to make the prenatal diagnosis, which reveals cardiac defects, a narrow thorax, shortening of the long bones, and hexadactyly of hands and feet. At birth, clinical examination aided by an X-ray of bones may be used to diagnose the disease. The DNA mapping technique based on homozygosity for a mutation in the EVC and EVC2 genes may be used to make a reliable diagnosis [4-8]. In the present case, the diagnosis was made based on typical oral manifestations and polydactyly of the hands combined with nail dystrophy.

Since no definite cure exists for EVC syndrome, treatment is mainly symptomatic. Early dental care should be sought out by patients to restore the missing teeth, and correction of other deformities. Parental dental health education should cover oral hygiene advice, diet counseling, and physiotherapy [5-8].

CONCLUSION

EVC syndrome is a rare autosomal recessive disorder. Diagnosis is mainly clinical in cases with delayed presentations. Besides having some constant clinical features, there may be other variable components present in different patients. Awareness among clinicians about this rare entity is important, and a multidisciplinary treatment approach is recommended.

Consent

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

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Our Dermatology Online

Case Report

Drug-induced lupus induced by osimertinib (Tagrisso): A case report

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ABSTRACT

Osimertinib is an irreversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) used to treat patients with locally advanced or disseminated non-small cell lung cancer (NSCLC) with a T790M mutation in the gene encoding EGFR present. Among the most common complications of using this drug are various dermatological complications. In the following paper, we present the case of a 75-year-old woman treated with osimertinib for disseminated non-small cell lung cancer, who developed a rare skin complication of the applied treatment in the form of drug-induced lupus. After the discontinuation of anticancer treatment and the administration of systemic and topical corticosteroids, the withdrawal of skin lesions and subjective symptoms was observed. Correct diagnosis and appropriate therapeutic management allowed the resumption of optimal anticancer treatment in the following weeks, while eliminating the patient's bothersome skin lesions and associated complaints.

Key words: Osimertinib, Drug-induced lupus, Lung cancer

INTRODUCTION

Drug-induced lupus (DIL) is defined as a condition characterized by clinical symptoms, serum antinuclear antibodies, and other abnormalities in laboratory tests similar to those of idiopathic systemic lupus erythematosus (SLE), yet temporally associated with long-term intake of various drugs [1]. The associated prognosis of the disease is good, with symptoms usually resolving within several weeks after the discontinuation of the causative drug [2]. Glucocorticosteroids are used for treatment, especially when symptoms are severe, such as the symptomatic presence of pericardial fluid (in the case described here, pericardial tamponade occurred) [3]. EGFR inhibitors, unlike traditional chemotherapy, do not affect most dividing cells; they primarily act on pathways crucial for tumor growth and survival [4]. Numerous studies have shown that the use of first- and second-generation EGFR-TKIs in the treatment of patients with locally advanced or disseminated non-small cell lung cancer with a mutation in the gene encoding EGFR present prolonged the time before tumor progression and reduced the number of side effects compared to patients receiving standard chemotherapy [5]. However, therapy with EGFR-TKIs is associated with side effects especially often related to the skin, the most common of which include acne-like rash and paronychia [6]. The mechanism of the aforementioned side effects is related to the effect of EGFRI on basal keranocytes. It leads to the inhibition of their growth and increased apoptosis, reducing cell migration and increasing their differentiation, as well as stimulating the development of a local inflammatory response [7]. Osimertinib, which is a third-generation EGFR-TKI, shows longer survival times among patients compared to older-generation drugs and has a similar safety profile [8]. In addition, the use of osimertinib is associated with a statistically significant lower risk of serious side effects in comparison with older-generation drugs [9]. The risk of grade 3 or 4 rash with

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osimertinib is about 1% [10], compared to 2–16% with first- and second-generation EGFR-TKIs [11]. The described case of drug-induced lupus is rare. In the available literature, we found only one description of its occurrence associated with the use of osimertinib [12].

CASE REPORT

A 75-year-old woman treated with osimertinib for non-small cell lung cancer at the disseminated stage and with chronic hypertension was referred to the department by her primary care physician because of increasing dyspnea and lower limb edema that had been present for two weeks. Prior to the onset of symptoms causing hospitalization, the patient was in good general condition (ECOG 1). She had a history of a rash on the lower limbs in August 2023, which resolved after the dose of antineoplastic drug was reduced by half. On admission, the patient was in average general condition, reporting slight dyspnea and the presence of itchy lesions on the skin of the back, chest, and arms (Figs. 1a and 1b). On physical examination, the patient's abnormalities included a papular rash on the skin of the back, chest, and arms, a decrease in saturation to 92% without supplemental oxygen, muffled heart sounds, and moderate lower limb edema extending to the knees. Chest CT showed the presence of a significant amount of fluid in the right pleural cavity and the pericardial sac. Therapeutic thoracocentesis and pericardiocentesis were performed, and treatment for exacerbation of heart failure was administered, resolving dyspnea. A biopsy of skin lesions was performed, which revealed drug-induced lupus (SCLE-DI). Osimertinib was discontinued and systemic treatment with 10 mg of prednisone and topical treatment with mometasone-containing steroid ointment was administered. The disappearance of skin lesions and associated subjective symptoms was observed (Fig. 2), accompanied by an improvement in the patient's mood and quality of life. The patient was referred to the oncology outpatient clinic for the modification of oncological treatment. In view of the disappearance of skin symptoms, the administration of the drug was resumed at a reduced dose.

DISCUSSION

Skin complications are among the common side effects occurring in patients undergoing EGFR-TKI treatment. Usually, especially with newer-generation drugs, they take the form of benign lesions. The

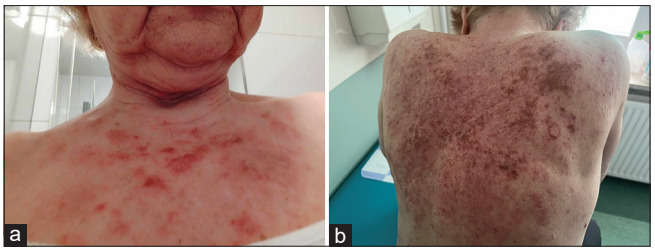

Figure 1: (a) Lupus-like lesions on the anterior surface of the chest. (b) Diffused skin lesions of the lower limbs.

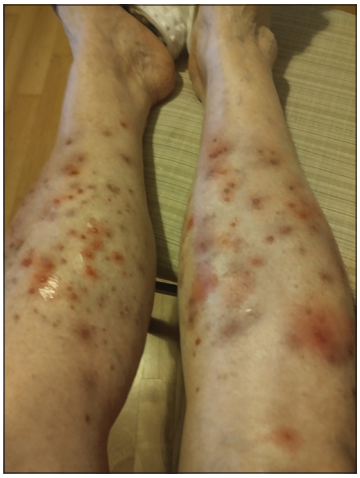

Figure 2: Healing skin lesions on the surface of the back as a result of the applied treatment.

interruption of oncological treatment, which has a higher efficacy and better safety profile than conventional chemotherapy, is then not required [13]. It is clinically important to recognize grade 3 or 4 side effects, as these require the discontinuation of the drug for up to three weeks with the resumption of treatment if symptoms resolve within this time. In the case described here, the preferred regimen was applied. This allowed the patient to continue optimal cancer therapy, while the patient's troublesome side effects subsided, which in turn significantly increased her comfort of life. An important role in the optimal management of skin lesions developed in the course of osimertinib treatment proved to be the knowledge of rare complications of the applied treatment, such as SCLE-DI.

CONCLUSION

Drug-induced lupus is a disease entity characterized by clinical symptoms and serum antinuclear antibodies temporarily associated with long-term drug intake. The prompt recognition of recognized SCLE-DI associated with the use of osimertinib allows for rapid modification of oncological treatment. This gives the

chance to continue optimal oncological therapy while reducing the occurrence of side effects.

Consent

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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.

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Our Dermatology Online

Case Report

Peutz–Jeghers lentigines revealing epidermodysplasia verruciformis in two siblings

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ABSTRACT

Peutz–Jeghers syndrome (PJS) is an autosomal dominant disease characterized by skin and digestive involvement. Epidermodysplasia verruciformis is a ubiquitous disease characterized by abnormal susceptibility to infection by about twenty human papillomaviruses of group B. Herein, we report two siblings followed for Peutz–Jeghers syndrome with lentiginous skin lesions and pityriasis versicolor-like macules confused with the diagnosis of epidermodysplasia verruciformis. The association of these two rare entities has not yet been reported. However, the cutaneous dyschromic lesions observed in Peutz–Jeghers syndrome are highly characteristic and may be confused with the signs of epidermodysplasia verruciformis, especially for macular lesions in an acral location. This case highlights the value of a skin biopsy in confirming the diagnosis in the face of the appearance of lesions of pityriasis versicolor-like and keratotic papules in a patient with Peutz–Jeghers lentigines.

Key words: Epidermodysplasia verruciformis, Human papillomavirus, Peutz–Jeghers, Morocco

INTRODUCTION

Peutz–Jeghers syndrome (PJS) is an autosomal dominant disorder characterized by polyposis of the gastrointestinal tract [1], pigmentation of the skin and mucous membranes, and a predisposition to oncological diseases. Its association with epidermodysplasia verruciformis (EV) has not been reported in the literature. Generally, EV is an autosomal recessive genodermatosis characterized by the persistent presence of beta group papillomavirus (HPV) in the skin. Recently, a new classification of EV has been proposed distinguishing a classical genetic form, a non-classical genetic form, and an acquired form. Herein, we report the first description of epidermodysplasia verruciformis associated with Peutz–Jeghers syndrome in two siblings.

CASE REPORT

A sixteen-year-old patient, without any notion of consanguinity, followed in pediatrics with his sister for Peutz–Jeghers syndrome with digestive polyposis, admitted to our training for dyschromic lesions on the face, neck, trunk, and upper limbs present since the age of ten years, whose evolution was marked by the appearance of other asymptomatic lesions on the back of the hands and perioral for which he was referred (Figs. 1a – 1c). A clinical examination revealed multiple lentigines on the back of the nose, lips, and palms, hyperpigmented macules on the lips and face, and millimeter-sized papules with keratotic surfaces on the back of the hands associated with a poorly defined pityriasis versicolor-like patch on the back, which was negative on Wood's light (Fig. 1d). We considered the cutaneous manifestations of his pathology or epidermodysplasia verruciformis given the dyschromic patch on the back. A skin biopsy was taken from the dorsal aspect of the hand and confirmed the diagnosis of epidermodysplasia verruciformis. An examination of his sister revealed the same clinical finding (Figs. 2a and 2b). Unfortunately, the patient refused any medical treatment. No genetic studies were performed in either patient.

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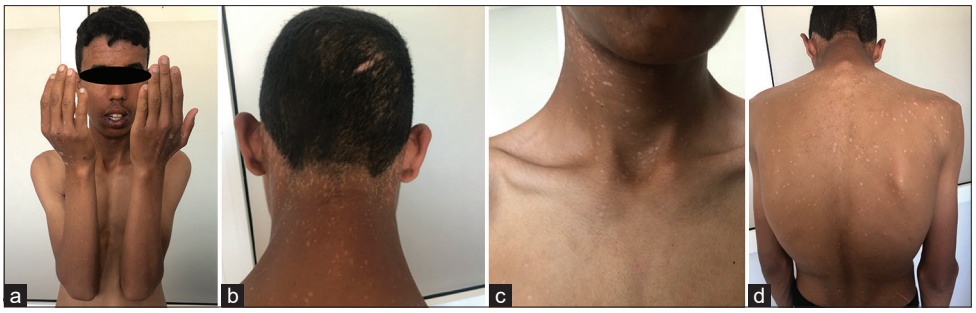
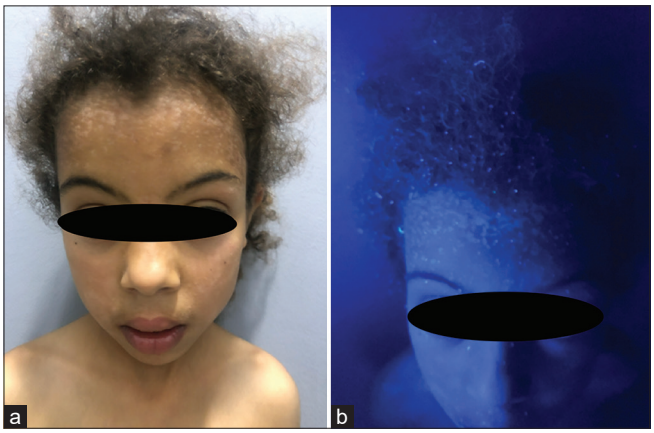


Figure 1: (a) Multiple papules with a keratotic surface on the forearms and dorsal surface of the hands associated with pigmented macules on the lips. (b and c) Multiple hypopigmented and pigmented macules on the neck.(d) Dyschromic pityriasis versicolor-like plaques on the back.



Figures 2: (a and b) Hypochromic macules on the face not taking contrast in Wood's light on the forehead in the sister.

DISCUSSION

SPJ is a rare autosomal dominant disease defined by the combination of periorificial lentiginosis-like skin involvement and digestive, pulmonary, and reproductive organ involvement [1]. The prevalence is estimated at 1 in 200,000, with no sex or race predominance, and the average age of diagnosis was 22 years in a review of 75 cases [2]. In 1921, Jan Peutz, [3], a Dutch physician, reported a family with gastrointestinal polyposis and mucocutaneous lentiginosis. In 1949, Harold Joseph Jeghers [4] published a detailed description of patients with intestinal polyposis and skin pigmentation, [1]. In a literature review of seventy cases, skin signs appeared earlier in boys (5–10 years) than in girls (10–15 years), which was not the case in our two patients [3]. These skin manifestations are a revealing sign of the disease, yet they are not the first to appear. In all cases, they are lentigines, brown- or buff-colored macules, oval, and generally less than 5 mm in diameter. They are most often found on the nose, lips, and oral mucosa, as was the case in our patient. The nasal mucosa, periorbital areas, elbows, dorsal surface of the fingers, toes, and plamo-plantar areas may also be affected [5], as in our patient.

This condition poses a problem in differential diagnosis, especially with epidermodysplasia verruciformis, a rare skin condition of genetic origin characterized by abnormal sensitivity of the skin surface to papillomavirus. Clinically, EV manifests itself in childhood between the fourth and eighth years of age, most often before the age of twenty, and lasts throughout life with flat, wart-like lesions and a macular rash similar to that known in pityriasis versicolor (pityriasis versicolor-like), disseminated and persistent [6] as was the case in our patient. The lesions usually begin on the back of the hands and forehead, progressively spreading to the limbs, neck and trunk, in rare cases reaching generalized forms, with the mucous membranes usually respected [7].

EV is associated with mutations in the EVER1/TMC6 and EVER2/TMC8 genes. Recently, a new classification of VE has been proposed distinguishing between a classical genetic form, a non-classical genetic form, and an acquired form. Recent discoveries of other genes involved in EV, including RHOH, MST-1 and CORO1A, have complicated the classification of EV and EV-like syndromes. In our patient, we assume that it was a classical form due to the presence of a familial case, as well as the age of onset of the lesions and the absence of an infection or immune deficiency [8].

In general, both conditions have a high risk of malignant transformation in both children and adults, with a lower prevalence in children [3], requiring regular and long-term follow-up.

There is no standardized treatment for mucocutaneous pigmentation, which is present in the majority of patients. Treatment is mainly cosmetic for the dermatological manifestations of Peutz–Jeghers and involves cryosurgery, dermabrasion, and Q-switched laser [4]. While for EV, complete regression of the

lesions has never been observed, as they are refractory to conventional wart treatments, preventive treatments for complications and symptomatic treatments of the lesions may be proposed, including alpha and beta interferons or imiquimod, yet their efficacy is inconsistent and temporary [9]. Cosmetically intrusive, benign tumors are treated with oral retinoids, yet results are inconsistent with a relapse on dose reduction or discontinuation. Photodynamic therapy and cryotherapy appear to be effective on viral lesions. [10]. Given the limited economic means of our two patients, only depigmenting and keratolytic creams and an early, permanent, and rigorous photoprotection were proposed.

CONCLUSION

This case was interesting because of the association between the two rare entities as well as the interest of a skin biopsy in confirming epidermodysplasia verruciformis in front of the appearance of pityriasis versicolor-like and keratotic papules in a patient with Peutz–Jeghers lentigines.

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.

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Our Dermatology Online

Review Article

150 years of Dermatology in the Municipal Hospital Dresden-Friedrichstadt

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ABSTRACT

The Department of Dermatology at the Municipal Hospital Dresden-Friedrichstadt was founded in 1874 and is the second oldest non-university department in the German-speaking countries. Founded in a former summer palace of nobles, the hospital has seen a tremendous development over time. In the early years cutaneous tuberculosis and sexually transmitted diseases dominated with limited treatment options, resulting in hospitalization and prolonged therapy. In the last decades derma-oncology and dermato-surgery become more important, but the COVID-19 pandemic has demonstrated that infectious diseases remain a challenge.

Key words: Dermatology, Dresden-Friedrichstadt, History of Medicine, Development

INTRODUCTION

In the German states, revolutions began in March 1848, propagating a National Assembly which prepared the first constitution (Reichsverfassung) for Germany. People in Dresden, Saxony, were faced with the repression of the democratic movement by the Saxonian king Friedrich August 2nd. As a result, the May Uprising began with prominent participants such as the publisher, composer and conductor August Röckel, the anarchist Mikhail Bakunin, the composer Richard Wagner, and the architect Gottfried Semper.

The number of dead rebels was later estimated at around 200, however, there is no data about the wounded people [1]. The Hospital Dresden-Friedrichstadt was founded 175 years ago in response to the needs resulting from the causalities of the revolution of 1848. It is basically located on a ground that was owned before by the Earl Heinrich von Brühl (*1700; †1763), one of the Saxonian king's favorites [2]. The character of the hospital was deeply influenced by its history as a noble palace with historic artifacts and a beautiful park (Figs. 1a and 1b) [3].

THE EARLY YEARS WITH JULIUS OTTO MARTINI

Dermatology started in the year 1874 when the II. External Department, Department of Skin and Venereal Diseases and Minor Surgery was founded. It was descended from the Department for Syphilitic Women, which belonged to Surgery. The Department consisted of 71 inpatient beds, nursing staff and physicians. It was the second Municipal Department of Dermatology in the German-speaking countries after Nürnberg (Nuremberg) which opened 1845. Although Dresden had no Medical College until 1954, when the Medical Academy "Carl Gustav Carus" was founded, the Hospital Dresden-Friedrichstadt was highly regarded.

The first leading physician in the position of a Senior Physician (Oberarzt) was Julius Otto Martini (*1829; †1909) from the start of the department until 1901. Martini attended the Princely and Country School Grimma. He studied Medicine at the University of Leipzig. Before he got his employment by the Hospital Dresden-Friedrichstadt in 1866, he worked as a Military Doctor and General Practitioner. Under his leadership

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Figure 1: (a) The Hospital Dresden-Friedrichstadt, main entrance of the Marcolini palais, 19th century.(b) Historical part of the Hospital Dresden-Friedrichstadt in recent times from inside with the Küfer (cellarman) fountain (U. Wollina).

the inpatient capacity was expanded to 140 by 1888. He was involved in "Carl Christian Schmidt's Yearbooks of Domestic and Foreign Medicine" (Carl Christian Schmidts Jahrbücher der in– und ausländischen Medizin) on systematic dermatology and treatment of skin diseases, which were published by Otto Wigand in primarily Leipzig and later also in Bonn (Fig. 2) [4]. He cooperated with the urologist Felix Martin Oberländer (*1850; †1915). Oberländer and the technician Maximilian Nitze (*1848; †1906) developed later the first cystoscope (Fig. 3) [5].

JOHANNES WERTHER AND HIS COLLECTION OF MOULAGES

Martini was followed by Johannes Werther (*1865; †1936), who got his education in Dresden. He studied medicine at the University of Leipzig and completed his specialized training in Dermatology at the Hospital Dresden-Friedrichstadt and the Charité Berlin. Under his leadership the Department received its own laboratory facilities including rooms for microscopy and photography, and a procedure room for surgery. In 1907 an X-ray machine and a quartz lamp completed the equipment. Werther had an interest in venereal diseases, lupus vulgaris, bullous skin disorders, and psychogenic skin diseases. He is considered the first describer of the Naevus syringadenomatosus papilliferus in German speaking countries [6,7] (Fig. 4).

On his initiative the Association of Dermatologists and Urologist in Dresden was founded, which held regular training evenings [8]. In 1903, he established the "Collection of Waxen Images of the Outer Department of the City Hospital of Dresden-Friedrichstadt" (Wachsbildersammlung der Äußeren Abteilung des Stadtkrankenhauses Dresden–Friedrichstadt) (Figs. 5a and 5b) [9].

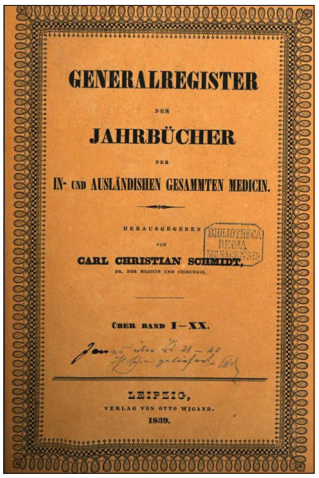

Figure 2: Year Books of Domestic and Foreign Medicine.

Figure 3: Julius Otto Martini (Plate 1116; CC BY-NC-SA @ Stadtmuseum Dresden).

Moulages are three-dimensional individualized wax models to depict the important features of skin diseases. Originating from the 19th century they became very popular for education of ongoing physicians in dermatology until the 1930ies. The moulageurs Fritz Kolbow and Emmy Kürschner-Ziegfeld produced most of the wax models in Werther's collection [10]. The

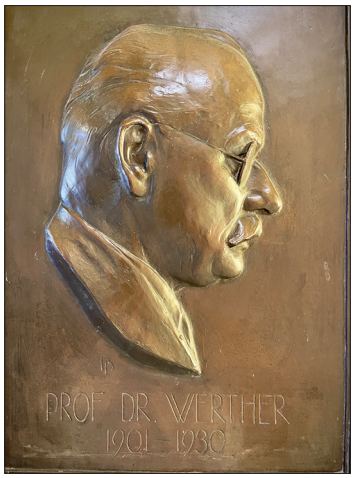

Figure 4: Prof. Dr. Werther, bronze plate.

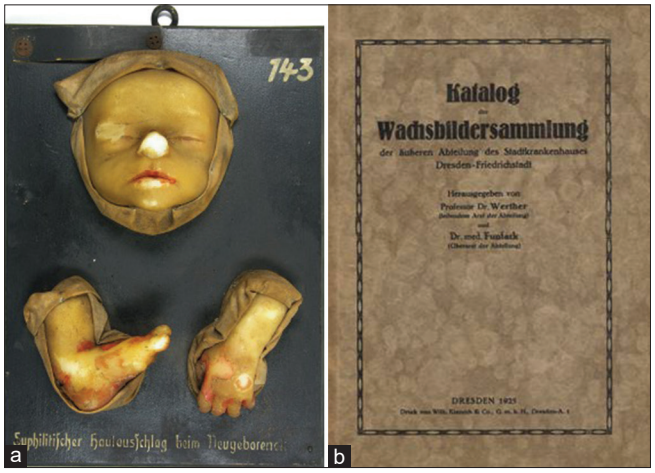

Figure 5: (a) Moulage from Werther's collection "Syphilitic rash in a newborn". (b) The catalogue of Werther's collection of moulages.

collection was expanded to 368 moulages until 1930 and survived the II. World War. However, during post-war years most of the artifacts were destroyed. Several years ago, the last moulages were transferred to the Dresden Museum of Hygiene for conservatory reasons [11].

Werther and Galewsky organized in 1925 the 14th Congress of the German Dermatological Society, for the first time at a place without a Medical University. This reflects the high appreciation for both dermatologist from Dresden, and the Department of Dermatology and Venereology in Dresden-Friedrichstadt. Werther's grave is on the Johannes cemetery in Dresden-Tolkewitz [12].

HANS MARTENSTEIN AND THE LEAGUE OF NATIONS

Hans Martenstein (*1892; †1945) became the successor of Werther in 1930. Martenstein studied Medicine at the University of Leipzig. At the University of Breslau (Wrocław) he acquired his dermatological education. His teachers were Albert Neisser (+1855; †1916), Joseph Jadassohn (*1863; †1936), and Heinrich Adolf Gottron (*1890; †1974). The University of Breslau was a Mecca for dermatologists and of outstanding impact on dermatology and venerology at the time [13].

His main interests during the years in Breslau were radiobiology and radiotherapy, cutaneous tuberculosis, and lupus erythematosus [14-18]. His investigations in syphilis culminated in his review article "Syphilis Treatment: Part I. Enquiry in Five Countries Carried out under the Auspices of the Health Organisation of the League of Nations." [19]. This may be considered as the first international guideline for diagnostics, treatment and follow-up for patients affected by syphilis.

The Committee of Experts headed by Jadassohn, made the following comments and recommendations:

(1) Treatment should be recommended as early as possible in the sero-negative primary stage. In this connection, the fullest possible use should be made, for purposes of diagnosis, of the microscopical examination of secretion from primary lesions or from lymph glands.
(2) It should be emphasised that, prior to the institution of either of the systems of treatment outlined below, there should be an adequate physical examination to determine the absence or otherwise of any indication for caution in respect of the dosage.
(3) It is essential that, in carrying out the treatment, a strict supervision of the patient be exercised, especially in respect of mucous membranes, skin, kidneys and liver.
(4) Observation, clinical and serological, after completion of treatment, should be adequate and in any case for not less than three years.
(5) Adequate examination of the spinal fluid, at least before dismissal from observation, is essential.
(6) The principles to be followed in carrying out the actual treatment should be as follows:
    (a) To employ a comparatively heavy individual dosage of the arsenobenzene and of the bismuth or mercurial compounds, the doses being administered in comparatively rapid succession, especially at the commencement.
    (b) To maintain a persistent attack on the disease, avoiding intervals of such length as to afford the parasite an opportunity of recovering.
    (c) To administer approximately as much treatment to primary as to secondary cases.

There was a lot of discussion on the optimal way to treat syphilis, which was discussed in detail in other papers, especially between US-American and European Physicians [20,21].

Bruno Bloch (+1878; †1933) and Josef Jadassohn recommended Martenstein as a successor of Georg Arndt (*1874; †1929) at the Department of Dermatology, Charité Berlin, but eventually he got no vocation [22]. Instead, he moved to the capital of Saxony, to Dresden.

In 1933 the Dermatologist Eugen Galewski (*1864; †1935) prepared the commemorative document for Jadassohn's 70th birthday. For this purpose, he was in close contact to Martenstein. But in this year the political situation in Germany changed dramatically, especially for Jewish people.

In a letter to Felix Pinkus (*1868; †1947) Galewsky wrote: „Under today's circumstances Martenstein and I believed to abstain from all preparations to honor Jadassohn until circumstances have been clarified." („Unter den heutigen Verhältnissen glaubten Martenstein und ich vorläufig von allen Vorbereitungen für die Ehrung von Jadassohn absehen zu müssen, bis sich die Verhältnisse geklärt haben werden.") [23]. Eugen Galewsky died in 1935, probably by suicide.

The foundation of an independent Department of Dermatology and Venereology in 1937 at the Hospital Dresden-Friedrichstadt is a merit of Martenstein. The clinic had 225 inpatient beds and was one of the most modern Departments of Dermatology in Germany.

Martenstein has never been a member of the NSDAP, which was quite unusual for Chief Medical Doctors during the III. Reich [24]. He died from suicide in May 1945 (Fig. 6).

Figure 6: The grave of Hans Martenstein (https://commons.wikimedia.org/wiki/File: DD-AKF-Grabmal-Martenstein.jpg).

THE POST-WAR PERIOD AND HEINZ HERING

After the II. World War the clinic was managed for short periods by Karl Gottfried Linser (*1895; †1976), Rolf Bettermann (*1917, † unknown), and Roderich Helmke (*1906; †1980). Linser studied Medicine in Würzburg and Heidelberg. From 1933 to 1945 he was the Chief Physician of the Dermatologic Unit of the Forest Park Hospital (Waldparkkrankenhaus) and the Pediatric Policlinic of the Hospital Dresden-Johannstadt before he headed the Department of Dermatology and Venereology Dresden-Friedrichstadt in 1945-1946. Later he became Ordinary of the Department of Dermatology at the University of Leipzig.

During post-war years gonorrhea and syphilis showed a dramatic increase. In Eastern Germany, the Soviet Military Administration in Germany (SMAD) released the SMAD-instruction No. 030/46 on February 12th 1946 "About the measures to combat sexually transmitted diseases". Several related instructions were published during the following years. Patients with syphilis and gonorrhea were treated in the Dermatological Hospitals, usually as inpatient treatment.

The Department of Dermatology and Venerology in Friedrichstadt had 300 inpatient beds. In 1947 the venereal patients were transferred to the Department of Infectious Diseases in Dresden-Trachau and to the Venereological Unit in the Bodelschwingh street which had nearly 180 inpatient beds. The free space was used for the Dermatological Policlinic to serve outpatients.

Heinz Hering (*1913; †1998) became the Chief Physician in 1950 and continued until 1974.

He studied Medicine in Jena, Breslau and Leipzig. Martenstein was his teacher during the dermatological specification training. In the year 1937, he habilitated on lipid metabolism in psoriasis [25]. In the same year he became a member of the NSDAP but left the party in 1944 probably while he was hold in captivity.

For several years he had a private practice. In the postwar period Hering was leading several makeshift hospitals to combat sexually transmitted diseases (STD). This made him qualified to head the Department of Dermatology

and Venereology in Friedrichstadt. In 1958-59 he achieved a reconstruction of the Department with 150 dermatological inpatient beds and a separate unit of 30 beds for patients with STD. In 1961 the number of inpatient beds was reduced to 150.

His clinical engagement at the Hospital Dresden-Friedrichstadt was focused on X-ray therapy, allergology, cutaneous tuberculosis, phlebology, venereology, and occupational dermatology. He established the varicose sclerotherapy according to Paul Linser (*1871; †1963) in Dresden-Friedrichstadt.

On the initiative of Hering, the Society of Dermatologist of Leipzig and the Association of Dermatologist of Dresden merged in 1957 to create the Assembly of the Saxonian Dermatological Society [26].

His view on patients with STD would be unacceptable today. Patients with changing sex partners were characterized as "impulsive", "moronic", and "unrestrained". He argued against ambulatory treatment of patients with gonorrhoea, because he feared that this would cause a higher promiscuity [27]. This statement cannot conceal the Janus face of East German health policy and morality. Prostitution was officially prohibited, but the Ministry for Internal Affairs used prostitutes to obtain information from visitors from Western countries [28].

In 1961 a secured ward for STD patients was founded that existed until 1974. Compulsory admissions to the venereological inpatients units were partially politically motivated based on the regulations of the SMAD in 1947 and continued until the mid 60ies [29].

The Department of Dermatology and Venereology also served as a burn center [30]. In the late 60ies Volker Tempel (*1939; †2022) raised a dermato-surgery unit which was also used for the treatment of burn patients. He was a surgeon and worked in the Department of Dermatology and Venereology.

After Hering had left the clinic, the department was managed for the next two years by senior physician Gerhard Goßrau (*1934), who was a specialist in photodermatology.

CLAUS SEEBACHER – A NEW START IN MYCOLOGY AND MELANOMA RESEARCH

In 1976 Claus Seebacher (*1935) became the new Head of the Department. He studied Medicine at the Universities of Greifswald, Leipzig and the Medical Academy in Dresden. Under his leadership, the department was modernized. In 1991 the reconstruction was completed, and the department had now 102 inpatient beds. He also established a special laboratory for mycology and the first digital database for cutaneous melanoma [31]. Mycology is his life. Together with Renate Blaschke–Hellmessen (*1931; †2022), microbiologist at the Medical Academy Dresden (later University Dresden) he edited in 1990 the definitive book "Mykosen: Epidemiologie - Diagnostik - Therapie" (Mycoses: Epidemiology – Diagnostics - Treatment) [32]. For many years, Seebacher served as Head of the Sub-Commission "Mycology" of the German Committee on Guidelines in Medicine (Fig. 7).

Seebacher connected to the tradition of the "Verein Dresdner Dermatologen", and founded in 1977 an annual symposium known as "Dresdner Dermatologische Demonstration" (Dresden Dermatological Demonstration). The tradition was only interrupted in 2020-2023 by the COVID-19 pandemic. It consisted of live patient demonstrations, short speeches on interesting case reports, and invited lectures [33,34].

Together with H. Bernhardt and Renate Blaschke-Hellmessen he organized the 5th Congress of the European Confederation of Medical Mycology and 33rd Congress of the Mycological Society of German Speaking Countries (DMyk) in June 1999 in Dresden [35]. He wrote reviews on the history of mycology in German-speaking countries and in former

Figure 7: Prof. Claus Seebacher (left) and Prof. Uwe-Fritjof Haustein (right) at the Symposium on the 80th birthday of Prof. Seebacher in the Marcolini Palais.

East Germany [36,37]. Seebacher was awarded as Honorary Member of the DMyk [38].

During Seebacher's leadership, Erich Köstler (*1943; †2007) habilitated on cutaneous porphyria. He studied medicine at the University of Leipzig. In 1969 he began his special training in Dermatology at the Hospital Dresden-Friedrichstadt. He worked closely with the Centre for Porphyrias in Chemnitz, the largest in Germany, headed by Ulrich Stölzel (*1955). In 1990 he became Privat-Dozent and in 2003 he became an adjunct professor at the Technical University of Dresden. He was an excellent clinician and dermato-surgeon [39]. He published several papers on porphyria diagnostics and treatment and the role of hemochromatosis (HFE) gene mutations [40-42].

THE LAST 2 DECADES

The successor of Claus Seebacher was Uwe Wollina in 2001. He studied Medicine at the Friedrich-Schiller-University of Jena. He headed the department for 22 years. The main interests of his clinical and scientific work were skin cancer, wound healing and chronic wounds, dermato-rheumatologic disorders, psoriasis, and dermato-surgery. The cooperation with the Porphyria Center Chemnitz was continued with Dr. André Koch, who is also connected to the Allergy Center of the Technical University of Dresden. Together with Birgit Heinig (Physical Therapy and Rehabilitative Medicine) Wollina established the Center for Lymphatic Diseases Dresden for patients with lymphedema and lipedema in conjunction with an outpatient clinic. The Department of Dermatology and Allergology became a certified Center for Dermato-Oncology (European Cancer Centers) with Dr. Gesina Hansel as Secretary. The spectrum of Dermato-Surgery was expanded for skin cancer and leg ulcers. Liposuction and laser surgery were established. Dr. Claudia Krönert became the Senior Physician for the surgery ward.

In 2011, the Department of Dermatology and Allergology moved to a modern new building, which significantly improved working conditions for the staff and comfort for the patients (Fig. 8). Processes were optimized and quality management was implemented.

Wollina was a co-founder of the very popular interdisciplinary training series "Psoriasis and Psoriatic Arthritis" in conjunction with Hubert Nüsslein (Rheumatology) and Leonore Unger (Rheumatology, Osteology).

Figure 8: The new building for the Department of Dermatology and Allergology, the ENT Department and the Department of Ophthalmology.

He organized the Congress of the European Society of Cosmetic and Aesthetic Dermatology COSMODERM XVI in 2010, the 5. Joint Lymphology Congress of the German Society of Lymphology and the Austrian Society of Manual Lymphdrainage (Dr. Vodder) in 2008, and the 1st International Dermatology Symposium and Regional Meeting of the International Society of Dermatology in Dresden [43,44].

A major challenge was the flooding of Dresden and the Hospital Dresden-Friedrichstadt in 2002 when 900 patients had to be evacuated from the hospital within a day [45].

The COVID-19 pandemic also had a strong impact on the Hospital and the Department of Dermatology and Allergology. Available inpatient beds and human resources became sustained restricted in university and non-university dermatologic departments, although necessary surgical interventions in cancer patients could be performed during the pandemic [46].

Wollina was last President of the Saxonian Society of Dermatology, Past-President of the ESCAD, and former Chairman of Regional Officers of the International Society of Dermatology (ISD). He is an Honorary Member of the Maltese Association of Dermatology and Venereology (MADV), Honorary Member of the Cosmetic Dermatology Society of India, and Honorary Member of the Jordanian Dermatological and Venereological Society. Wollina received the Certificate

of Appreciation 2014 of the International League of Dermatological Societies (ILDS) for his engagement in the International Society of Dermatology [47].

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Our Dermatology Online

Clinical Image

Tattoo removal by caustic products complicated with erysipelas

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Tattoo art has been present for thousands of years in all cultures and is currently flourishing in all age groups, social classes, and occupations. Despite the rising popularity of tattoos, demand for their removal has also increased. Caustic products are used as affordable alternatives for laser tattoo removal [1]. Herein, we report a case of tattoo removal performed by non-medical professionals and complicated by erysipelas.

A 27-year-old female presented with fever and a painful left forearm after having a tattoo removed chemically with lactic acid by a non-medical professional (Fig. 1). A physical examination revealed an infiltrated, erythematous, edematous, and painful skin patch surrounding a necrotic and purulent area (Fig. 2). We also found axillary lymphadenopathy. A neurological examination was normal; there were no defects in finger spacing capacity or the overall grip of the hand. Oral antibiotic therapy based on amoxicillin and clavulanic acid with silver sulfadiazine cream was prescribed with the disappearance of the fever after 24 hours and the beginning of healing of the area of the removed tattoo and the elimination of the necrotic crusts.

Clinicians in the field of dermatology and plastic surgery are in their work now and are confronted with tattoo complications. Acute conditions are dominated by bacterial infections needing antibiotic treatment. Systemic infection is a matter of urgency and requires intravenous treatment in a hospital immediately to prevent septic shock [2,3]. Products are obscured and liability and consumer protection are unacceptable; limitation is needed.

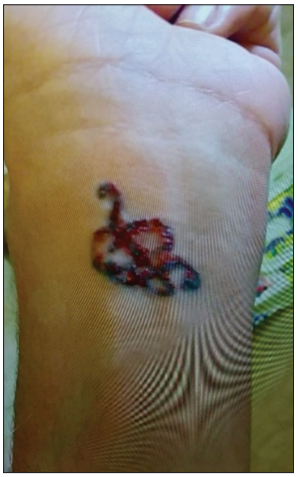

Figure 1: The appearance of the skin thirty minutes after removing the tattoo.

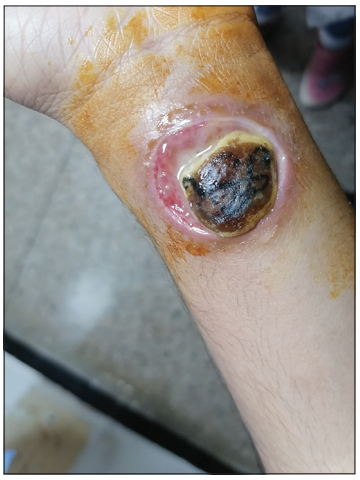

Figure 2: The appearance of the skin on the consultation after fifteen days.

Consent

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

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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.

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Our Dermatology Online

Research Letter

Quality of life of patients with melasma: Is there a correlation between the Melasma Area and Severity Index (MASI) and the Melasma Quality of Life Scale (MelasQoL)?

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Sir,

Melasma, one of the most common causes of acquired hyperpigmentation, is characterized by light to dark brown macules located on photo-exposed areas [1], having a significant impact on appearance and psychosocial and emotional distress, making the assessment of QoL in patients with skin disorders increasingly important [2].

Is this deterioration in the QoL of melasma patients mainly related to disease severity or are other factors involved?

The aim of this study was to assess patient quality of life and to investigate the different clinical factors associated with this disease that may influence the quality of life of melasma patients.

This was a prospective analytical study of seventy subjects with melasma conducted over a period of seven months.

Melasma severity was assessed using the MASI score.

The study subjects completed the MelasQoL questionnaire.

The MelasQoL is a ten-item questionnaire on the impact of melasma on the patient's emotional state, social relationships, and daily activities. Each patient indicates how they feel about their skin condition on a scale from 1 (not bothered at all) to 7 (bothered all the time). The total score is calculated as the sum of all scales for each question (the total score varies from 10 to 70).

The data was analyzed using SPSS software. The association between categorical variables was tested using the $\chi 2$ test. The p value was considered significant if it was less than or equal to 0.05.

All patients were female. The mean age of onset and duration of melasma were 32.14 and 9 years, respectively.

The majority of the patients had no family history of melasma (81.6%).

The MelasQoL analysis showed that 92% of the patients felt self-conscious about the appearance of their skin, 58.9% were frustrated and embarrassed by their skin condition, 51.6% were depressed, and 79.5% felt unattractive.

However, for 85.53% of the patients, the skin condition did not affect their relationships with others and, for 75%, it did not affect their desire to socialize, communicate or spend time with others. In addition, 88% of the patients did not find it difficult to express affection, 54.2% did not feel that their importance or productivity had decreased, and 54.83% did not feel that their freedom had been restricted (Table 1).

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Table 1: Answers for the MelasQoL questions (*n*=70).

	Not bothered at all (%)	Not bothered most of the time (%)	Not bothered or sometimes bothered (%)	No feeling either way (%)	Sometimes bothered (%)	Bothered most of the time (%)	Constantly bothered (%)
Skin appearance	0	1	6	1	2	80	10
Frustration due to skin condition	20	14	7	0	6.9	40	12
Embarrassment at skin condition	13	25	8	1	7	30	22
Depressed by skin conditio	48.4	5	11	0	20.4	10.2	5
Effects of the skin condition on the desire to be with people	60	15	2	13	6	4	0
Difficulty in showing affection	75	13	2	12	8	0	0
Effects of the skin condition on relations with other people	80.03	3.5	2	6.5	7	1	0
Feeling unattractive due to skin blemishes	2	10	18.3	10	22	17	10.2
Reduced sense of importance/ productivity	30	24.2	10.8	15	10	8	2
Restricted sense of freedom	50	4.8	15.2	10	7	10	3

The analytical study showed no statistically significant association between the MelasQoL and MASI scores ($p > 0.05$) or with other associated parameters such as family history or phototype. However, a younger age and longer disease duration were significantly associated with higher MelasQoL scores ($p < 0.05$).

The negative influence of various pigmentation disorders, including melasma, is well documented [1].

In line with previously published studies, our study confirmed that melasma has a major impact on the patient's quality of life, causing emotional distress due to feelings of dissatisfaction, frustration, embarrassment, and depression related to their skin condition [3].

On the other hand, and contrary to previous studies, the social life of our patients was, paradoxically, less altered by the pathology [3].

Several studies have analyzed the relationship between quality of life and lesion severity using the MASI score, yet most have reported that they are not related or that the correlation is weak [4-6]. Clinical severity should not be the only criterion to assess the psychological impact of the patient's skin condition [2]. This was consistent with our results.

Therefore, some authors have tried to obtain demographical factors influencing MelasQoL scores to explain this situation [6].

In fact, several factors have been analyzed in previous studies, especially age, family history, the patient's educational level, and duration of evolution, with these inconsistent results.

The effect of patient age on MelasQoL score has also been analyzed, with most studies finding no correlation between these two parameters [3-6]. Some found a correlation between a younger age and a higher MelasQoL score, as in our study, while others concluded that, on the contrary, an older age is more likely to lead to greater impairment of quality of life [1-3].

Our study found no association between the patient's family history of melasma and impaired quality of life, which was consistent with the literature [3].

Regarding the patient's educational level, some authors described the MelasQoL scores of patients with lower educational level as significantly higher than those with higher educational level [7]. The authors suggested that a lack of knowledge about the disease leads to greater anxiety and that patient education is, therefore, of paramount importance [6]. However, other studies reported no difference in MelasQoL scores regardless of education level [6].

In addition, several studies found no significant effect of the duration of development on the MelasQoL score [1-6], while others concluded that a longer duration of evolution is significantly associated with a higher MelasQoL score and, thus, with a significant

deterioration in quality of life, which was consistent with our findings [3-5].

In light of our results, we conclude that factors other than disease severity were associated with decreased quality of life in our patients, particularly a young age and longer disease course.

Given the conflicting results of the various studies analyzing the factors influencing the MelasQoL score, further studies are needed to determine the factors contributing to the altered quality of life in our melasma patients.

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Our Dermatology Online

Case Letter

Zosteriform metastasis of Burkitt lymphoma as evidence of disease relapse

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Sir,

Burkitt lymphoma is a highly aggressive B-cell non-Hodgkin lymphoma that represents less than 5% of cases of lymphoma in adults [1]. It commonly affects the lymph nodes and extranodal sites, in particular, the ileocecal area, central nervous system, and bone marrow [2]. Skin involvement is highly rare and may occur by hematogenous dissemination, direct extension, or iatrogenic tumor seeding of the skin and subcutaneous tissue during an invasive procedure, such as the excision of the primary tumor, celioscopy, or the insertion of a catheter into primary lesions [3,4]. It may reflect a systemic involvement or relapse of the disease. A zosteriform pattern appears to be unusual [4]. Only one case has been reported in the literature [5], which was an elderly Asian male who primarily developed a skin rash with the clinical presentation of a dermatomal distribution on the face, which had been erroneously diagnosed as herpes zoster infection and treated with acyclovir without improvement; a biopsy was performed in front of the appearance of new skin lesions confirming the diagnosis of Burkitt lymphoma. This pattern has also been reported in some cases of primary solid and hematologic malignancies, such as colon and breast cancer, melanoma, cutaneous squamous cell carcinoma, Kaposi's sarcoma, and T- and B-cell lymphomas [6,7]. The suggested pathogenic mechanism was a Koebner-type reaction at the site of a previous herpes zoster [5]. The diagnosis is confirmed by an anatomopathological study and the treatment is based on polychemotherapy [1]. Herein, we report a new observation of zosteriform metastasis of Burkitt lymphoma as evidence of disease relapse.

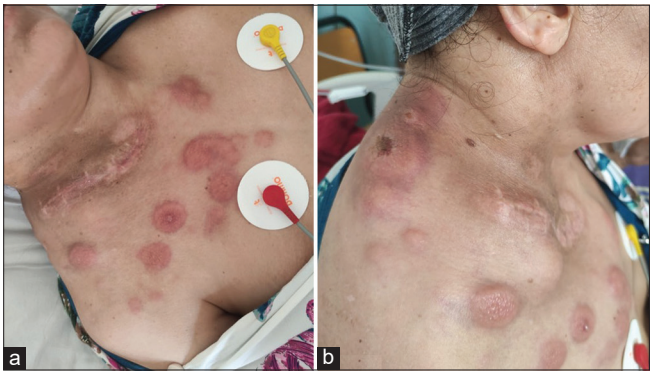

Figure 1: (a and b) Indurated, erythematous nodules with a zoster-like arrangement in the right C3-C4 dermatomes.

A 43-year-old female with no history of herpes zoster, followed for non-metastatic Burkitt lymphoma initially, diagnosed on a biopsy of a right laterocervical mass, having received four courses of chemotherapy combining cyclophosphamide, vincristine, adriamycin, and prednisone, with an 80% response at re-evaluation after three courses, consulted one week after the fourth course of treatment for an intracranial hypertension syndrome and an asymptomatic skin rash. A physical examination revealed a group of indurated, erythematous nodules, with some excoriated lesions at the center, measuring 1.5 cm in the case of the largest, linearly distributed on the upper back on the right side, the shoulder, and the ipsilateral subclavicular region, compatible with right C3-C4 dermatomes (Figs. 1a and 1b). A skin biopsy was performed and an anatomopathological study revealed a cutaneous localization of her lymphoma. The patient had also undergone a lumbar puncture with a study of the cerebrospinal fluid, which showed the presence of malignant cells, and a re-evaluation scan, which showed

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a progression of her lymphomatous disease with an increase in the size of the laterocervical mass and the appearance of hepatic and cerebral localizations. The patient died several days later following a septic shock.

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.

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Our Dermatology Online

Case Letter

Nummular eczema on an old burn scar

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Sir,

Herein, I describe two cases of nummular eczema on an old burn scar.

CASE 1

A 72-year-old male visited our department complaining about itchy eruptions on the lower leg during the winter season. A physical examination revealed a depigmented oval scar with peripheral brownish pigmentation on the right lower leg and erythema with slight scales on the scar (Fig. 1). Although diffuse dry skin was observed, eczema was confined to the scar, and there were multiple senile leukoderma lesions near the scar. The patient stated that the scar was the result of a burn injury caused by contact with healed metal that had occurred more than 30 years previously. He had no medical history and was not taking any medications. Itchy erythema improved by topical corticosteroid ointment within two weeks.

CASE 2

A 60-year-old male visited our department complaining about an itchy eruption on the lower extremity during the winter season. A physical examination showed scaly erythema on the left lower leg (Fig. 2). The patient stated that erythema initially appeared on a scalded scar by boiling water fifty years previously and spread around the scar. A closer physical examination revealed hair loss on the deep burned site (Fig. 2 *arrow*). He had no medical history and was not taking any medications. The lesions improved with topical corticosteroid ointment within one month.

Herein, I presented two cases of nummular eczema on an old burned scar, which were considered to be induced as a result of Köbner response. Boyd and Nelder [1] previously classified the pattern of isomorphic response of Köbner into four categories: true Köbner response, pseudo-Köbner response, occasional traumatic localization of lesions, and

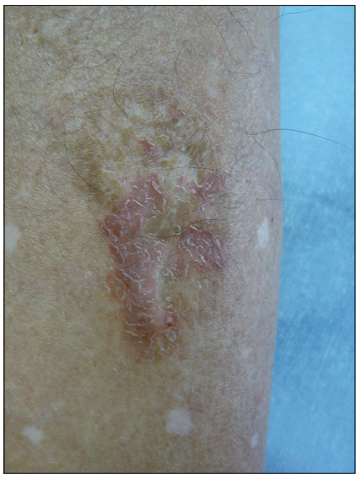

Figure 1: Nummular eczema confined to the burn scar on the lower extremity (case 1).

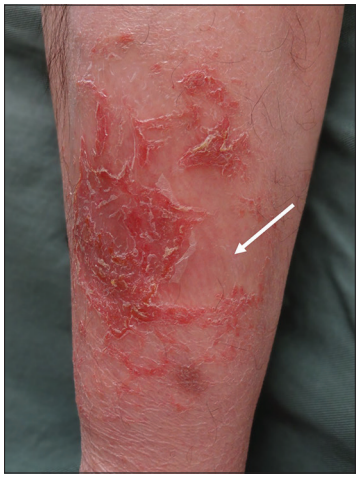

Figure 2: Nummular eczema on the old scar with hair loss (*arrow*) on the lower leg (case 2).

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poor/questionable trauma-induced processes. Eczema is included in the last category, along with a number of conditions.

Injured skin is not normal and is susceptible to developing other lesions. We have recently reported a case series of nummular eczema that developed on an old surgical scar [2]. Epidermal T cells, including tissue resident memory T cells (T_{RM}), exist in the epidermis of the surgical scar [3]. T_{RM} in the scar epidermis may be involved in the development of nummular eczema; however, the stimuli that activate resting T_{RM} and convert into activated T_{RM} have not yet been clarified. Köbner response may be associated with vascular, immunologic, neural, and hormonal factors. Environmental factors such as xerosis or dry season may also be triggers for an eczematous reaction. The patients in the present two cases had 30- and 50-year-old burn scars, suggesting the long-term local presence of T_{RM} at scar sites.

Another possible mechanism of the nummular eczema on the scar may involve the role of absent in melanoma 2 (AIM2). AIM2 activation in keratinocytes drives the development of immune disorders such as psoriasis, as well as the wound healing process, suggesting that AIM2 might be the key marker modulating trained immunity in inflammation-experienced epidermal keratinocytes [4,5]. Further studies are necessary to clarify the mechanism of the development of nummular eczema on the scar.

Consent

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

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

Our Dermatology Online

Case Letter

Phytophotodermatitis, report of four cases

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Sir

Phytophotodermatitis is a non-immunological inflammatory reaction of the skin to phototoxic substances, typically triggered by contact with botanicals sensitive to ultraviolet A light. Clinically, it may present with lesions characterized by erythema, blisters, and burning sensation, resembling a burn, and in the final phase, it can leave pigmentation.

A 30-year-old male presented with dark spots on his back, evolving over 5 days. Upon evaluation, he exhibited localized dermatosis on the back characterized by linear and irregular spots, along with two rounded ones (Fig. 1).

A 20-year-old male consulted due to the presence of brown spots on his back, evolving over 4 days. He exhibits localized dermatosis on the upper third of the back, consisting of a map-like dark spot and linear streaks resembling drips (Fig. 2).

A 40-year-old male consulted due to the presence of dark spots on his left leg, evolving over 8 days. Initially, he developed blisters which subsequently ruptured, leaving behind that dark hue, prompting the consultation. He exhibits localized dermatosis on the anterior aspect of the left leg, characterized by rounded dark spots (Fig. 3).

A 45-year-old female consulted regarding the presence of black spots on the anterior chest and exposed areas of the upper limbs, characterized by dark spots. She mentioned that one of them blistered. She presents disseminated dermatosis on the anterior chest and upper third of the upper limbs, characterized by irregularly shaped brown spots. The largest spot has a plaque with an erythematous center and surrounding scales, as well as hyperpigmented skin around it (Fig. 4).

All these patients were diagnosed with phytophotodermatitis, without any significant personal or family history. They all had a history of being at the beach for vacation and consuming salads, guacamole, beer, tequila, and rum with lemon.

Phytophotodermatitis is a cutaneous phototoxic inflammatory eruption, its name comes from Greek roots: "phyto" meaning plant, "photo" referring to light, and "dermatitis" indicating skin inflammation [1]. It occurs by ingestion of or topical exposure to furocoumarins, which are present in some plants like: carrots, citrus fruits, bergamot, buttercup, peppers and celery [2,3].

These substances respond to UVA radiation by utilizing their main component, psoralen, resulting in skin reactions of erythema, edema, tenderness, burning sensation, pain, inflammation, itching and bullae with subsequent hyperpigmentation can develop [2,3].

Previous sensitization is not necessary for the rash to occur because it is a non-immunological reaction. The skin lesions can be irregularly shaped, typically painful rather than itchy, and appear exclusively on sun-exposed areas. This characteristic helps distinguish the condition from contact dermatitis caused by plants [3].

The signs and symptoms of Phytophotodermatitis usually start 24 hours after contact with the skin and reach their peak between 48 to 72 hours afterward [4]. Acute dermatitis is self-limiting and resolves within a period of days to weeks, but resulting hyperpigmentation, caused by increased melanin production stimulated by psoralens, can last weeks to months [1,5].

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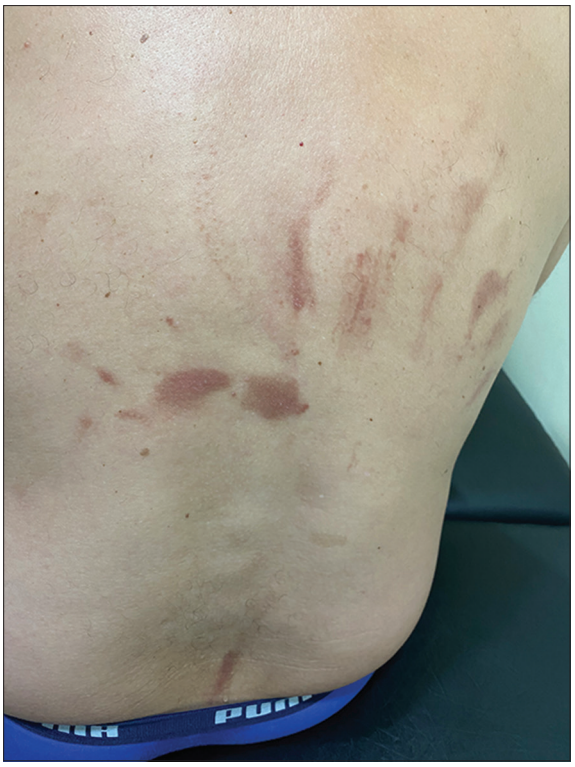

Figure 1: Linear scattered spots on the back.

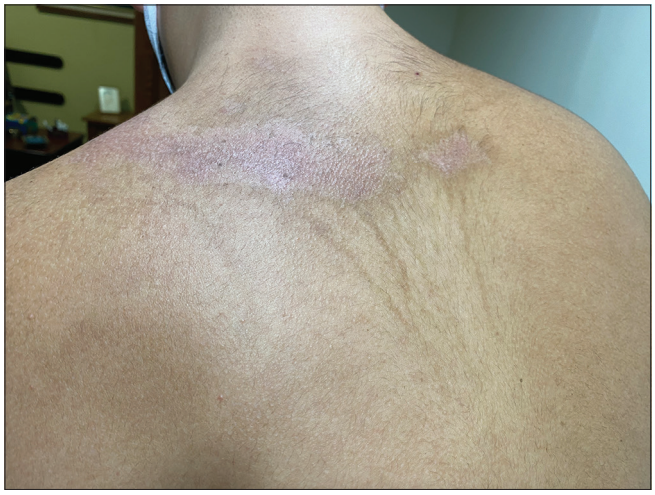

Figure 2: Blackish cartographic and linear spots resembling streaks.

All patients should be instructed to steer clear of sunlight and photosensitizing substances after experiencing the initial reaction. Typically, phytophotodermatitis resolves on its own without lasting effects, so treatment is generally unnecessary [4].

For acute lesions, applying cool, damp compresses can help. Moderate symptoms may benefit from short-term use of corticosteroids or antihistamines to relieve discomfort. In severe cases with swollen eruptions, topical steroids may be prescribed. Adults might take

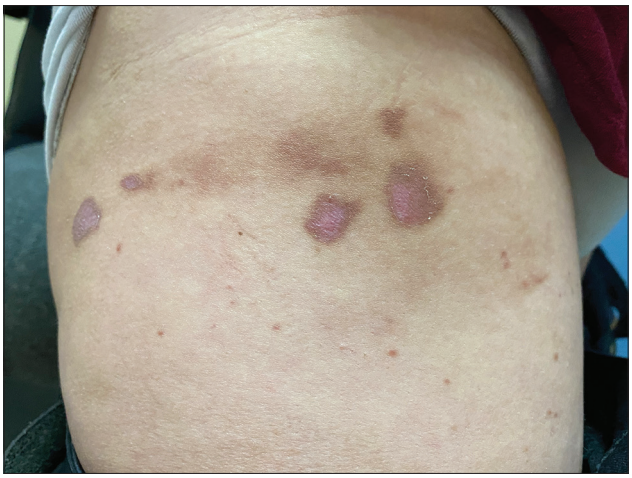

Figure 3: Presence of rounded blackish spots on the anterior aspect of the left leg.

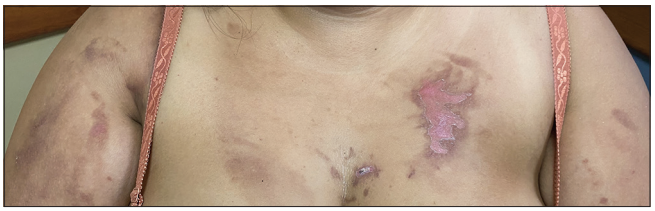

Figure 4: Disseminated dermatosis on the anterior chest and upper third of the upper limbs with the presence of blackish spots of variable shape and size.

Indomethacin orally (50-75 mg). If the condition worsens or affects more than 30% of the body, it is recommended to seek admission to a burn unit for specialized local wound care [4].

This condition could be mistaken for cellulitis, allergic contact dermatitis, or a fungal skin infection [6].

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.

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

Case Letter

Punctate lesions on palmar creases: An enigma decoded

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Sir,

A 33-year-old male presented with complaints of lesions on the bilateral palmar creases. The lesions had been present for one year and were otherwise asymptomatic. There was no familial history of similar lesions nor a history of lesions elsewhere in the body. On cutaneous examination, numerous, tiny, hyperkeratotic, skin colored, 2–4 mm pits were found on the palmar creases of both hands. The lesions had a predilection for the transpalmar crease and the proximal interphalangeal joint crease of both hands (Fig. 1a). He was in good condition and had no other skin lesions. On dermoscopy, there was a central crust in all lesions on the palmar creases (Fig. 1b).

The results of a complete blood cell count and blood chemistry studies were normal. The above findings were consistent with keratosis punctata of the palmar creases (KPPC).

A microscopic examination of the punctate keratosis of the palm revealed orthokeratotic hyperkeratosis, hypergranulosis, and acanthosis. Hyperkeratosis forms a conical horn overlying a depression in the epidermis. No abnormalities were observed in the dermis. The patient was treated with retinoic acid and local keratolytics, which temporarily improved the condition.

KPPC is a hyperkeratotic benign dermatosis primarily found among people of African descent. They have hyperkeratotic plugs, which break off, leaving characteristic pits. The lesions begin in adolescence or early adulthood [1].

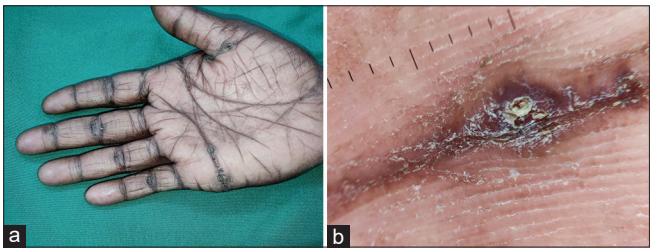

Figure 1: (a) Multiple tiny hyperkeratotic lesions on the palmar surface with a predilection on the creases. (b) Dermoscopy showing the prominent central crusting.

The cause of KPPC remains unknown. Several etiologic theories have been proposed. Although few cases have been reported with a history of arsenic exposure and latent syphilis, many others seem to be due to an abnormal hyperproliferative localized response in predisposed persons possibly induced by trauma. The relationship between the keratotic plug and the acrosyringium has been found in some cases. Yet, in our patient, the acrosyringium was normal. Additionally, KPPC has been reported to occur in association with Dupuytren's contractures, pterygium inversum unguis, dermatitis herpetiformis, psoriasis, and ichthyosis vulgaris [2].

This condition has to be differentiated from keratosis punctata palmoplantaris (KPPP), a rare condition with diffuse pitting of the palmoplantar surfaces, as opposed to its occurrence limited only to the palmar creases [3]. KPPC is a benign process while KPPP carries the associated risk of colorectal malignancy. Hence, it is very important to evaluate the patient and exclude the differentials.

Our case showed characteristic hyperkeratotic pits confined only to the palmar creases. In addition, the other differentials include basal cell nevus syndrome,

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arsenic exposure, palmoplantar porokeratosis, latent syphilis, verrucae vulgaris focal acral hyperkeratosis, and acrokeratoelastoidosis. Treatment with topical retinoids and emollients has been documented [4]. Surgical treatment has also been used for severe and localized disease.

Consent

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

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

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

Our Dermatology Online

Case Letter

Pyoderma gangrenosum mimicking mycobacterial infection

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Sir,

A 79-year-old female was referred to our hospital complaining of painful, elevated nodules and plaques with ulcers on the extremities, which appeared two months previously. Because oral antibiotics were ineffective, she was referred to our hospital. She had not engaged in agricultural work nor kept tropical fish. A physical examination showed a painful, elevated, edematous swelling with partial ulcerations on the right forearm and the dorsum of her left foot (Figs. 1a and 1b). The surface was a reddish granulation, and the ulcer was surrounded with erythema. A laboratory examination showed an increased white blood cell count (5,800/μL, with 82% neutrophils), elevated levels of C-reactive protein (4.29 mg/dL), while β-D-glucan and T-SPOT were normal. We attempted taking a skin biopsy, yet she developed transient loss of consciousness twice due to vagal reflex by local anesthesia. In the meantime, the lesions on the extremities worsened with larger ulcerations, and new ulcers appeared on the buttocks (Fig. 2). A biopsy specimen from the edge of the ulcer showed dense infiltration of neutrophils and mononuclear cells in the lower dermis and subcutaneous tissue (Figs. 3a and 3b). Stain with Grocott and Ziel–Neelsen was negative. Cultures for bacteria, deep fungus, and mycobacterium were sterile in both superficial pus and biopsied tissues. Examination by respiratory medicine excluded either lung tuberculosis or fungal pneumonia. She was initially treated with systemic prednisolone (20 mg/day), which resulted in sufficient effects. However, during prednisolone tapering, ulcers relapsed, and adalimumab was added with successful results.

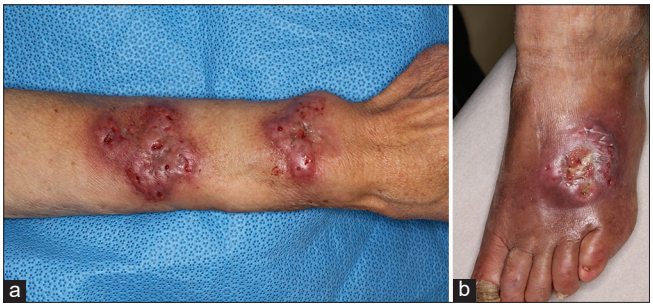

Figure 1: (a) Elevated, reddish plaques on the forearm. (b) Elevated, granulomatous plaque with central ulceration on the dorsum of the feet.

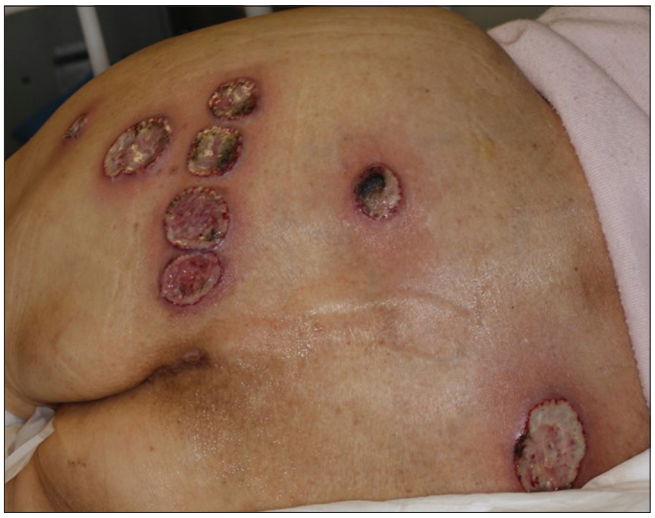

Figure 2: Multiple, round ulcerations with elevated borders on the buttock.

The diagnosis of pyoderma gangrenosum (PG) is sometimes difficult, because the histopathological features of PG are non-specific. Therefore, clinical findings are important for the diagnosis of PG; however, there are a number of disorders presenting with refractory skin ulcers mimicking PG, due to various causes, such as occlusive venous diseases, vasculitis, cancer, primary infection, drug-induced, exogenous tissue injury, and other inflammatory disorders [1]. Among the 95 cases

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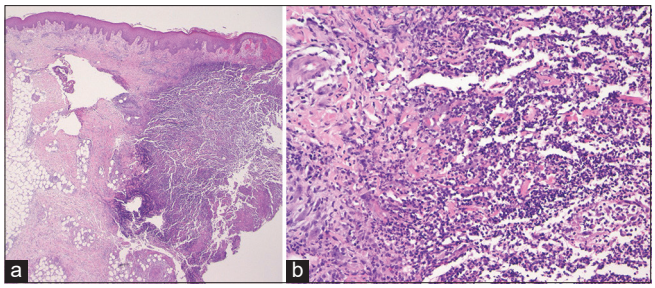

Figure 3: a) Histological features showing prominent infiltration of neutrophils (H&E; 40×). b) Higher magnification revealing dense neutrophil infiltration (400×).

presenting with PG-like skin ulcers, 14 were primary cutaneous infection, and among them, 10 had deep fungal infection [1]. There have been several cases of cutaneous cryptococcosis [2], sporotrichosis [3], deep fungus [4], and Buruli ulcers [5], which showed PG-like appearance or were misdiagnosed as PG. Thus, mycobacterial or deep fungal infection may present with clinical features mimicking PG. On the contrary, cases of PG showing mycobacterial infection are not numerous. In the present case, judging from the granulomatous clinical appearance, mycobacterial infection was initially suspected; however, mycobacteria culture was sterile, and the patient developed multiple ulcerations with edematous borders on the buttock during the skin biopsy, which was postponed. Finally, PG was diagnosed by histopathological examination. To date, some diagnostic criteria have been proposed, which described the clinical features as ulcers with irregular, violaceous, and undermined borders [6]. Differentiation from other diseases presenting with leg ulcers is necessary. Clinicians should be aware that PG may assume a varying clinical appearance, and a multifocal approach is required to differentiate other diseases presenting with ulcers. Finally, our patient was successfully treated with oral prednisolone and adalimumab. Adalimumab has recently been approved for PG in Japan [7] and is useful for cases showing steroid resistance or steroid-tapering difficulty.

Consent

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

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Our Dermatology Online

Case Letter

Miliaria crystalline in adults

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Sir,

Miliaria crystalline, is a common condition affecting the sweat glands, particularly, the eccrine ducts, and is typically observed in the immature sweat glands of newborns. However, it is uncommon for adults to experience this condition. This article presents two cases of miliaria in adults. Sweat glands are distributed throughout the body, primarily serving to regulate body temperature during high-heat exposure. However, dysregulation of the skin surface may lead to various causes, including inflammation and bacterial infection, resulting in glandular blockage, which will be further elaborated upon.

One patient was a fifty-year-old female hospitalized in the intensive care unit for decompensated diabetes and severe sepsis due to urinary tract infection under medical treatment. During her stay, she presented with a disseminated dermatosis on the anterior chest, back, and abdomen consisting of vesicles (Figs. 1a and 1b). The rest of the physical examination revealed the patient in poor overall condition and with fever. The patient passed away eight days after hospitalization.

The other patient was a 32-year-old female hospitalized in the intensive care unit for sepsis following a surgical wound infection. During her stay in the service, she presented with a disseminated dermatosis on the anterior chest, back, axillae, and abdomen characterized by multiple vesicles on healthy skin (Fig. 2). The rest of the physical examination revealed the patient in poor general condition and with fever. The patient was discharged four weeks after her stay in the service.

In both patients, the clinical diagnosis of adult-onset miliaria crystallina was made, which was favored by the

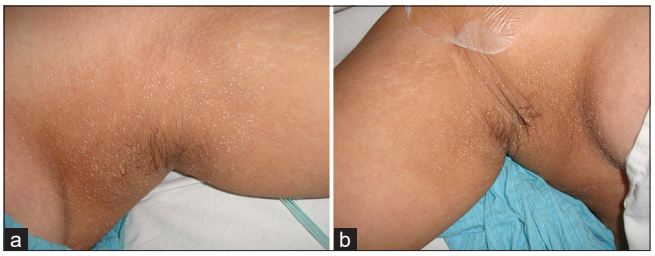

Figure 1: (a and b) Vesicular lesions in both armpits.

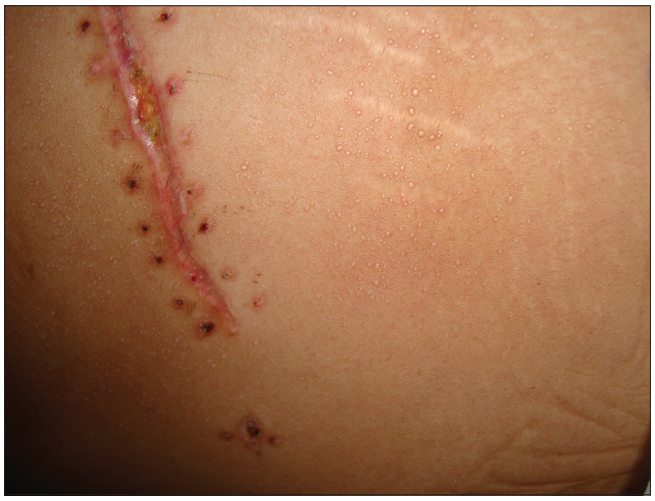

Figure 2: Abdominal vesicles on healthy skin.

feverish state secondary to the sepsis that they both had. In this study, we aim to highlight this uncommon dermatological aspect in adults.

Miliaria is a structural and functional alteration of the eccrine excretory ducts due to the body's exposure to high temperatures and extreme humidity conditions, resulting in a generally pruritic dermatosis on the skin [1].

This dermatosis may occur in patients of any age, yet children, especially in the early years of life, are the

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most affected. It is believed that miliaria in childhood is the result of immaturity of the eccrine structures, with partial closure and sweat retention. Interestingly, little is known about miliaria in adults [1].

There are three forms of miliaria: miliaria crystalline, when obstruction of the eccrine duct occurs in the stratum corneum; miliaria rubra, when sweat is retained in the stratum Malpighii; and deep miliaria, when the aforementioned occurs in or below the dermoepidermal junction. This translates into different clinical presentations, with progression from superficial to deep forms, influencing responses to various treatments [1,2].

For adults, miliaria arises from the obstruction of the sweat gland ducts by dead skin cells or bacteria such as *Staphylococcus epidermidis* and *Staphylococcus aureus*. These bacteria produce a sticky substance which, when combined with excessive sweat and dead skin cells, may lead to blockage. The acute inflammation of sweat ducts is triggered by the blockage of pores due to macerated skin, and it is believed that over-hydration of the stratum corneum is adequate to cause temporary blockage of the acrosyringium, which is the most superficial region of the sweat gland duct [3].

Nevertheless, mere sweating does not suffice to trigger duct disruption and miliaria. Increased levels of sodium chloride on the skin, elevated humidity, and wearing occlusive clothing may contribute to eccrine duct disruption due to the maceration of the stratum corneum. Additionally, damage to epidermal cells induced by ultraviolet radiation may also result in ductal disruption [3].

Since miliaria arises in hot and humid environments, the main approach for treating and preventing it involves managing heat and humidity to prevent excessive sweating. This may be achieved by removing tight-fitting clothing, relocating to a cooler environment, reducing physical activity, and taking frequent cool showers [3].

Consent

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

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

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Our Dermatology Online

Case Letter

A mutilate form of a metatypical carcinoma of the face

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Sir,

Metatypical carcinomas are rare, aggressive, non-melanoma skin cancers, combining both basaloid and squamous cell proliferation with metastatic potential [1]. Herein, we report a case of metatypical carcinoma mutilating the face responsible for the invasion of the homolateral eye with blindness.

A 94-year-old patient presented to our clinic with an ulceration on the face evolving for four years and gradually increasing in size. A clinical examination revealed a well-limited ulceration with regular contours, a clean surface, a budding background with infiltrated and pigmented border measuring 15 cm in the left frontotemporal area with the invasion of the homolateral eye responsible for its complete destruction with blindness, as well as multiple BCCs on the rest of the face (Fig. 1a).

A dermoscopic examination revealed bluish-gray pigmented border and hemorrhagic crusts (Fig. 1b).

A histological examination revealed basaloid tumor cells and signs of dyskeratotic maturation in favor of a metatypical carcinoma.

Extension workup with ultrasound of the lymph nodes and parotid area was normal, and a craniofacial CT scan revealed infiltration of fronto-temporal and orbital tissue, infiltration of the temporal and masseter muscles, destruction of the lacrimal gland, and bone lysis without endocranial extension. The patient was discussed in RCP and was a candidate for treatment with radiotherapy.

Metatypical carcinoma is a rare entity with an incidence ranging from 1.7% to 2.7% [2]. As defined by the WHO, "basosquamous carcinoma is a term used to describe basal cell carcinomas that are associated with squamous differentiation" [3].

They have a metastatic capacity more similar to SCCs than BCCs [4].

The tumor usually develops in elderly individuals with a strong male preponderance [2].

The clinical presentation of metatypical carcinomas is non-specific. The most common clinical presentation is a long-standing nodule that gradually becomes ulcerated in sun-exposed areas [1].

Due to the rarity of this entity, very few studies evaluating the dermoscopic features of these tumors have been conducted until now, with the most common dermoscopic criteria for metatypical carcinomas being arborescent vessels, yellowish keratin parches, white areas without structures, scales, hemorrhages, and ovoid nests [5].

Histologic examination remains the gold standard diagnostic method for metatypical carcinomas. Numerous authors have described the presence of histological features of basal cell carcinoma as well as those of squamous cell carcinoma with a transition zone between them [2].

Metatypical carcinomas have an aggressiveness comparable to that of squamous cell carcinoma. Indeed, the tumor is characterized by a rapid increase

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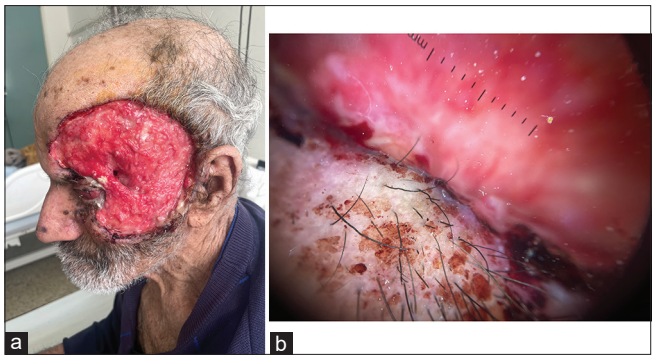

Figure 1: (a) Clinical picture of the ulceration of the face with the destruction of the eye. (b) Dermoscopic image showing a bluish-gray, pigmented border and hemorrhagic crusts.

in size, a high risk of recurrence, and a high metastatic potential.

The bad prognostic factors of these tumors are the male sex, invasive excision margins, lymphatic invasion, and peri-nervous involvement [6].

To date, there have been no established standard therapeutic guidelines for the treatment of metatypical carcinomas.

Several therapeutic modalities may be proposed [1]:

- Wide surgical excision yet with a high risk of recurrence;
- Mohs micrographic surgery as the best treatment option for metatypical carcinomas, with a 8.9% recurrence rate;
- Radiotherapy and chemotherapy in adjuvant or palliative therapy;
- New emerging therapies: Hedgehog pathway inhibitor (vismodegib).

Metatypical carcinomas are highly rare, aggressive, non-melanoma skin tumors that combine features of basal cell carcinoma and squamous cell carcinoma.

Histology is the gold standard of diagnosis.

Early recognition of these tumors allows for rapid management and a better long-term 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.

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Our Dermatology Online

Case Letter

Non-pruritic lichen planus in sickle cell anemia: Is there a role for hydroxyurea?

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Sir,

Herein, we report a case of non-pruritic lichen planus in a 21-year-old male who had been on treatment with hydroxyurea for sickle cell anemia since nine years of age.

A 21-year-old male was admitted with multiple non-pruritic, hyperpigmented, raised lesions in a generalized distribution of three weeks' duration. He was diagnosed to have had sickle cell anemia since nine years of age and had been on treatment with hydroxyurea 500 mg daily and iron and folic acid supplements since then. On examination, he had pallor, bilateral pitting and pedal edema, and there were generalized, bilaterally symmetrical, well-defined, violaceous, and hyperpigmented discrete and confluent papules and plaques of sizes varying from 0.5 x 0.5 cm to 2 x 2 cm with adherent grayish-white scales and Koebner's phenomenon (Figs. 1a and 1b). The mucous membranes and nails were normal. The differential diagnosis considered were acute generalized lichen planus and lichenoid eruption to hydroxyurea.

Peripheral blood smear revealed microcytic hypochromic anemia with poikilocytes such as elliptocytes, pencil-shaped cells, target cells, and some sickle cells. Sickling test was positive. Serology for syphilis, HIV, hepatitis B, and hepatitis C were negative. Histopathological examination of the lesional skin in low power showed acanthosis, focal hypergranulosis, saw toothing of rete ridges, basal cell degeneration, and band-like lymphoplasmacytic infiltration in the dermo-epidermal junction (Fig. 2a). Civatte bodies and pigment incontinence were seen in high power view (Fig. 2b). The diagnosis of acute generalized lichen planus was made. Due to the generalized and extensive nature of the disease, systemic steroids were initiated. As the sickle cell disease was active and histopathology showed no features of lichenoid eruption, hydroxyurea was not discontinued. The skin lesions resolved with hyperpigmentation and there was no recurrence on stopping systemic steroids (Fig. 3).

There are several reports of lichenoid eruption to hydroxyurea [1]. However, in this case, there were no clinical or histopathological features to suggest lichenoid eruption. Furthermore, there was no exacerbation or recurrence of skin lesions in spite of continuing hydroxyurea. Itching is one of the

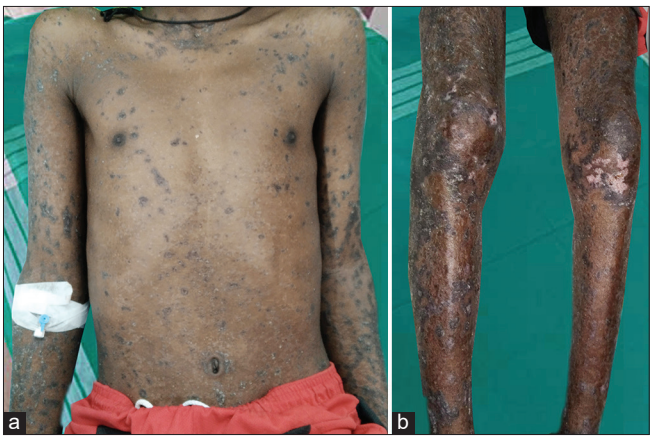

Figure 1: (a) Generalized, bilaterally symmetrical, well-defined, violaceous and hyperpigmented, discrete and confluent papules and plaques of sizes varying from 0.5 x 0.5 cm to 2 x 2 cm with adherent grayish-white scales and Koebner's phenomenon on the trunk. (b) Bilaterally symmetrical, well-defined, violaceous and hyperpigmented, discrete and confluent papules and plaques of sizes varying from 0.5 x 0.5 cm to 2 x 2 cm with adherent grayish-white scales on the legs.

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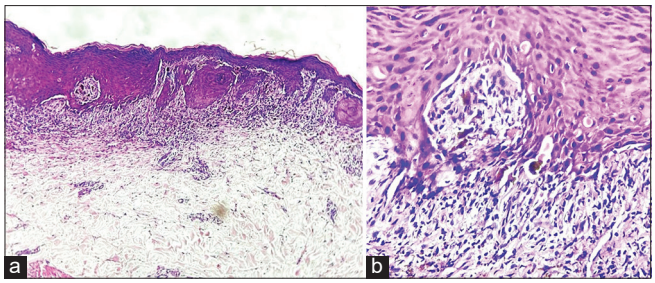

Figure 2: (a) Epidermis showing acanthosis, focal hypergranulosis, saw toothing of rete ridges, basal cell degeneration, and band-like lymphoplasmacytic infiltration in the dermo-epidermal junction (H&E, 40x). (b) Epidermis showing acanthosis, focal hypergranulosis, saw toothing of rete ridges, basal cell degeneration, and band-like lymphoplasmacytic infiltration in the dermo-epidermal junction with Civatte bodies and pigment incontinence (H&E, 100x).

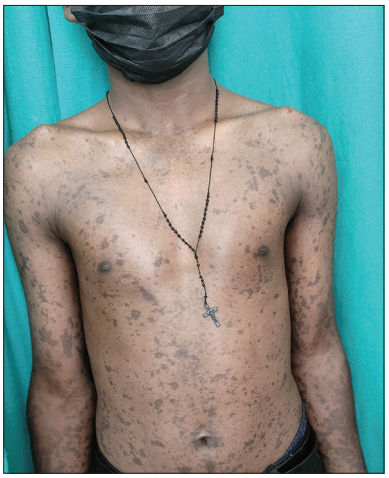

Figure 3: Skin lesions subsided with hyperpigmentation.

important symptoms of lichen planus. It is produced when pruritogenic stimuli activate primary afferent C fibers. Endogenous pruritogens, such as histamine, kinins, proteases, neurotrophins, some opioids, and cytokines produced by keratinocytes, leukocytes, mast cells, fibroblasts, endothelial cells, and cutaneous nerves directly activate the itch-sensitive C-fibers or indirectly induce the release of pruritogenic mediators and modulators from other cells. Some of the newer pathogenetic factors for itch in lichen planus include increased levels of IL-31 and TNF-α; increased expression of IL-31 receptors and protease activated receptors; and the activation of μ-opioid receptors and toll-like receptors (TLRs) [2].

Hydroxyurea has anti-inflammatory action by decreasing the levels of TNF-α and IL-6. Treatment with hydroxyurea leads to a significant decrease in neutrophil-to-lymphocyte ratio, which is positively correlated with serum levels of CRP, TNF-α, and IL-6 [3]. In our patient, hydroxyurea could have made the lichen planus non-pruritic by decreasing the levels of the chemical mediators of itch. This needs to be confirmed by further studies. Drugs such as hydroxychloroquine, dapsone, PUVA, phenytoin, and isotretinoin known to cause lichenoid eruption or trigger lichen planus have found a place in the treatment of the same [4,5]. Whether hydroxyurea like these drugs have a therapeutic role (for pruritus) in lichen planus also needs to be explored.

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Our Dermatology Online

Case Letter

Inflammatory nodule of the scalp: Not always surgical

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Sir,

The appearance of an inflammatory nodule on the scalp initially leads general practitioners to suspect bacterial origin, leading to puncture-aspiration or outright surgical excision. Herein, we report the case of a child who was mistakenly operated for a scalp abscess.

The patient was a three-year-old child with an inflammatory scalp nodule that developed over eight days, for which he consulted the pediatric emergency room, where he was treated surgically. As his condition did not improve, he was referred to our clinic for further treatment. We found domestic animals (pigeons, cats) during the interrogation, yet no similar cases in the family. A dermatological examination revealed irregularly sized, alopecic plaques with a rounded ulceration adjacent to the excision of the nodule. The traction sign was positive (Figs. 1a and 1b). Dermatoscopy showed an erythematous area with yellowish scales. The examination of the lymph nodes found three subcentimetric cervical adenopathies bilaterally. Mycological samples revealed colonization by *Trichophyton violaceum*. The sample was subjected to oral corticotherapy (1 mg/kg/d) for ten days, then to daily washing with a ketoconazole sachet and to oral and local griseofulvin with favorable results (Fig. 2).

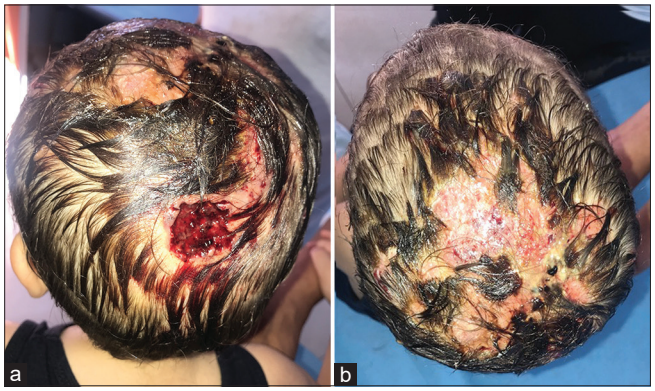

Figure: (a) Alopecic plaques involving the vertex, erosive with pus to pressure. (b) Rounded ulceration corresponding to the exeresis of the nodule.

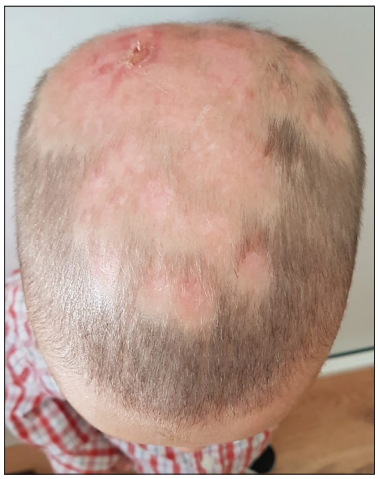

Figure 2: Healing of the ulceration with scarring alopecia.

Kerion is an inflammatory variant of the scalp ringworm caused by an exaggerated immune response to the fungus [1,2]. It begins as inflammatory follicular papules, gradually coalescing into a soft mass, destroying the hair follicles, thus potentially leading to scarring and alopecia [3]. However, because of the obvious inflammation of the hair follicle and the surrounding area, it is often misdiagnosed and treated as scalp pyoderma, anthrax, or cellulitis. Our patient had this problem.

Diagnostic criteria are proposed indicating a consultation with dermatology before surgical manipulation, and

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diagnosis includes culture, dermoscopic examination, and Wood's lamp examination [2]. Treatment requires the use of oral antifungal agents with adjuvant topical treatments to prevent the spread of the infection. Incision and drainage aggravate the infection and delay the treatment of the disease [1,3].

Kerion is often misdiagnosed and mistaken for an abscess, which delays appropriate treatment and allows the infection to spread. Therefore, early diagnosis and prompt treatment may prevent scarring and psychological complications.

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.

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