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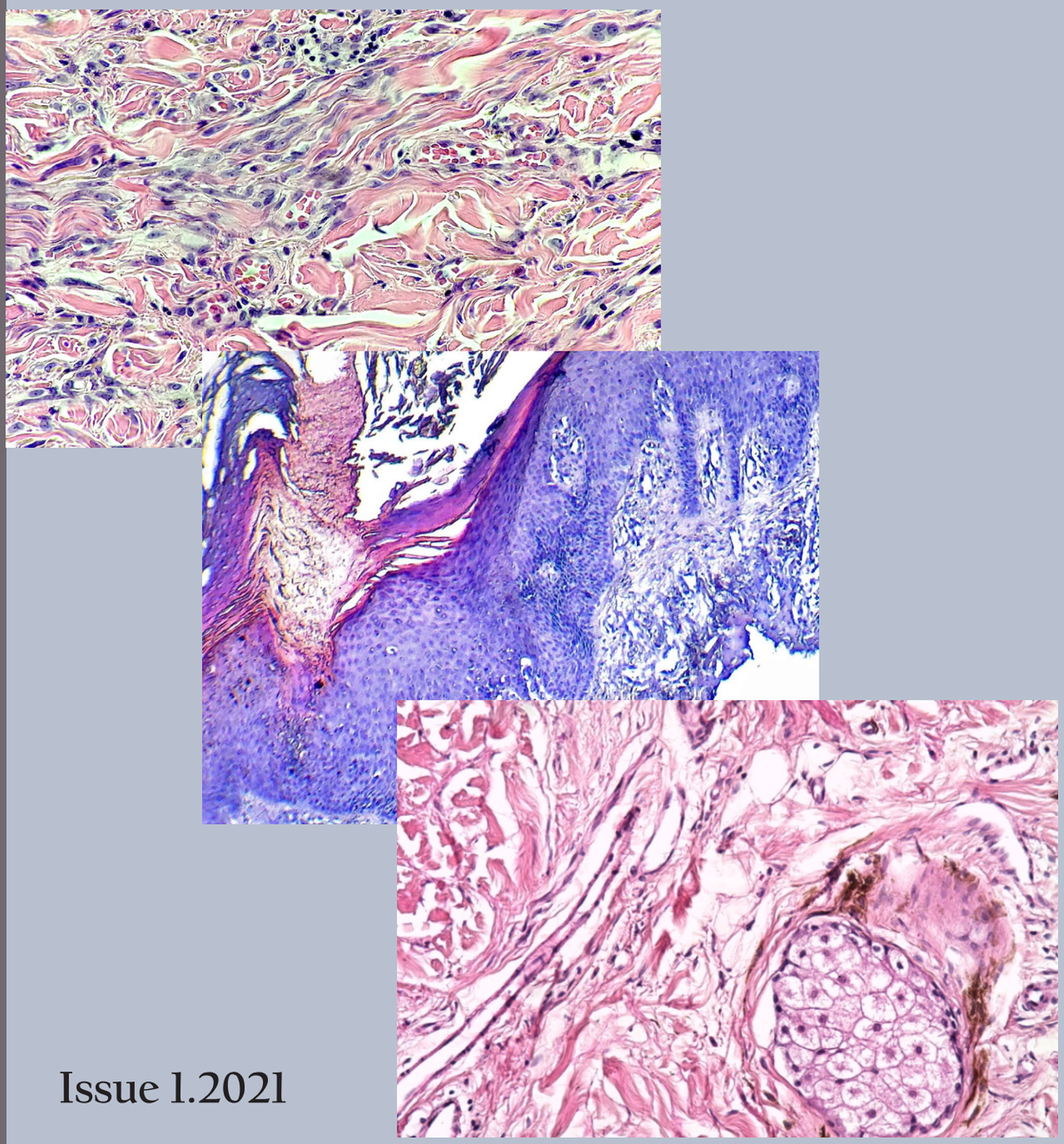

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Original Article

Atopic dermatitis in adults from sub-Saharan Africa: epidemiological and clinical patterns, severity, and quality of life

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ABSTRACT

Background: Atopic dermatitis (AD) is a chronic and recurrent inflammatory dermatitis often associated with other atopic manifestations, such as asthma and allergic rhinitis. This study aimed to determine the epidemiological and clinical aspects of AD and to assess the quality of life (QoL) of patients suffering from AD in our setting. Materials and Methods: This was a cross-sectional study conducted from February through April 2017 in seven hospitals in Cameroon. The study included patients above 18 who presented themselves to a dermatology consultation, were diagnosed with AD, and gave their consent. To assess the severity of AD and evaluate the QoL of the patients, standardized scales, such as SCORAD and QoLIAD, were employed. Results: The study enrolled 46 patients between 18 and 69 years of age with a mean age of 31 ± 12 years and the prevalence of AD at 1.5%. Most of the participants were females, with a sex ratio of 0.4:1, living in urban areas (93.5%). Food (34.8%) and cosmetic products (21.7%) were found as the main risk factors in the occurrence of AD. Upon physical examination, the upper and lower limbs were found to be the most affected in 84.8% and 54.3% of cases, respectively; in addition to cutaneous xerosis (45.7%), lichenification (43.5%), and excoriations (37%). Of the 46 patients, 9 (20%) had severe AD, 32 (70%) had moderate AD, and 5 (10%) had mild AD. QoL was impaired in 43 of the 46 patients (93.5%). Conclusion: Atopic dermatitis is a pathology that impacts the QoL of adults. A QoL assessment is, therefore, an important step in the management of AD.

Key words: Atopic dermatitis; Quality of life; Adults; Cameroon; Sub-saharan Africa

INTRODUCTION

Atopic dermatitis (AD) is a common chronic and pruritic skin condition characterized by progression through relapsing, whose long-term management can be difficult and daunting [1,2]. Its increasing prevalence and the overall cost of its treatment constitute a real public health problem in industrialized countries [1]. As its onset often falls onto infancy, AD is commonly seen in the practice of pediatric dermatology, beginning within the first year of life in 60% of cases and before the fifth year in 85% of cases [2].

The rapid increase in the prevalence of AD in the past twenty years can be due to many factors, such as industrialization, pollution, and reduced exposure to infectious agents. This observation derives from the "hygiene theory," which claims that insufficient exposure to infectious agents in early childhood increases susceptibility to allergies and autoimmune diseases [3].

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Most often reported in children, AD can also occur in adults, and its prevalence has, in recent decades, increased considerably in industrialized countries [4]. In general, AD affects 1–3% of adults worldwide, and can be either *de novo* in adults or continue from childhood into adulthood [5].

Furthermore, the chronic nature of AD and its evolution by relapsing over multiple years and its generation of itching can ultimately impact the quality of life (QoL) of both patients and their families [6-9].

Aside from a 2017 study by Kouotou et al. [9], which described a significant change in the QoL of children and their families brought about by AD, there have been none in Cameroon to evaluate the QoL of adults with AD. Because, to the best of our knowledge, data on AD in sub-Saharan Africa is lacking, we have conducted a study on Cameroonian adults suffering from AD in order to determine their epidemiological and clinical profiles and to assess the impact of AD on their QoL.

MATERIALS AND METHODS

Study Design and Setting

The following was a cross-sectional descriptive study conducted from February through April 2017 in the outpatient dermatology services of five health facilities in Yaoundé, Cameroon: Central Hospital of Yaoundé (CHY), Yaoundé Gynecology, Obstetrics and Pediatrics Hospital (HGOPY), University Teaching Hospital of Yaoundé (UTHY), Biyem-Assi District Hospital (BADH), Elig-Essono District Medical Center (EEDMC); and two health facilities in Douala, Cameroon: Laquintinie Hospital of Douala (LHD) and Douala General Hospital (DGH). These facilities were chosen based on the availability of experienced dermatologists providing dermatology consultations.

Study Participants

We included patients over 18 years of age who presented themselves to a dermatology consultation in one of the study facilities during the recruitment period with manifestations of AD and who gave their consent to participate in the study. Patients with other skin conditions that could impact the estimation of the severity of AD were excluded from the study. Participants were recruited consecutively and non-exhaustively during the period of the study.

The diagnosis of AD was made by clinical recognition using the criteria of the United Kingdom Working Party.

Procedure and Data Collection

We used a standardized data collection form to obtain information on sociodemographic (age, sex, place of residence, profession, level of education, marital status, profession) and clinical (sites and types of lesions) characteristics and to assess the severity of each case of AD and each patient's QoL. Specific standardized scales were used to conduct these assessments. The evaluation of the severity of AD was performed during the consultation after the confirmation of the diagnosis. At the end of the process, the patient received a prescription, advice on the pathology, and an appointment date for a follow-up. Each patient's QoL was assessed after the consultation.

To assess the severity of AD, we used a clinical scoring system for AD, specifically SCORAD (Scoring Atopic Dermatitis), whose measurement range is 0 to 103. The formula of the SCORAD index is as follows: $(A/5 + 7B) / (2 + C)$. Its classification of AD is as follows: mild (0–24), moderate (25–50), and severe (51–103).

A represents the extension of AD, which measures the affected surface by noting the extent of the patient's inflammatory lesions and is calculated using the rule of nines (same as for burns). The total score ranges from 0% to 100%.

B represents six clinical features of varying disease intensities: erythema/darkening, edema/papules, oozing/crusting, excoriation, lichenification/prurigo, and dryness (evaluated on noninflamed skin), each on a scale of 0–3. The total score ranges from 0 to 18.

Finally, C represents the subjective symptoms as experienced by the patient, in particular daily pruritus and sleep loss, each on a scale of 0–10. The total score ranges from 0 to 20.

The QoL of each patient was assessed using the Quality of Life Index for Atopic Dermatitis (QoLIAD) [10], which is a scale that specifically assesses the impact that AD has on the QoL of a patient. QoLIAD comprises a questionnaire of 25 items intended for patients over 16 years old with answers either *true* (score = 1) or *not true* (score = 0) and scores from 0 to 25. The result is expressed as a percentage of the maximum possible score of 25. The higher the QoLIAD score, the greater and more significant the impact AD has on a patient's

QoL. Fig. 1 illustrates our process for recruiting our participants.

Statistical Analysis

Data was coded and entered using the software CSPro and subsequently analyzed using SPSS Statistics, version 21.0, and R. Tables and figures were used to present the results, which were expressed as frequencies (percentages) of qualitative variables and means and standard deviations (SD) of quantitative variables. The comparison of the qualitative variables employed the Chi-square test or Fisher's exact test, and the independence t-test or the one-factor were employed in the comparison of the quantitative variables where appropriate. Statistical significance was set at a p of 5%.

Ethics Statement

We conducted the study in accordance with national and international ethical rules and in accordance with the revised Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS).

The study was granted ethical clearance by the Ethical Review Board of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I, Cameroon. In addition, we received administrative authorization from the directors of all hospitals comprehended by the study. The anonymity of the patients and the confidentiality of information gathered were respected.

The informed consent form was only obtained after signing the consent sheet by each of the patients. The study involved no major risk for the participants because no examination or invasive sampling was performed.

RESULTS

Prevalence of Atopic Dermatitis

From February through April 2017, 3132 patients visited the outpatient dermatology clinics of the selected hospitals. Of these 3132 patients, 46 suffered from AD and met the inclusion criteria, thus giving the prevalence of AD of 1.5% (95% confidence interval at 1.1–1.9).

Sociodemographic Characteristics of Patients

The age of the patients ranged from 18 to 69 years, with an average of 31 ± 12 years. There was a female predominance, with a sex ratio of 0.4/1. In addition, these patients were mainly single (65.2%), with a university education (73.9%), and resided mainly in urban areas (93.5%), as illustrated in Table 1.

Patient Medical History

The AD cases were either isolated (21/46; 45.7%) or associated with at least one other atopic condition (25/46; 54.3%), including allergic rhinitis (45.6%), asthma (8.7%), and allergic conjunctivitis (23.9%). Furthermore, a family history of atopy found in our patients concerned the ascendants, the collaterals, and the descendants (Table 2).

The risk factors in the occurrence of AD in the participants were dominated by food (34.8%) and the usage of cosmetic products (21.7%) (Table 3). Among foods, sugar (17.4%) and fish (13.0%) were the most incriminated; and perfumes (10.9%) were the first cosmetic products to be mentioned by the participants (Table 3).

The patients experienced an average of 1.7 ± 0.94 relapses of AD per year, with extremes varying from one to four relapses.

Pruritus was present in 43 of the 46 patients (93.5%), while 16 of the 46 patients (34.8%) reported a loss of sleep.

Clinical Data

Upon physical examination, the upper and lower limbs were found to be the most affected in 84.8% and 54.3%

Table 1: Sociodemographic characteristics of patients with AD (N = 46)

Variable		Number	Percentage
Age (years)	18–20	8	17.4
	21–30	17	37
	31–40	11	23.9
	>41	10	21.7
Sex	Female	33	71.7
	Male	13	28.3
Level of education	University	34	73.9
	Secondary	10	21.7
	Primary	2	4.3
Marital status	Single	30	65.2
	Married	16	34.8
	Student	23	50.0
Profession	Employed	20	43.5
	Unemployed	3	6.5
Residence	Urban	43	93.5
	Rural	3	6.5

Table 2: Past medical history of the patients

Atopic diseases in the participants				
	Presence of atopic disease	**Yes (%)**	**No (%)**	**Total (%)**
Atopic disease	Allergic rhinitis	21 (45.7)	25 (54.3)	46 (100)
	Asthma	4 (8.7)	42 (91.3)	46 (100)
	Allergic conjunctivitis	11 (23.9)	35 (76.0)	46 (100)
Associations of atopic diseases				
	Associations	**Number**	**Percentage (%)**	**Total (%)**
Atopic disease associations	AD alone	21	45.7	46 (100)
	AD + allergic rhinitis	14	30.4	
	AD + allergic rhinitis + allergic conjunctivitis	4	8.7	
	AD + allergic conjunctivitis	3	6.5	
	AD + allergic rhinitis + asthma + allergic conjunctivitis	3	6.5	
	AD + asthma + allergic conjunctivitis	1	2.2	
Family history of atopic diseases				
	Atopic disease	**Parents**	**Siblings**	**Children**
		Number (%)	**Number (%)**	**Number (%)**
Family history	Allergic rhinitis	10 (21.7)	14 (30.4)	3 (6.5)
	Asthma	5 (10.9)	5 (10.9)	4 (8.7)
	Allergic conjunctivitis	5 (10.9)	2 (4.3)	1 (2.2)
	AD	4 (8.7)	7 (15.2)	1 (2.2)

Table 3: Factors associated with AD

Variables		**Number (%)**		**Total (%)**
		Yes (%)	**No (%)**	
	Alimentation	16 (34.8)	30 (65.2)	46 (100)
	Cosmetic or washing products	10 (21.7)	36 (78.3)	46 (100)
	Stress	3 (6.5)	43 (93.5)	46 (100)
	Infection	1 (2.2)	45 (97.8)	46 (100)
Different components of triggering factors				
		Component	**Number**	**Percentage (%)**
Triggering factors	Food allergy	Sugar	8	17.4
		Fish	6	13.0
		Dairy	1	2.2
		Spices	1	2.2
		Groundnut	1	2.2
	Cosmetics and washing products	Fragrance	5	10.9
		Body wash	2	4.3
		Body lotion	1	2.2
		Detergent	2	4.3

of cases, respectively. The elbows and popliteal fossa were the most affected areas in 35 (89.7%) and 16 (64.0%) patients, respectively. The physical signs were moderate skin dryness (45.7%), moderate lichenification (43.5%), and moderate excoriation (37%) (Table 4).

The severity of AD was classified according to the SCORAD score: mild (5/46; 10.9%), moderate (32/46; 69.6%), and severe (9/46; 19.6%) (Fig. 2).

Quality of Life

QoL was impacted in 43 patients (93.5%). QoL scores ranged from 1% to 20%. We, thus, found 9 (19.6%) and 34 (73.9%) patients whose QoL scores varied between 11% and 20% and between 1% and 10%, respectively. Furthermore, the score was 0% in 3 patients (6.5%) (Fig. 3).

The most incriminated factors in the changes in QoL concerned appearance: in particular, questionnaire items "I struggle with my appearance" (80.4%) and "I feel embarrassed about my skin appearance" (65.2%) (Table 5).

DISCUSSION

The study took place from February through April 2017 in seven health facilities in the cities of Yaoundé and Douala with the aim to determine the epidemiological and clinical profiles of patients with AD, and to assess the impact of AD on their QoL. During the study's time frame, 46 adult patients were diagnosed with AD.

Prevalence of Atopic Dermatitis

In our study, AD in adults represented 1.5% of the dermatology consultations, which is less than the 3.4% reported by Pesce et al. in Italy [11]. This might be explained by the fact that our sample was much smaller. Our prevalence might also be explained by the fact that AD is classically described as an uncommon condition in adults. Indeed, the prevalence of AD decreases as an individual matures from a child to an adult, according to the literature [12,13].

Table 4: Sites and types of lesions

Sites of lesions					
Sites	**Site distribution**	**Number**	**Percentage (%)**		
Upper limbs (N=39)	Elbows	35	89.7		
	Hands	15	38.5		
	Forearms	6	15.4		
Lower limbs (N=25)	Popliteal fossa	16	64.0		
	Feet	11	44.0		
	Thighs	10	40.0		
	Legs	4	16.0		
Torso (N = 12)	Thorax	9	75.0		
	Back	8	66.7		
Head and neck (N = 6)	Face	6	100.0		
	Scalp	3	50.0		
	Neck	1	16.7		
Genital organs (N = 1)	Scrotum	1	100		
Clinical features (N = 46)					
Feature		**Absent**	**Mild**	**Moderate**	**Severe**
Erythema	Number	11	6	27	2
	Percentage (%)	23.9	13.0	58.7	4.3
Edema/papulation	Number	8	10	26	2
	Percentage (%)	17.4	21.7	56.5	4.3
Oozing/crusting	Number	30	10	4	2
	Percentage (%)	65.2	21.7	8.7	4.3
Excoriations	Number	14	14	17	1
	Percentage (%)	30.4	30.4	37.0	2.2
Lichenification/prurigo	Number	18	6	20	2
	Percentage (%)	39.1	13.0	43.5	4.3
Dryness	Number	7	17	21	1
	Percentage (%)	15.2	37.0	45.7	2.2

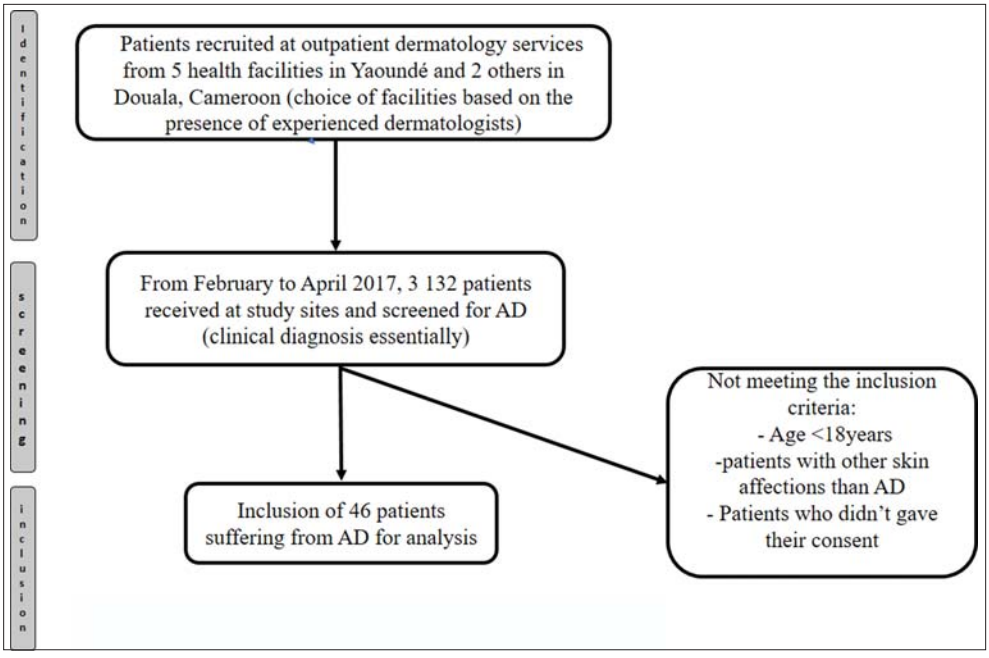

Figure 1: Flow diagram of the section "Materials and Methods."

Sociodemographic Characteristics of Patients

The mean age was 31 ± 12 years, with extremes of 18 and 69 years. This result is close to the 30.4 years achieved by Zeppa et al. [14].

Women constituted 73% of the study population, with a sex ratio of 0.4. This might be explained by the fact that women, in general, exercise more apprehensiveness about their physical appearance and, thus, consult more readily, whether the pathology is visible or not.

Table 5: Quality of life perception in patients suffering from AD (QoLIAD)

Quality of life perception in patients	(N=46)					
	Sex					
	Female		Male		Total	
	N	%	N	%	N	%
I struggle with my appearance.	26	56.5	11	3.9	37	80.4
I lack self-confidence.	10	21.7	3	6.5	13	28.3
I try to avoid physical contact or touching other people.	12	26.1	6	13	18	39.1
I feel embarrassed about my skin appearance.	14	30.4	7	15.2	21	45.7
I worry about my life because of my eczema.	6	13	2	4.3	9	19.6
I am nervous.	9	19.6	5	10.9	14	30.4
I want to hide.	2	4.3	2	4.3	4	8.7
I can't wear the clothes that I want.	20	43.5	9	19.6	29	63.0
I feel as if other people don't want to touch me.	8	17.4	4	8.7	12	26.1
It's always on my mind.	6	13	3	6.5	9	19.6
I try to hide my eczema.	21	45.6	9	19.6	30	65.2
I have difficulty concentrating.	5	10.9	0	0	7	15.2
I want to cry sometimes.	6	13	3	6.5	7	15.2
I am afraid of being rejected.	3	6.5	3	6.5	6	13.0
I hate seeing myself in the mirror.	5	10.9	3	6.5	7	15.2
I am nervous.	5	10.9	2	4.3	6	13.0
I can't concentrate on anything else.	0	0	1	2.2	2	4.3
I am losing time because of my eczema.	5	10.9	2	4.3	8	17.4
I feel embarrassed about my skin appearance.	22	47.8	3	6.5	30	65.2
There is no liberation.	9	19.6	8	17.4	16	34.8
I am afraid of being rejected.	3	6.5	7	15.2	7	15.2
I can't do the things that I want.	5	10.9	4	8.7	7	15.2
I have to force myself to do something.	3	6.5	3	6.5	5	10.9
I feel overwhelmed by my eczema.	1	2.2	2	4.3	3	6.5
I can't tolerate it when someone touches me.	7	15.2	3	6.5	11	23.9

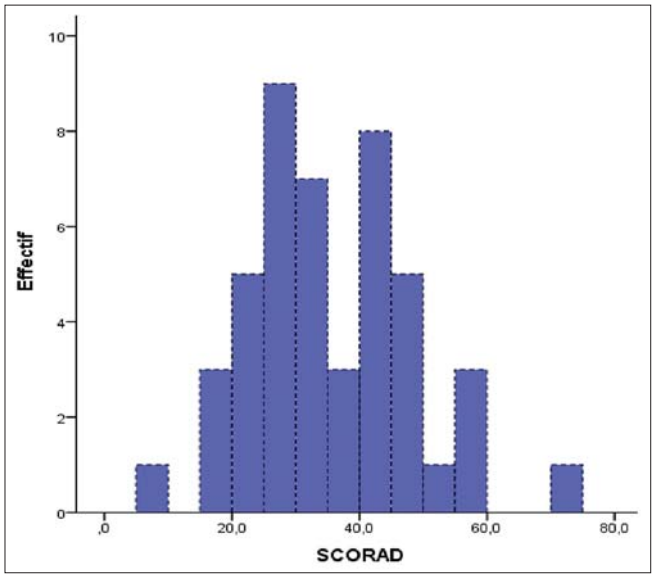

Figure 2: Distribution of patients according to SCORAD.

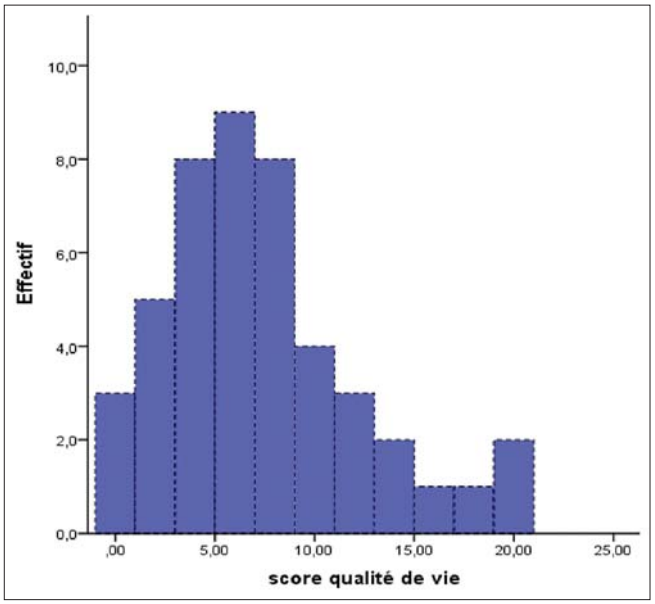

Figure 3: Evaluation of QoL according to QoLIAD.

The same tendency has also been noted in Italy and India [5,11].

Our patients resided mainly (43/46; 93.5%) in urban areas, which is similar to the results obtained by Yemaneberhan et al. in Ethiopia [15]. In addition, a Chinese study highlighted a clear gradient in the prevalence of urban vs. rural AD: 10.2% vs. 4.6% [16]. The increased risk of atopy in urban areas might be explained by the industrialization of cities, air pollution, and various dietary habits [4,15,16].

Patient Medical History

In our study, we found that 54.3% of the patients had a personal history of allergic rhinitis, asthma, and allergic conjunctivitis. This result is close to that obtained by Ahogo et al. [2], who found that 54.2% of cases studied had a personal history of atopy.

Food allergy was the first risk factor in AD and accounted for 34.8% of cases. The relationship between AD and food allergy has been well-established in children, unlike adults, who are more sensitive to environmental allergens, such as molds, mites, and pollens [17,18].

Clinical Data

The upper limbs (84.8%) and lower limbs (54.3%) were the most affected, with a predominance in the elbows (96%) and popliteal fossa (64%). Zeppa et al. [14] found lesions to be located predominantly on the upper limbs (66.6%), followed by the face (45.9%) and the lower limbs (34.6%). In fact, these sites are described as the most affected in adults with AD [19] and these adults had lesions in at least three sites [20].

In our patients, the most common clinical signs were dry skin (45.7%), lichenification (43.5%), and excoriations (37.0%). The lichenoid aspect of the lesions might be due to the chronicity of the lesions and the intensity of the pruritus.

Moderate AD (69.6%) was the most common in our sample, which is higher than the 18.7% found by Zeppa et al. [14], who determined severe atopic dermatitis to be predominant (54.8 %).

Quality of Life

In our study, we employed QoLIAD, an AD scoring scale for adults [10], to find that QoL was impacted in 43 of all our 46 patients (93.5%). This result is close to the 88.6% noted by Cheok et al. [21]. Similar impact of AD on the QoL of patients, both children and adults, was discovered by other studies [7,9]. Health-related QoL is defined as a multidimensional construction comprised of impacts on different aspects of life, such as physical, emotional, mental, and social health, as well as daily functioning. In our case, changes in QoL can be explained not only by the chronic and relapsing nature of the pruritus but also by the sociocultural factors for which modern medicine can offer no definite solution.

In our study, we found a high percentage of positive responses to items in the QoLIAD questionnaire, mostly two: "I struggle with my appearance" (80.4%) and "I feel embarrassed about my skin appearance" (65.2%). This might be explained by the aesthetically displeasing nature of AD in a society in which appearance carries significant importance in interpersonal relationships and professional settings.

Nevertheless, our study, which concerned adults with AD, posed some limitations, in particular: 1) the fact that the sample was limited to hospital settings and, therefore, may not have been representative of the general population; 2) the choice of convenience made for the various hospitals where patient recruitment took place; and 3) the short period of data collection, which might have influenced the end results.

CONCLUSION

Atopic dermatitis (AD) is an infrequent finding in adults made by dermatology consultations in the Cameroonian cities of Douala and Yaoundé. It is predominantly found in females, and can either be isolated or associated with other forms of atopy. It is also found in patients with a family history of atopy. In most cases, its clinical presentation is quite moderate, but significantly affects the quality of life (QoL) of patients with AD. Therefore, in addition to medical treatment, educational and psychological support has to be provided. Such a combination of therapies could significantly improve the long-term condition of patients with AD. Assessing the QoL of adults with AD is an important step in their treatment and follow-up care.

ACKNOWLEDGMENTS

The authors are most grateful to the directors and heads of the dermatology services of the seven hospitals—five in Yaoundé and two in Douala—where this study was conducted, and to all personnel for their kind help in the process of collecting data.

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

Dermatology residency research policies and support: A national USA survey

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ABSTRACT

Background: Dermatology residency programs are considerably varied in regard to their resident research requirements and resources. The authors examined the availability of 12 key resident research-related criteria in 30 ACGME dermatology residency programs in the United States. **Objective:** To assess the degree to which dermatology residency programs require and support their new physician graduates in scholarly research. **Methods:** This cross-sectional study employed a 12-item survey administered online that was informed and created by literature search, expert feedback, and a thorough review and revision process. The primary purpose of the study was to examine the differences in programs' policies and structure around resident research. **Results:** Thirty out of 114 PDs (26%) responded to the survey. We found that while most programs had publication and QI project requirements for residents, the majority did not have required research rotations, research electives, or a formal mentorship program. Thus, in spite of a growing need for new physician–scientists coupled with the various benefits associated with conducting research during residency training, considerable hurdles dissuade new physician graduates from pursuing careers in clinical research. **Conclusions:** Our survey findings supply timely, objective data on dermatology resident research requirements across the country. Medical schools, residency programs, and the ACGME/ AMA may all find our results valuable in further enhancing, evolving, and systematizing dermatology residency policies and provisions.

Key words: Dermatology, Residency, Survey, Research, ACGME

INTRODUCTION

The dermatology residency is one of the most competitive residencies available to medical school students. Applicants who successfully matched into dermatology have the second highest mean USMLE Step 1 scores across all residency applicants [1]. Over 1,000 Dermatology applicants applied to an average of 82.2 programs. Over half of them were AOA members and over 40% graduated from one of the top 40 medical schools in the United States based on NIH funding. Finally, applicants who matched into Dermatology had a mean number of 11.7 abstracts, presentations, and publications; 10.1 volunteer experiences; and 4.7 research experiences [1].

In contrast to the highly structured application process, Dermatology programs themselves vary widely in their features, approaches, demographics, and requirements for research. A minority of Dermatology residency programs have formally allotted time devoted to research within their curricula, and many programs' requirements for research are much broader and more open-ended [2].

The specific research requirements associated with Dermatology residency programs is poorly characterized in the literature, as far as we are aware. Given the heterogeneity of residency programs and the competitiveness in their selection criteria, attaining an improved characterization of program research requirements would be influential and important to applications and Dermatology programs alike. Indeed, research within other medical specialties indicates that prospective applicants consider a variety of factors

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when ranking residency programs, not limited to their reputation, geographical location, or personal interactions [3,4].

Our study aimed to collect data about and categorize the similarities and differences between research requirements and expectations amongst Dermatology Residency Programs in the United States [5-8]. Elucidating these mutable and heterogeneous factors has the potential to aid residency programs in emphasizing unique and distinguishing characteristics of their program and attracting the most competent candidates. Meanwhile, our study provides a foundation to pave the way for greater transparency and even standardization of requirements amongst programs.

MATERIALS AND METHODS

Questionnaire Development and Dissemination

Our study was a cross-sectional survey utilizing a categorical, study-specific online questionnaire. Our initial draft was formulated subsequent to a review of the relevant published literature utilizing PubMed. The survey was subsequently assessed and edited by the authors as well as a team of content experts including Dermatologists, Dermatology PDs, and medical school students.

Our study was developed using the REDCap platform. We chose to use the REDCap application as it is HIPAA-compliant, user-friendly, and can be used to collect virtually any type of data. It is further optimized to be able to support both online and offline data capture for research.

Our study obtained Not Human Subjects Research IRB approval (COMIRB #17-1634) from the University of Colorado, Denver, Institutional Review Board. It was exempt from the requirements of written consent due its nature of being a survey.

In addition to collecting demographic data, our final survey (Appendix I) contained 12 items including 11 yes/no questions and 1 numerically-coded question asking respondents how many days off per year residents in their program have to attend academic events such as research symposia or professional conferences. All "yes" responses was givens space to elaborate.

All 114 Accreditation Council for Graduate Medical Education (ACGME) approved dermatology programs were eligible in our study. Contact information for the programs was gathered and organized via a structured search in the ACGME, American Medical Association (AMA), American Academy of Dermatology (AAD) websites. Contact information for those programs whose contact information was unavailable or found to be no longer in use after consulting these sources was retrieved directly from individual program websites.

Our survey was sent to each program via an email that outlined our study's objectives and contained a secure and specific URL link to the survey. Emails were sent between January 2018 and November 2018. Programs that did not respond to our initial request for completion were contacted again an average of 3 times. Data were downloaded from the REDCap database and analyzed as survey responses were gathered.

Outcomes and Objectives

The primary aim of our study was to characterize the differences in the standards and specifications of dermatology residency research requirements (if present) between individual programs. Our criteria included requirements for publication, QI projects, and research rotations, as well as the availability of research electives, funding for AAD Annual Meeting attendance, research mentors, and the presence of a formal written statement describing the program's policies regarding resident research and conference attendance.

The secondary outcome of our study was to assess the nature of these program differences and to categorize and systematize our findings for possible future use by and benefit for the ACGME, residency programs, and prospective applicants alike.

RESULTS

We collected a total of 30 responses to our questionnaire. The majority of respondents (n=19) reported having publication requirements for their residents. An even larger proportion of respondents (n=23) reported having Quality Improvement (QI) requirements for residents. On the other hand, only 3 respondents reported having a required research rotation for residents, while just 11 respondents reported even offering a research elective option.

Meanwhile, though 25 programs reported having a written statement outlining program policies on

resident research and conference attendance, only 7 programs allotted 10 or more days for residents to attend academic events such as research symposia or professional conferences. Despite this finding, 26 programs reported having funding allocated for residents to attend the AAD Annual meeting as well as participate in other conferences or educational activities.

Interestingly, even though most programs reported financially supporting conference and meeting attendance, close to half of the programs surveyed (n=11) reported lacking funding for residents to present research at these events. Even more programs (n = 19) reported lacking a formal mentorship program to connect residents with research mentors. Nevertheless, all but 1 program report research mentor access for residents.

DISCUSSION

Research from numerous specialties have described the nature of research and research policies during residency training [9-12]. In contrast to most other specialties prior to the implementation of strict duty-hour rules in 2003 [13], dermatology residency programs have historically been structured to be able to support research activities.

There are myriad advantages associated with research during residency. Residents' research may result in improved patient care by cultivating clinical reasoning, critical appraisal skills, and lifelong learning [14,15]. Since publication during residency is associated with careers in academic medicine [16], research during postgraduate training may also help bolster the declining numbers of clinician investigators [17]. Publication and presentation of research by interns may also improve the reputation of residency programs, allowing them to draw more competitive applicants [18,19]. Lastly, research experience during residency is beneficial to residents applying for jobs or fellowships [20].

In spite of the various advantages associated with research during residency, our findings suggest that program policies, procedures, structure, and support concerning resident research is highly variable.

Even though there is a growing need for new physician–scientists, considerable hurdles dissuade new physician graduates from pursuing careers in clinical research. Physicians who are considering research careers weigh mounting financial challenges against the unpredictability of decreased federal research budgets and insufficient mentorship opportunities [21–23]. As a result, morale among aspiring investigators is deteriorating, with many choosing to give up their research interests in order to pursue full-time clinical careers [24,25].

Though much has been done to expand research exposure and training for medical students and fellows, there are a scant number of formal programs specifically designed to target resident physicians. It is probable that residency was deemed too busy to accommodate research, due to its demanding schedule and emphasis on clinical training and subspecialty selection. The formidable growth of technology, data, and medical innovations needed to be mastered during residency in the current healthcare setting, coupled with higher acuity, shorter hospital stays, and growing patient turnover, has only heightened the challenge. The ongoing demands to reduce "length of stay" may also have the unintended consequence of deterring some residents from pursuing careers in research by compromising scientific inquiry into their patients' health conditions due to the focus on patient "disposition" [13].

Adding to these challenges is the trend towards greater reliance on hospitalists as attending physicians on inpatient wards at teaching hospitals. This trend may improve clinical care but almost always reduces residents' exposure to researchers who can serve as potential mentors [26]. Residency in the time in which most graduates are finalizing their career trajectories; thus, this lack of exposure during residency is likely to result in a dearth of researchers in the future. The ultimate impact of these trends has yet to be fully realized and is particularly worrisome, given healthcare's move towards more precise and faster-paced care delivery and technological innovation [13].

Authors have described research curricula or research rotations, but there is a paucity of empirical studies describing specific components of an effective resident research program. Previous surveys suggest that residents [25] report lacking both interest in and time for research. Our study adds to this body of literature by revealing that the majority of dermatology program directors surveyed report a lack of research requirements, curricula, guidelines, mentors, and funding as further barriers to research.

Some study limitations should be taken into account. First, our sample size was limited to roughly one quarter (26.3%) of all ACGME Dermatology residency programs. Our findings may thus not be representative of all programs and should not be used to draw conclusions about programs that were not surveyed. Nevertheless, our respondents included programs from all geographical regions of the United States, including several top 20 medical schools [27]. Second, while we left room for respondents to elaborate, not all participants responded to all of the open-ended questions, and the degree of clarification or description provided was highly variable.

Finally, it is important to keep in mind that our data represents programs of various types. We report average findings for a sample that included private, public, highly endowed, government-run, urban, rural, large, and small institutions.

CONCLUSION

According to the Accreditation Council for Graduate Medical Education (ACGME), graduate medical education should occur in "an environment of inquiry and scholarship in which residents participate in the development of new knowledge, learn to evaluate research findings, and develop habits of inquiry as a continuing professional responsibility." The Residency Review Committees (RRCs) of the ACGME specifically require that interns participate in scholarly activity such as original research, reviews of research, or case reports during their residency training [28]. Insufficient evidence of residents' scholarship is one of the most common causes that residency programs are cited by the RRC [29].

Conducting research during residency can be very challenging. Studies suggests that successful research training include the following elements: (1) designated research time; (2) training in basic research methods; (3) the availability and guidance of mentors; and (4) an environment that encourages research participation [30-32]. We found that several of these factors were included in the programs we surveyed.

Nevertheless, our survey suggests that many dermatology residency programs lack some or all of the necessary infrastructure and resources required to adequately and effectively support research among their residents. Our findings add to the extant body of literature that describes residency research rotations and curricula and can inform future research and interventions designed to address research deficiencies among programs.

In sum, the mandate for resident research has the potential to enhance the practice of medicine, improve quality, and reduce cost. However, for research to take place on a large scale, residency training programs must surmount various significant hurdles. Effective implementation demands a thoughtful methodology that focuses on overcoming specific barriers, starting with institutional culture change to foster an environment of inquiry and the financial investment to create the infrastructure needed to support the research endeavors.

Statement of Human and Animal Rights

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

Statement of Informed Consent

Informed consent was obtained from all patients for being included in the study.

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Our Dermatology Online

Original Article

Topical ivermectin in the treatment of pediculosis capitis

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ABSTRACT

Background: Head lice infestation is considered a prominent issue because of its worldwide distribution, especially among children. Millions of children are infested with pediculosis capitis every year. The increasing rate of lice infestation has been reported even in the developed countries due to the resistance to known pediculicides. Besides, the louse is a vector for serious diseases, such as epidemic typhus fever. **Objective:** The aim of this work was the search for a new cheap and effective drug for pediculosis capitis. 2% ivermectin solution, a promising novel drug used for endoparasite and ectoparasite infections, was used in this study. **Materials and Methods:** This was a clinical trial study. The in vitro study was carried out in a period of five months. Samples of nits and lice were collected from female patients of the Department of Dermatology and Venereology, Baghdad Teaching Hospital. The study was conducted during a period from October 2002 through November 2003. One hundred fifty children from four primary schools in Hayy Al-A'amel, Baghdad, participated in this part of the study. The preparation was applied to the children by the author. One hundred children were tested with ivermectin solution and fifty children with rectified spirit. The first part of the study involved a parasitological evaluation (in vitro study) of pediculicidal and ovicidal activity, in which 4% ivermectin solution was discontinued because of contact dermatitis. Therefore, 2% ivermectin solution was used instead. Pediculicidal and ovicidal activity was examined half an hour afterward. The second part of the study involved a clinical evaluation (in situ study) of 2% ivermectin solution for half an hour. Results: Topical 2% ivermectin solution in rectified spirit is a good pediculicidal (100%) and a good ovicidal (88%) drug with good therapeutic efficacy (82% after the first application, 90% after the second application) against pediculosis capitis. **Conclusion:** The study described a novel topical preparation for pediculosis capitis, which was proven effective and safe.

Key words: Ivermectin; Pediculosis capitis; Iraq; Topical solution

INTRODUCTION

Population-based studies in European countries show a highly divergent prevalence of pediculosis capitis, ranging from 1% to 20% [1]. With an increasing rate of treatment failure, it is worthwhile to consider the issues of misdiagnosis, lack of adherence, inadequate treatment, reinfestation, lack of ovicidal or residual killing properties of the pediculicide, and/or resistance of lice to the pediculicide [2]. Resistance to topical pediculicides is an emerging concern in most parts of the world [3]. The problem of resistance is directly related to the frequency of its use [4,5] in genotyping, demonstrating that head lice exhibit resistance to compounds such as DDT, the pyrethrins, and the pyrethroids [6]. Numerous treatment options have been used to control the spread of pediculosis capitis with various drawbacks. For instance, 1% lindane exhibits central nervous system toxicity and may cause severe seizures in children [7]. 5% benzyl alcohol was the first non-neurotoxic pediculicide, and pruritus, erythema, pyoderma, and ocular irritation are its usual side effects. It is also non-ovicidal [8]. The percentage of patients who were louse-free after treatment with a product containing tea tree oil and lavender oil and a head lice suffocation product was higher than with a product containing pyrethrins and piperonyl butoxide [9]. Eucalyptus oils have been used against permethrin-resistant pediculosis [10].

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Grapefruit juice [11], coconut, and anise spray have been found to be more effective than permethrin in pediculosis capitis, thereby demonstrating clinical resistance [12].

In head lice infestations that are difficult to treat, oral ivermectin may prove more effective [13] or as effective as topical 0.5% malathion lotion [14]. Oral ivermectin demonstrates high efficacy and tolerability in the treatment of pediculosis capitis. A significant number of children required a second dose to ensure complete eradication [15]. A single oral dose of ivermectin 400 μg/kg repeated throughout seven days has been shown to be more effective than 0.5% malathion lotion [13]. It has also been used successfully in school children [16]. In head lice infestations that are difficult to treat, oral ivermectin given twice every seven days had superior efficacy when compared with topical 0.5% malathion lotion [17]. After a single dose, complete healing was achieved in 77.5% and 87.5% of ivermectin and malathion groups, respectively. No major adverse effects were observed in either group. Oral ivermectin is a promising and effective approach for the treatment of head lice and might be an ideal substitute for conventional pediculicides [14]. Community-based treatment with oral ivermectin in susceptible, and poor sections of the society has given us promising results [18].

MATERIALS AND METHODS

In vitro parasitological evaluation: The activity of the test preparation was evaluated on the Pediculus capitis in ovicidal and pediculicidal tests. Samples of nits and lice were collected from female patients of the Department of Dermatology and Venereology, Baghdad Teaching Hospital. The study was conducted during a period from September 2002 through November 2003. 2% ivermectin solution l gm/50 cc rectified spirit was used and tested by parasitological evaluation (in vitro study). A control test was included as part of the parasitological evaluation as well. Rectified spirit was the control preparation. Ovicidal tests of each type of test and control preparation were tested half an hour after washing in tap water.

Pediculicidal test: lice and nymphs were collected from the patients' heads with a fine-tooth comb, gently transferred with forceps onto a clean Petri dish, closed with self-adhesive tape, and identified. Lice were examined microscopically. Lice that were dead, damaged, or less than fully mobile were discarded. Fully mobile (active) lice were transferred to another clean Petri dish. A hundred fully mobile lice were exposed to test preparations by immersion at room temperature. The number of live and dead lice was recorded. After three minutes, the lice were washed in tap water, then microscopically examined. A louse was considered dead if it lacked signs of internal and external movement. Fifty fully mobile lice were exposed to rectified spirit half an hour after washing, then microscopically examined. The percentage of dead lice represented the pediculicidal activity of the test preparation.

Ovicidal Test

Hair shafts with attached viable ova (nits) were removed with forceps and scissors, transferred onto a sterile Petri dish, closed with self-adhesive tape, and identified. An ovum was judged viable if it was plump, had an intact operculum and ideal eyespot, and was yellow or creamy white. Dark tan to brown or black ova with shriveled or shrunken shells were judged nonviable. An ovum that had the operculum popped open and a translucent shell without a brown residue was considered hatched. Nits were examined with a binocular microscope. Empty (hatched) or possibly dead (nonviable) nits were excluded from the ovicidal test, whereas the plump (viable) nits were transferred to another clean Petri dish. The viable ova, firmly fixed to their support (hairs), were exposed to the test preparation by immersion for half an hour at room temperature. Afterward, the nits were washed three times in tap water. Nits were allowed to dry at room temperature and incubated again in similar conditions at room temperature for two weeks for hatching. Next, unhatched nits were counted under the microscope. The percentage of unhatched nits represented the ovicidal activity of the test preparation. Then, the same was done but with the control preparation after the completion of the parasitological evaluation.

In Situ Study

Ivermectin solution was tested for its therapeutic efficacy on primary school children infested with pediculosis capitis. One hundred fifty children from four primary schools in Hayy Al-A'amel, Baghdad, participated in this part of the study.

The children were in grades one to six. The preparation was applied to the children by the author. One hundred children were tested with ivermectin solution and fifty children with rectified spirit.

To be eligible for participation, each patient had to have a diagnostically active head lice infestation confirmed by direct visual identification of live adult lice or nymphs. The presence of nits on the hair shafts was insufficient to qualify a child for inclusion in the study. A child was excluded if there were any other dermatological conditions present or if a pediculicide was used within two weeks of the initial evaluation.

The parents agreed not to wash the hair of their children for half an hour of solution application and not to use pediculicides, medicated shampoos, or lotions, other than ordinary shampoo, during the study. During the first visit, a visual estimation of live adult louse and nymph populations in the children's hair was conducted and the test preparation was applied to the dry scalp in amounts sufficient to thoroughly wet the hair and skin of the infested areas. An amount of 25–50 mL was sufficient to wet the hair and scalp, but extremely long and thick hair sometimes required larger amounts. During the application of the test preparation, the children were instructed to protect their eyes from the preparation by holding a folded towel against their forehead. The hair was covered with a cup for half an hour, then washed.

The therapeutic index (i.e., eradication of live lice and nymphs) was evaluated on days seven and fourteen following the treatment. The children were examined for a minimum of five minutes for the presence of one or more live adult lice or nymphs on either evaluation. The first application of the preparation was given at the first visit, and the second application was given at the second visit (after one week) with the same procedure as on the first application. The parents of the children were instructed to boil or steam sheets, pillowcases, and other formats for about 15–20 minutes.

A clinical evaluation was performed 30–60 minutes following day fourteen. The children were examined for three dermal signs (edema, erythema, and rash) and five dermal symptoms (pruritus, burning, stinging, numbness, and tingling).

Ethics Statement

All authors hereby declare that the study has been approved by the scientific committee of the Scientific Council of Dermatology and have, therefore, been performed in accordance with the ethical standards defined by the Iraqi Board of Dermatology and Venereology.

RESULTS

A total of 150 lice were included in the study. A hundred were tested with ivermectin and fifty with rectified spirit.

The following pediculicidal activity was observed:

1. 2% ivermectin solution

After exposure for three minutes, all of the 100 ova were dead. The pediculicidal activity of the preparation was 100%.

2. Rectified spirit

After half an hour, 7 ova out of the 50 were dead. The pediculicidal activity was 14%.

Ovicidal Test Results

A total of 150 eggs were included in the study.

1. Out of the 100 eggs, 88 eggs were dead. The ovicidal activity of the ivermectin solution was 88% after half an hour.
2. Out of the 50 eggs, 6 eggs were dead. The ovicidal activity of the rectified spirit was 12% after half an hour.

The lice were found to be able to survive for 2–4 days at 30°C without food (away from the human host).

In Situ Study Results

Hundred fifty primary school children infested with active pediculosis capitis were included in the study. One hundred of them were treated with 2% ivermectin solution at the first and second visit and fifty with a control preparation (rectified spirit). All children were female, and their age ranged from 6 to 12 years with a mean of 9 years.

Eighty-two children had no live lice at the first examination (one week after the first application of the test preparation). The therapeutic efficacy of the test preparation after one application was 82%, and 90% after two applications.

While out of the 50 children infested with pediculosis capitis treated with rectified spirit applied for half an hour before washing, 47 children had live lice (adults or nymphs) at the first examination (one week after the first application), and 43 children had live lice (adults or nymphs) at the second examination (one week after the second application). Therefore, the therapeutic efficacy

of the control preparation (rectified spirit) was 6% after the first application and 14% after the second application.

A burning sensation was reported in twelve children (12%) 15–30 minutes after the application of the test solution (2% ivermectin solution). No other dermal symptoms or signs were observed after the application of either preparation.

DISCUSSION

Ivermectin was chosen because of its role in the treatment of ectoparasitic infestations and its relative lack of toxicity as compared with other modalities by recent studies and, because of the increasing number of treatment failures, possibly due to the development of resistance, a change in treatment is to be considered.

Ivermectin is a new drug for the treatment of ectoparasites. To determine its effect on pediculosis capitis, in this study, we applied it as a topical 2% solution in rectified spirit and found that the in vitro pediculicidal activity of the ivermectin solution after three minutes was exceptionally good (100%) and that its ovicidal activity was good as well (88%).

After the first application of 2% ivermectin solution for half an hour, the therapeutic efficacy (percentage of dead lice and ova) was very good (82%) and, after the second application, it was still very good (90%).

A burning sensation was reported in twelve children 30 minutes after the application. These results support that topical ivermectin solutions produce a low frequency of side effects, whereas, with the use of lindane, toxicity has been reported [7].

The result of the study indicates that a 2% ivermectin solution is a good pediculicidal and ovicidal drug that appears to be a suitable alternative, especially considering the reported worldwide spread of resistance to both pyrethroids and malathion.

Therefore, 2% ivermectin solution is a good and cheap pediculicide with a low frequency of side effects. Its main advantages are low adverse reactions and rapid insecticide action, which requires a short contact time and makes it suitable for home treatment.

The study suggests that topical ivermectin may be a promising treatment for head lice and that a second dose on day seven might be appropriate.

2% ivermectin solution was found to have good ovicidal activity (88%) and, if the time of exposure is increased, the ovicidal activity may increase; therefore, a second application is of extreme importance.

In the study, the lice were able to survive for 2–4 days without food (away from the human host).

Causes of treatment failure: Active lice, adults and nymphs, in parasitological evaluation, exposed to the test preparation under optimal conditions with complete exposure of all lice to the preparation in a Petri dish, while the application of the preparation on the hair of the children may not be in close contact with all the lice. Some nits may need more than one week to hatch. Therefore, the nits will hatch on the second application, and this may lead to failure in treatment and reinfestation since all failed cases in our study had live lice. Most of them were small (nymphs) but several were of a mature size (adults), suggesting that these children had been reinfested.

CONCLUSION

This is the first Iraqi study on the use of topical ivermectin for pediculosis capitis.

Topical 2% ivermectin solution in rectified spirit is a good pediculicidal (100%) and a good ovicidal (88%) drug for the in vitro treatment of pediculosis capitis. However, a second application seems to be necessary because of its incomplete ovicidal activity.

It is deemed safe and has no or few side effects.

It is a good pediculicide drug, with 82% therapeutic efficacy on the first application and 90% therapeutic efficacy on the second application, and a good choice for a primary treatment of pediculosis capitis and resistant cases.

At the time of the study, there had been few similar studies, which shows that there is a need for more clarification on Iraqi patients because of the geographical diversity of resistant cases.

Recommendations

1. Further studies regarding ivermectin solutions for longer periods of exposure.

2. Further comparative studies of ivermectin solutions with other pediculicides.
3. There is an urgent need for monitoring the development of resistance through official control of sales and prescriptions.
4. New products such as topical ivermectin are required and, once introduced, careful control of their use would be of benefit.
5. Control of head lice can be attempted by head shaving and wet combing.
6. We recommend the use of a fine-toothed louse comb in addition to treatment for its role in:
    a. The prevention of lice infestation;
    b. Anti-louse treatment methods as an accessory tool;
    c. The removal of nits.

Mass family treatment is necessary.

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Statement of Human and Animal Rights

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

Statement of Informed Consent

As per the national standard, written consent has been collected from the patient or a parent of the patient and preserved by the author(s).

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Our Dermatology Online

Brief Report

The relevancy of patch testing in the exploration of the cutaneous side effects of herbal medicine

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ABSTRACT

Background: Data on the cutaneous side effects of herbal medicine is scarce, especially with regard to allergy skin testing. Our objective was to determine the relevancy of patch testing in the exploration of the cutaneous side effects of herbal medicine. **Material and Methods:** A prospective study was conducted in the Department of Dermatology of the Hospital Institute of Social Hygiene of Dakar over a one-year period. Patch tests were given to patients with cutaneous side effects related to the exclusive use of herbal medicine. The plants recovered were turned into macerates and powders and mixed with Vaseline at concentrations of 5%, 20%, and 30%. **Results:** Patch tests were given to 31 of the 53 patients included. They were positive in 11 patients (35.48%). Positive patients displayed systemic eczema (n = 7/15 of cases), Stevens–Johnson syndrome (n = 2/3), contact eczema (n = 1/1), and fixed pigmented erythema (n = 1/2). Positive tests were obtained for 11 medicinal plants identified: *Jatropha chevalieri* (n = 2), *Terminalia avicennoïde* (n = 2), *Detarium microcarpum*, *Acacia seyal*, *Acacia albida*, *Acacia italic*, *Sesamum indicum*, *Mangifera indica*, *Momordica charantia*, *Nauclea latifolia*, and *Anogeisius leiocarpus* (in one case each). There was no statistically significant relationship between the type of cutaneous side effect and the test result (p = 0.388) and between the nature of the plant used and the test result (p = 0.402). **Conclusion:** In view of their high rates of positivity, patch tests could prove promising in the exploration of the cutaneous side effects of herbal medicine.

Key words: Herbal medicine; Patch tests; Cutaneous side effects

INTRODUCTION

Despite scientific advances in modern medicine, the World Health Organization (WHO) estimates that 80% of the African population continues to use traditional medicine in primary health care [1]. In Senegal, most of the population has been moving toward unconventional medicine to treat various diseases, with rates up to 90% in some locations [2]. The extent of the use of herbal medicine and the potential severity of the possible cutaneous reactions are well known, but few studies have been devoted to this subject, particularly with regard to allergy skin testing. Patch testing plays a major role in the diagnostic approach to cutaneous adverse drug reactions caused by conventional drugs, often establishing a causal link between drug intake and the occurrence of cutaneous adverse events. Their sensitivity can reach 70% depending on the type of cutaneous reaction and the nature of the drug involved [3,4]. We conducted this study in order to determine the frequency of positive patch tests in cutaneous adverse effects related to herbal medicine and to search for a link between test results and the type of cutaneous reaction or the variety of medicinal plant administered.

MATERIAL AND METHODS

The following is a cross-sectional, descriptive, and analytical study with a prospective data collection

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conducted from May 1, 2016, through June 1, 2017 (i.e., for almost one year), in the Department of Dermatology of the Hospital Institute of Social Hygiene of Dakar in collaboration with the Laboratory of Organic and Therapeutic Chemistry of the Faculty of Medicine, Pharmacy and Odontology of Cheikh Anta Diop University of Dakar. Included were cases of a cutaneous reaction related to the exclusive use of herbal medicine. Inclusion necessitated a voluntary informed consent from each patient. Patients who had, at the time of the study, been taking a conventional drug were excluded. All patch tests were free of charge. Each plant recovered was both pulverized and macerated in an acetone extract. The substrates obtained (powder and macerate) were mixed with Vaseline at concentrations of 5%, 20%, and 30%. Ointments were packaged in labeled syringes. Some plants were brought by patients in solution form; these were tested as delivered. Patch tests were performed at least 6 weeks after the disappearance of cutaneous reactions. Finn Chambers cups were used as a support system for allergenic ointments and were applied on the back in occlusion. In the case of fixed pigmented erythema, tests were also applied to lesion sites. The lecture of the tests was performed at 48h and 72h. The criteria used were those of the ICDRG (Table 1). Test relevance was always verified. Data was stored in an Excel file and analyzed using the software Stata 14. First, a descriptive study of quantitative and qualitative variables was made, followed by an analytical study. A Pearson's chi-squared test was used to search for a correlation between the dependent variable (positive patch test) and the covariates. The significance threshold was at $p < 0.05$.

RESULTS

53 patients were enrolled in the study. The average age was 45 years old with the minimum and maximum age of 5 years and 75 years, respectively. The sex ratio was 0.77. A personal history of atopy was reported in 24 patients (45.28%) with allergic rhinitis (n = 6), atopic dermatitis and asthma (n = 5 each), and an association of at least two allergic diseases (n = 8). An observation of allergy to penicillin (n = 2) and nonsteroidal anti-inflammatory drugs (n = 1) was also reported. The most common cutaneous adverse effects were systemic eczema in 22 patients (Fig. 1), contact eczema (n = 4) (Fig. 2), erythrodermic syndrome (n = 4) (Fig. 3), fixed pigmented erythema (n = 3), lichenoid rash (n = 3), and Stevens–Johnson syndrome (n = 3). An aggravation of a preexisting dermatosis was noted in 9 patients, including 6 cases of psoriasis. The average time of onset after the administration of the plants was 12 days. Table 2 shows the frequency of the various cutaneous adverse effects with the average time of their onset. Of the 104 plant medications brought by patients, 74 were identified. Those administered most often were *Detarium microcarpum* (n = 12), *Momordica charantia*

Table 1: Reading criteria of the ICDRG [13]

Symbol	Morphology	Assessment
-	No reaction	Negative reaction
?+	Faint erythema only	Doubtful reaction
+	Erythema, infiltration, possibly papules	Weak positive reaction
++	Erythema, infiltration, papules, vesicles	Strong positive reaction
+++	Intense erythema, infiltrates, coalescing vesicles	Extreme positive reaction
IR	Various morphologies, e.g., soap effect, bullae, necrosis	Irritant reaction

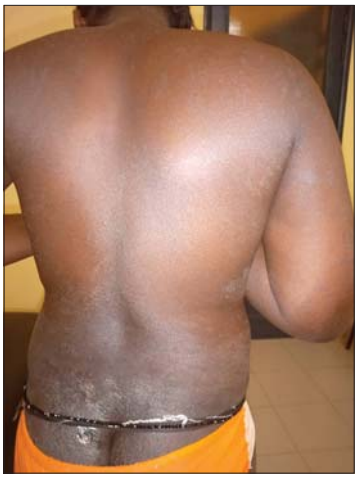

Figure 1: Systemic eczema 7 days after taking *Cassia italic*.

Figure 2: Contact eczema 3 days after the application of an unidentified powder.

(n =7), *Stereospermum kunthianum* (n = 6), *Jatropha chevalieri* (n = 5), *Anogeissius leiocarpus* (n = 4), *Acacia seyal* (n = 4), *Euphorbia balsamifera* (n = 4), and *Terminalia avicennoïde* (n = 3). Table 3 shows the distribution of plants according to the type of cutaneous reaction induced. Patch tests were given to 31 patients with 49 plant medications, 8 of which were unidentified solutions. The 31 patients tested displayed the following cutaneous adverse effects: systemic eczema (n = 15), contact eczema (n = 1), Stevens–Johnson syndrome (n = 3), erythrodermic syndrome (n = 2), fixed pigmented erythema (n = 2), lichenoid rash (n = 2), phytophotodermatitis (n = 1), and aggravated psoriasis (n = 5). Patch tests were positive in 11 cases, corresponding to the frequency of 35.48%. Patients tested positively showed the following cutaneous adverse effects: systemic eczema

Figure 3: Erythrodermic syndrome 30 days after taking *Detarium microcarpum*.

Table 2: Distribution of cutaneous side effects with the average time of their onset

Cutaneous reactions	Effective (n)	Frequency (%)	Average time of onset (days)
Systemic eczema	22	41.50	16.43
Aggravated psoriasis	6	11.32	13.33
Contact eczema	4	7.54	6.75
Erythroderma	4	7.54	11.5
Fixed pigmented erythema	3	5.66	5.66
Lichenoid rash	3	5.66	18
Steven Johnson syndrome	3	5.66	15.75
Erythema multiform	1	1.88	5
Acute generalized exanthematous pustulosis	1	1.88	2
Prurigo	1	1.88	7
Urticaria	1	1.88	2
Phytophotodermatitis	1	1.88	7
Aggravated lichen planus	1	1.88	7.5
Aggravated bullous pemphigoid	1	1.88	3
Aggravated pemphigus foliaceus	1	1.88	7
Total	53	100	

Table 3: Distribution of plant-induced cutaneous side effects

Plant	SE	CE	ES	FPE	SJS	EM	AGEP	Pr	Ur
Detarium microcarpum	5	2	2			1			
Momordica charantia	2		1				1		
Stereospermum kunthianum	2				1				
Jatropha chevalieri	1	2	1						
Anogeissius leiocarpus	2			1					
Acacia seyal	1	1	1						
Euphorbia balsamifera	2	1						1	
Terminalia avicennoïdes	1				1				
Nauclea latifolia	1								
Cassia sieberiana	1								
Cassia occidentalis	1	1							
Leptadenia hastate	1	1							
Euphorbia hirta								1	
Annona senegalensis		1							
Securidata longepe dunculata	1								
Nigella sativa			1						
Acacia albida	1								
Securinega virosa	1								
Mangifera indica	1								
Carapa procera	1								
Aloe vera	1								
Anacardium occidentale			1						
Xylopia aethiopica				1					
Azadirachta indica	1								
Sesamum indicum			1						
Aphania Senegalensis	1								
Fangara zanthoxyloïdes	1								
Khaya senegalensis	1								
Mitragyna inermis	1								
Guiera senegalensis	1								

SE: systemic eczema; CE: contact eczema; ES: erythrodermic syndrome; FPE: fixed pigmented erythroderma; SJS: Stevens–Johnson syndrome; EM: erythema multiform; AGEP: acute generalized exanthematous pustulosis; Pr: prurigo; Ur: urticaria.

in 7 cases, Stevens–Johnson syndrome in 2 cases, contact eczema in 1 case, and fixed pigmented erythema in 1 case. Depending on the nature of the plant, patch tests were positive for *Jatropha chevalieri* (n = 2), *Terminalia avicennoïde* (n = 2), *Detarium microcarpum*, *Acacia seyal*, *Acacia albida*, *Acacia italic*, *Sesamum indicum*, *Mangifera indica*, *Momordica charantia*, *Nauclea latifolia*, and *Anogeisius leiocarpus* (in one case each). No positive results were obtained for plant medicines in solution form. There was no statistically significant relationship between the type of cutaneous adverse effect and the test result (p = 0.388) and between the nature of the plant used and the test result (p = 0.402).

DISCUSSION

Studies on drug-test patches for cutaneous side effects related to herbal medicine are scarce. In a previous study from Senegal, Niang et al. reported 43 cases of cutaneous side effects related to medicinal plants, among which only 19 were tested by patches and pricks, with 62% and 26% positivity, respectively [5]. In India, out of 90 patients tested with patches, De et al. found a positivity rate of 26.7% [6].

Our study shows, once again, the high frequency and diversity of cutaneous reactions attributable exclusively to herbal medicine. This frequency is probably underestimated because of the systematic exclusion of patients who have simultaneously taken conventional drugs or in whom an interrogation did not initially establish the accountability of the plant.

Systemic eczema is the most common cutaneous side effect related to herbal medicine, observed in almost half of our patients. This result is in agreement with that obtained by Niang et al., in which systemic eczema accounted for 58% of cases [5]. In our study, plants most likely to cause systemic eczema were *D. microcarpum*, *M. charantia*, *S. kunthianum*, *A. leiocarpus* and *E. balsamifera*, *D. microcarpum* and *S. kunthianum*. These plants were found most conducive to systemic eczema also in the Niang et al. study, in addition to *Guiera senegalensis*. In the literature, cases of systemic eczema have also been reported with conventional drugs. The most frequently mentioned include amoxicillin, quinolones, acyclovir, and captopril [7,8]. In our research, no chemical similarities were found between conventional drugs and plants incriminated.

In view of these severe reactions, such as erythrodermic syndrome and Stevens–Johnson syndrome, which occurred in some of our patients, it becomes a necessity to improve the phytovigilance process. The high rate of positivity of patch tests observed in our study indicates their potentially significant contribution to the accountability process. Moreover, this rate could have been much higher if a late reading had been done at 96 hours or even a week. Nevertheless, a negative skin test does not exclude the relationship of a drug with the occurrence of a cutaneous reaction. The sensitivity of drug-test patches varies widely depending on the type of cutaneous reaction and the drug involved. Drug-test patches seem to help in exploring maculopapular exanthema, systemic eczema, acute generalized exanthematous pustulosis, and fixed drug eruption. Sensitivity is less important in the case of Lyell's and Stevens–Johnson syndromes: all of our 2 cases of Stevens–Johnson syndrome were positive. Patch tests are unhelpful in exploring vasculitis, urticaria, and angioedema [3]. Furthermore, the nature of the drug tested seems very important for the sensitivity of the drug-test patch [3,4]. The allergenic potential of plants needs no further demonstration. *D. microcarpum* contains in its composition coumarins, also present in the fragrance mix of the European Standard Series [9]. Meanwhile, *M. charantia* contains alpha-momorcharin, whose immunoallergenicity has already been demonstrated in rats [10]. Plants of the *Euphorbiaceae* family, such as *J. chevelieri* and *E. balsamifera*, contain sesquiterpenes known for their allergenic properties [11,12].

In our series, systemic eczema gave a greater number of positive results, with 7 cases out of the 11 positive tests. In the series of Niang et al., 5 of the 10 positive tests were cases of systemic eczema [5]. The absence of a significant statistical link between the type of cutaneous reaction and the result of a patch test could be explained by the small size of our series.

CONCLUSION

In view of their high rate of positivity, patch tests can prove promising in the exploration of cutaneous side effects related to herbal medicine. However, further and broader studies are necessary in order to identify the main allergens in medicinal plants, which will improve the accountability process in cutaneous side effects related to herbal medicine.

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Statement of Human and Animal Rights

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

Statement of Informed Consent

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

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Our Dermatology Online

Brief Report

Alopecia areata in Black African patients: epidemiological, clinical, and therapeutic aspects

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ABSTRACT

Background: The aim was to describe the epidemiological, clinical, and therapeutic aspects of alopecia areata in Black African patients. **Material and Methods:** This was a retrospective descriptive study conducted at the Dermatology and Venerology Department of the University Hospital Center of Treichville over a 5-year. **Results:** The prevalence of alopecia areata was 0.2%. The mean age was 24.6 years and the male-to-female ratio was 1.47. Stress preceding the symptomatology was found in 3 cases. As for the clinical distribution, there were 25 cases of plaque-type alopecia areata, 10 cases of total descending alopecia areata, and 7 cases of universal alopecia areata. There was no nail damage and no associated pathologies. Local treatment only was administered in 31 cases, local and systemic treatment in 8 cases, and systemic treatment only in 3 cases. **Conclusions:** Alopecia areata predominates in young male populations and pathologies associated with alopecia are very rare.

Key words: Alopecia areata; Black skin; Inflammatory dermatoses

INTRODUCTION

It leaves little doubt that hair is an important personal asset especially crucial for maintaining one's physical appearance, and losing it, in part or whole, can greatly affect their quality of life. Several pathologies can lead to hair loss. As for the scalp, alopecia areata is the second most common cause of alopecia in West Africa after ringworm [1,2]. Its frequency varies from region to region and its diagnosis is essentially clinical. Alopecia areata is often associated with other autoimmune diseases. It is difficult to deal with and results are often disappointing. Its occurrence in black people, and especially in sub-Saharan Africa, has received little study. A deeper knowledge of alopecia areata in the region of tropical Africa will make it possible to identify its particularities and to develop treatment protocols adapted to patients suffering from it. Herein, we describe the experience of the Dermatology Department of the University Hospital Center of Treichville after several years of treatment of alopecia areata. The objective of this study was to describe the epidemiological, clinical, and therapeutic aspects of alopecia areata in Black African patients in Abidjan.

MATERIALS AND METHODS

This was a cross-sectional, retrospective, descriptive, and monocentric study that took place from January 1, 2014, through December 31, 2018, for a total period of five years, at the Dermatology Department of the University Hospital Center of Treichville in Abidjan, Côte d'Ivoire. The department is the largest reference center for skin diseases in Côte d'Ivoire in general and chronic dermatoses in particular. Included in the study population were all patients seen in consultation for alopecia areata during the study period. Diagnoses of

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alopecia areata were reached on the basis of clinical and/or histological examinations. Caucasian patients and black patients residing outside of sub-Saharan Africa were excluded. The following epidemiological, clinical, and evolutionary parameters were sought: age, sex, medical history, type of alopecia areata, duration of evolution, treatment. Data were compiled and analyzed with the software Epi Info, version 3.5.1.

Ethics Statement

During the study, we did not conduct any examination on animals or humans. All the data were retrieved from medical files. No information concerning the identity of the patients was mentioned in the study.

RESULTS

During the study period, 39,603 patients were seen in consultation, including 42 cases of alopecia areata, giving a prevalence of 0.2%. The average age was 24.6 years, ranging from 6 to 44 years. There was a male prevalence, with 25 (59.5%) cases, and a male-to-female ratio of 1.47. The distribution of patients by sex and age group was predominantly male in all age groups (Fig. 1). Schoolchildren and students were in the majority, with 21 (50%) cases, followed by patients performing informal activities, in 11 (26.2%) cases. The majority of patients were from Abidjan or its suburbs (92.8%). Stress preceding the symptomatology was found in 3 (7.1%) cases. The symptomatology had evolved for 21.38 months (i.e., 1 year and 9 months) before the consultation. There were 25 cases of plaque-type alopecia areata (3 cases of ophiasis, 2 in the right temple, 2 in the vertex, and 18 sparse cases), 10 cases of total descending alopecia areata, and 7 cases of universal alopecia areata (Fig. 2). There was no nail damage and no associated pathologies. Local treatment only was administered in 31 cases, local and systemic treatment in 8 cases, and systemic treatment only in 3 cases. Local treatment involved the prescription of dermocorticoids in 25 cases, 2% minoxidil in 12 cases, and a rubefacient gel in 8 patients. Systemic therapy included prednisone in 10 cases and methotrexate in one case.

DISCUSSION

Alopecia areata is an autoimmune disease that destroys hair follicles. Its prevalence in the world population is estimated at around 2% [3]. In sub-Saharan Africa, especially in Burkina-Faso and Nigeria, alopecia areata represents 26.4% and 38.1%, respectively, of the causes of alopecia in hospitals [1,2]. The prevalence of alopecia areata in our department—estimated at 0.2%—is lower than what is reported in the literature: between 0.57% and 3.8% [4]. This might be due to selection bias. In fact, public health structures such as ours most often welcome patients who lack health insurance or are financially destitute. Thus, patients in a more advantageous financial position or who do have health insurance may consult in private facilities, reducing the prevalence of certain pathologies in hospitals. Alopecia areata predominates younger populations, with an average age of onset of 33 years and extremes ranging from 25.2 to 36.3 years [3,4]. The average age of the patients in our study, which was 24.6 years, was relatively lower than that reported by other studies [3,4]. In our study, males predominated in all age groups. This might be explained by the fact that alopecia areata tends to be upsetting and more disconcerting to young males because, what would otherwise be easier for most young females, the short hair typically worn by young males is not enough to camouflage the lesions. According to Salam et al., the most common etiology of nonscarring alopecia in African women is traction alopecia [5]. Several pathologies can be associated

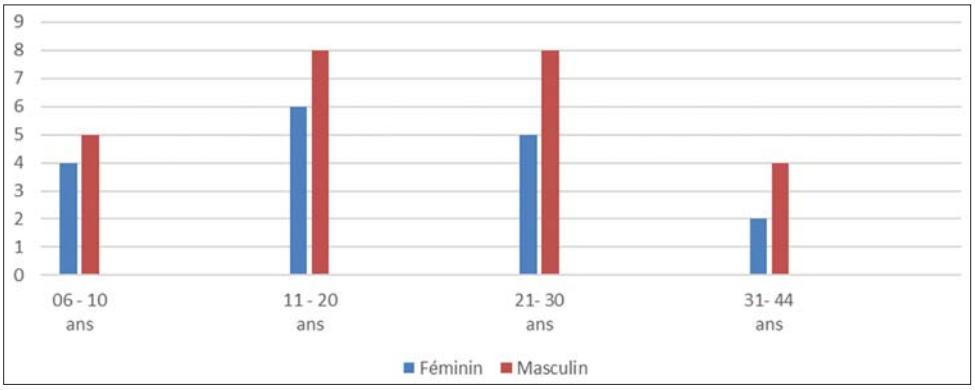

Figure 1: Distribution of patients by sex and age group.

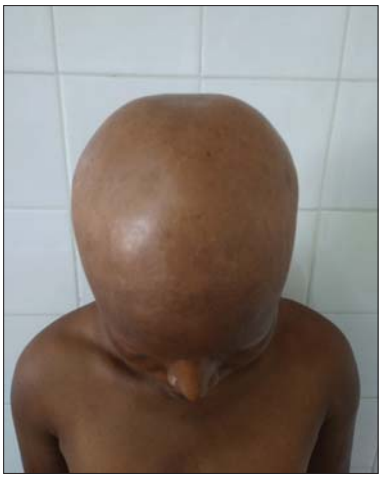

Figure 2: Universalis alopecia areata in a young female.

with alopecia areata, and these include thyroiditis, vitiligo, psoriasis, diabetes, lichen planus, atopic dermatitis, and numerous other diseases described in the literature [6-9]. However, our study found no pathologies associated with alopecia areata. Only stress was found in 23% of our cases, and this could have been due to the high prevalence of poverty among them. Indeed, people with insufficient financial means fail to return after the first consultation to see the doctor and receive further medical examination. Such a lack of resources also explains the long consultation time (21.38 months) found in our study. Apart from this, we believe that this observation might be a peculiarity of alopecia areata in Africa, given that certain pathologies may be clinically discovered. The clinical forms found were proportionally identical to those in the literature [3,4,6,7]. Treatment in our work context was based on locally applied topical remedies; these were mainly dermocorticoids and minoxidil solution, used in combination or not. In recent years, several treatments have been used for the management of alopecia areata [10-13]. However, despite the scientific advances in pathophysiology made in recent years, no treatment provides complete satisfaction, especially in the presence of ophiasis alopecia areata or total alopecia areata.

CONCLUSION

Alopecia areata is an inflammatory condition of the scalp with a relatively low frequency in our context. It occurs mostly in young males. Pathologies associated with alopecia areata are very rarely found and local treatment is still topical.

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

Case Report

Flat topped hypopigmented micropapules on the flank and neck

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ABSTRACT

Lichen nitidus (LN) is a rare inflammatory condition which presents as multiple small, shiny, pale to flesh colored papules measuring 1-2mm in diameter. Lesions typically occur on the abdomen, chest, genitalia and extremities. However, cases of LN involving the nails, oral mucosa and acral skin have been described. Although, it typically presents in children and young adults, there is no gender or racial preference. Clinical and histopathological findings are characteristic for LN and treatment is rarely warranted. Herein we report a case of LN in a 26-year-old African American female who presented with multiple areas of LN.

Key words: Lichen nitidus; Rash; Lichen planus; Papules

INTRODUCTION

(LN) is a rare condition with poorly understood pathophysiology [1,2]. Patients are usually asymptomatic but may have pruritis. Clinical presentation may be sufficient enough for diagnosis. However, patients with symptoms may warrant a biopsy, especially if seen by generalized practitioners. It is most common in children and young adults; however, it has also been described in older patients [3,4]. Both genders and all races may be affected. Many clinical variants of LN which have been described in literature including vesicular, confluent, generalized, perforating, follicular and linear forms [1,4]. Although LN is generally self-limited, clinical presentation and biopsy results may be needed for patient reassurance.

CASE REPORT

A 26-year-old pregnant African American female presented with complaints of a rash present on her right flank and the right side of her neck (Figs. 1 and 2). The rash was chronic in nature and present for approximately 2 years. Patient reported minor pruritis at times but denied dry, cracked, scaling skin, or any changes to the rash. She was evaluated for the rash previously at an outpatient clinic and was prescribed an antifungal cream for tinea. She used the antifungal cream for 3 months without any improvement. Clinically the rash was discrete with multiple pinpoint, flat-topped, pink colored papules. A shave biopsy was taken from the papules present on the flank and sent to pathology.

Sections of the biopsy revealed a patchy / multifocal lymphohistiocytic infiltrate obscuring the epidermal-dermal junction and enclosed within an epidermal collaret (Fig. 3). Subtle basal cell vacuolization and very rare apoptotic keratinocytes were noted in these areas. Overlying thinning of the epidermis was noted (Fig. 4). Eosinophils were not identified. The overlying granular cell layer, and stratum corneum with otherwise fairly unremarkable. These morphologic features of multiple small areas of a more mixed histiocytic and lymphocytic infiltrate surrounded by epidermal collarets was diagnostic for lichen nitidus.

The patient was informed of her biopsy results. However, she was pregnant and therefore, treatment

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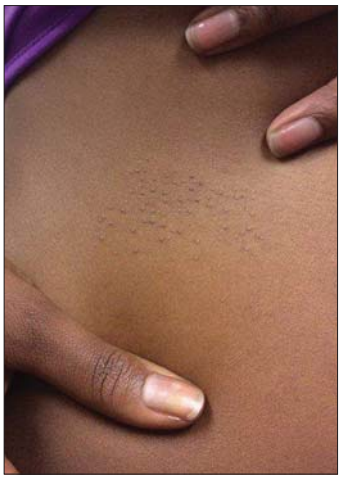

Figure 1: Discrete small flesh colored micropapules on the flank.

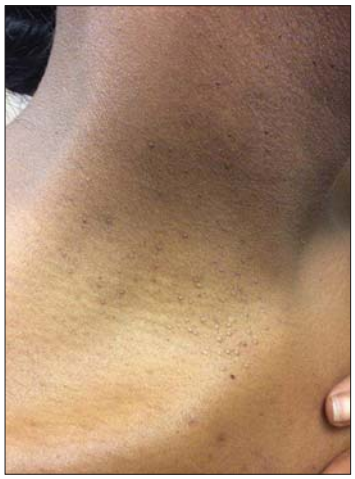

Figure 2: Shiny slightly hypopigmented micropapules on the neck.

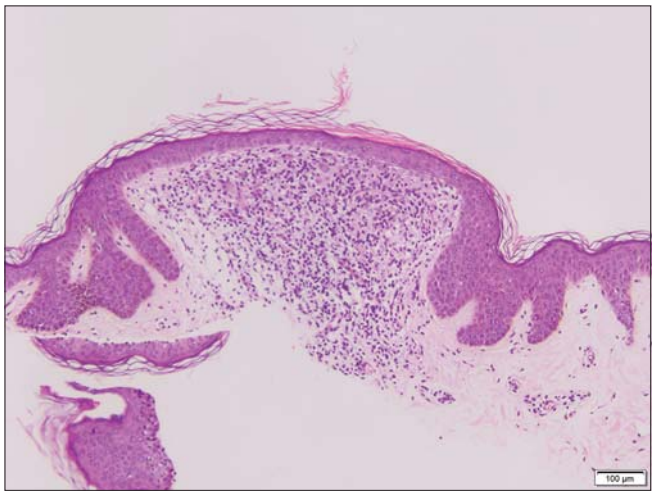

Figure 3: Multifocal lymphohistiocytic infiltrate obscuring the epidermal-dermal junction and enclosed within an epidermal collaret. H&E 100x.

was not recommended unless the rash became worse or more problematic. She was reassured and instructed to schedule a follow-up if the rash progressed.

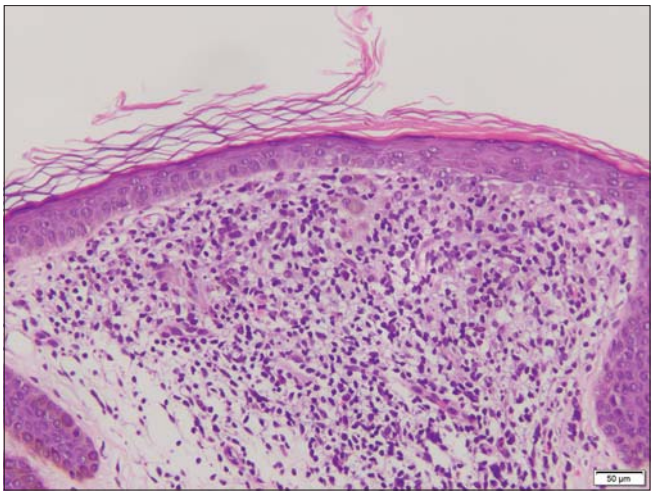

Figure 4: Mixed histiocytic and lymphocytic infiltrate, an overlying thinning epidermis, and scattered apoptotic keratinocytes. H&E 200x.

DISCUSSION

Histopathology of LN is very characteristic and consistent with a well circumscribed lymphohistiocytic infiltrate hugging the epidermis. The overlying epidermis is typically atrophic and parakeratotic. The rete ridges extend downward, making finger like projections enclosing the inflammatory infiltrate in a typical ball in claw appearance. [5] Basal cell hydropic degeneration and cytoid bodies may be seen [1,5].

Older lesions of LN may have granulomas and giant cells while earlier lesions typically consist of lymphocytes [5]. Immunohistochemical stains (IHC), although unnecessary can also be utilized. LN demonstrates a heterogenous population of CD4+ and CD8+ lymphocytes along with macrophages [6].

The differential diagnosis of LN includes lichen planus (LP) and in fact many authors have described LN and LP occurring in the same patient population. This has sparked the debate as to whether LN is merely a micropapular variant of LP [6]. However, both entities have distinct histopathological and IHC patterns. LP, in contrast to LN demonstrates a predominance of CD4+ helper T-cells along with HECA-452 staining as well as a more uniform lymphocytic infiltrate [1,6].

Although histology and clinical presentation are characteristic; features of dermoscopic findings are notable and thus, dermoscopy may provide to be a useful tool [1]. Jahkar et al, studied 8 cases of LN using polarized and non-polarized dermoscopy. Nonpolarizing dermoscopy was characteristic for shiny

elevated surface with the absence of dermatoglyphics as well as central depression. Polarizing dermoscopy showed the presence of ill-defined hypopigmentation, diffuse erythema as well as linear vessels [5]. Features of dermoscopic findings correlated with the histopathologic findings of LN. The absence of dermatoglyphics correlated with the flattening features of the epidermis overlying the inflammatory infiltrate and the central depression seen was characteristic for the well circumscribed ball like inflammatory infiltrate [5]. Therefore, dermoscopy can be used as a non-invasive diagnostic tool to help differentiate between other cutaneous lesions.

The pathogenesis of LN is unclear. It has been linked to immunologic alterations in patients [1,6]. Reports of LN associated with cutaneous disease such as lichen planus and erythema nodosum have been described, suggesting that an allergen may cause antigen presenting cells to activate a cell mediated response which results in the characteristic lymphocytic accumulation [1]. Furthermore, LN has been associated with a variety of systemic conditions including Niemen Pick's disease, HIV, Chron's disease and Down's Syndrome [1,6]. Generalized LN, on the other hand, has been reported following treatment using interferon alpha, ribavirin and anti PD-1 therapy such as nivolumab [1,7].

LN is generally a self-limiting eruption, however the clinical course is uncertain [8]. Patients typically have spontaneous resolution of symptoms and thus treatment is often not necessary given the asymptomatic nature [6]. However, patients who present with symptoms or have cosmetically disrupting lesions may be treated. Symptomatic patients or patients with chronic LN may benefit from topical or systemic corticosteroids [1,6]. Patients with the generalized form can be treated with PUVA or astemizole. Consequently, oral retinoids have proved to be beneficial in patients who have involvement of acral skin [1].

CONCLUSION

Most lesions of LN resolve within 1-3 years of onset [6,9]. However, the papules of LN may lead to post inflammatory hyperpigmentation. It is believed that as the papules heal, they are replaced by hyperpigmented post inflammatory macules which tend to resolve within months [1,9]. Treatment may be necessary for cosmetic purpose as well. It is important for practioners to be aware of LN. Our patient was originally misdiagnosed and treated for tinea unnecessarily. Fortunately, since biopsy and reassurance she has not had any further complaints.

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

Localized cutaneous argyria: A new observation

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ABSTRACT

A 27-year-old female, a radiotherapy technician, was referred to our consultation with a localized gray pigmentation of the perinasal area. The condition had been asymptomatic for its entire duration of 2 years. A dermatological examination found a localized bluish-gray pigmentation in the perinasal area. Dermoscopy revealed an annular bluish-gray patch. Her occupation involved the manufacture and micromanipulation of machines, which required handling pure iron, nickel, copper, and silver with bare hands. She also reported a tic of flaring the nose. A skin biopsy was performed and histology revealed deposits of fine granules in the basal cell layer of eccrine sweat glands and along the elastic fibers of the superficial dermis, conforming with the diagnosis of argyria. The patient was given laser Q-switching treatment and showed a measurable improvement. This case studies a currently rare dermatological curiosity. Argyria is a disease caused by chronic absorption of silver-rich materials. This is the first description of argyria following the manipulation of radiopaque caches with a tic of flaring the nose.

Key words: Argyria; Cerrobend; Occupational argyria; Skin pigmentation

INTRODUCTION

Argyria is an uncommon clinical condition caused by prolonged skin exposure to silver. Two known types of argyria exist: localized and generalized. Localized argyria has been reported to be the result of using topical medication and inadvertently implanting in the skin objects that contain silver. Several different types of exposure—accidental, therapeutic, occupational, and environmental—routes of administration—oral, intranasal, and percutaneous—and intervals of exposure—from 8 months to 5 years—have been described. The diagnosis is reached by histopathology, although certain cases may necessitate the identification of the presence of metal by electron microscopy (EM).

The following case report studies a patient with localized argyria caused by manipulation of focused custom caches (Cerrobend).

CASE REPORT

A 27-year-old woman showed a localized bluish-gray pigmentation in the perinasal area asymptomatic for 2 years (Fig. 1). The patient denied the use of drugs: phenothiazines, antimalarials, amiodarone, and minocycline. She did not report the use of a nasal decongestant or an antiseptic. Two years after beginning her professional occupation, she noted the appearance of bluish macules in the perinasal area. Rhinoscopy did not find any gray pigmentation on the anterior part of the nose. Dermoscopy revealed an annular bluish-gray patch with blurred borders (Fig. 2). We performed a biopsy and found deposits of fine granules in the basal cell layer of eccrine sweat glands and along the elastic fibers of the superficial dermis (Fig. 3). Since the patient admitted to manipulating focused custom caches containing silver and having a tic of flaring the nose, a final diagnosis of occupational argyria was established. The patient was treated with laser Q-switching and showed a measurable improvement (Fig. 4).

DISCUSSION

Argyria is a rare disease caused by chronic absorption of silver-rich materials [1]. Skin pigmentation is caused

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Figure 1: Localized bluish-black pigmentation in the perinasal area.

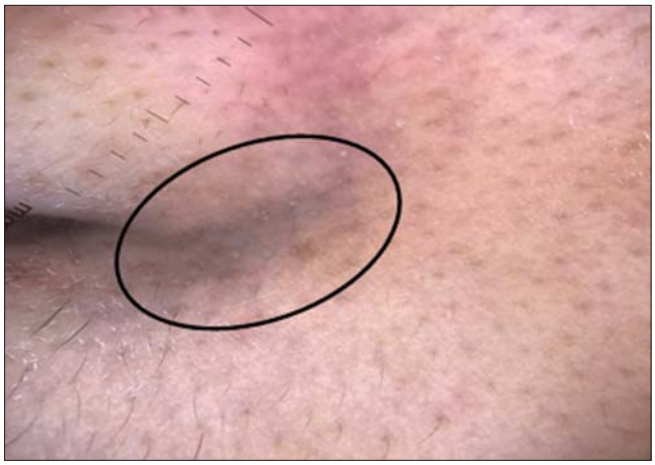

Figure 2: Dermoscopy showing annular structures on a gray background area (black circle).

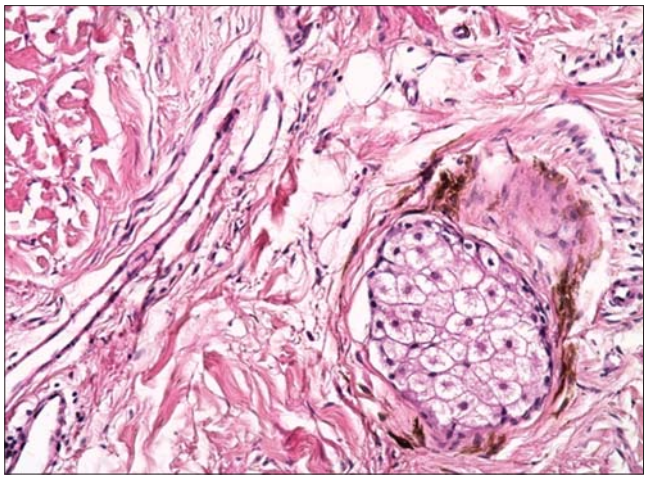

Figure 3: Histology showing deposits of fine granules along the elastic fibers of the superficial dermis.

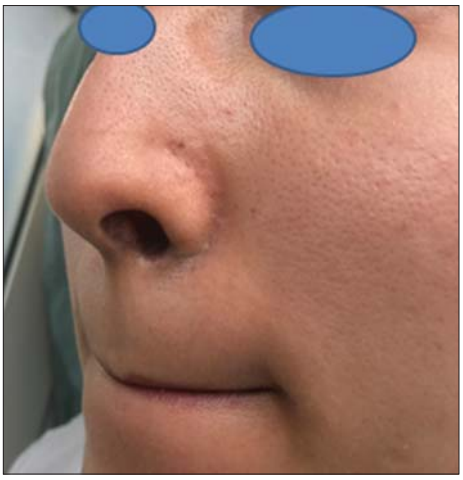

Figure 4: Control image after laser.

not only by silver deposition—in sulfite or selenite forms—in the dermis but also, according to some, by stimulation of melanin synthesis [2].

In localized argyria (LA), lesions may appear as asymptomatic slate, gray, or blue macules resembling blue nevi. The reason as to why the gray color is more evident in photoexposed skin areas is unknown. It is believed that silver assumes a brownish-black hue through a chemical reduction reaction or through a photomediated exacerbation of its stimulatory effect on melanin synthesis [3].

These compounds are deposited following slow tissue flux and are captured by elastic fibers and the basement membrane before reaching the epithelium. The bluish-gray color of dermoscopic structures was most probably produced via the Tyndall effect, which gives the appearance of bluish-gray pigment located deep within the dermis. The bluish-gray annular structures were observed by dermoscopy due to the presence of pigment deposition around eccrine glands. A histopathological examination showed an accumulation of brownish-black granules with no appreciable inflammatory infiltrate; such granules lie in compact bands parallel to the mucosal surface and/or in black cloud-like aggregates close to the surface. The basic requirements to identify such granules as an exogenous pigment are their Perls stain negativity and persistence after tissue section bleaching [4]

Different treatments can be proposed to this benign condition; these may include topical depigmenting agents such as hydroquinone, but they give little improvement. However, in most reported cases, laser Q-switching led to noticeable improvements [5].

To the best of our knowledge, this is the first description of argyria following manipulation of radiopaque caches

with bare hands. Radiation therapy caches contain tin, an alloy of silver and copper.

Our case highlights the adverse consequences of manipulating focused custom caches that may be ignored in a limited clinical setting.

CONCLUSION

Localized argyria is a benign condition unassociated with systemic disorders or malignant development. Even so, a manifest location, such as the face, can disturb and alarm patients.

Consent

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

The authors certify that they have obtained all appropriate patient consent forms, in which the patients have given 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

Effective treatment of alopecia universalis with oral tofacitinib: A case report

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ABSTRACT

Alopecia areata is a common autoimmune disease presenting itself with patches of hair loss on the scalp, eyebrows, eyelashes, or any part of the body. It may manifest itself as a single patch, involving the entire scalp (alopecia totalis), or affecting the entire body, thus the name *alopecia universalis*. Multiple lines of treatment may be employed, but no single most effective treatment exists, especially if the condition is generalized and, thus, becomes more difficult to treat. Herein, we report a case of alopecia universalis treated with oral tofacitinib with an excellent and persistent response one year after.

Key words: Alopecia areata; Alopecia universalis; Tofacitinib

INTRODUCTION

Alopecia areata (AA) is a common autoimmune disease with a lifetime incidence of 2% worldwide [1]. Its clinical presentation ranges from a single patch of non-scaring hair loss, the involvement of the entire scalp, also known as alopecia totalis (AT), or generalized hair loss involving the entire body, also known as alopecia universalis (AU) [2].

Its pathogenesis is a complex immune-mediated response with predominant CD8 T-cells leading to an attack on a hair follicle [3]. It has been documented as an increase in CD8/CD4 cells around a hair follicle in an area known as the bulb causing non-scaring hair loss [4,5]. An increase in substance p that mediates the transition of the hair cycle from anagen to catagen has been reported, thus resulting in hair fall [6].

There are several lines of treatment available for alopecia universalis, including topical and oral steroids, topical immunomodulators, but no FDA approved therapy as of yet. Recently, Janus kinase (JAK1–3) and tyrosine kinase TYK2 have been reported to be relevant [7]. JAK enzymes are implicated in a series of transcribing inflammatory proteins, which are involved in the pathogenesis of numerous autoimmune diseases, such as vitiligo, rheumatoid arthritis, atopic dermatitis, psoriasis/psoriatic arthritis, and alopecia areata. By blocking these enzymes, targeted treatment is achieved [5,7,8].

Many cases are resistant to some, if not all, lines of treatment, especially long-standing cases. Thus, the possibility of a targeted treatment that is effective for cases such as alopecia universalis is promising.

CASE REPORT

We present the case of a 29-year-old female with a history of alopecia totalis present since 2015. It started with patchy hair loss limited to the scalp. The patient was previously seen in another hospital, where she was started on minoxidil 5% once daily initially with a good improvement for one year. She had been a known case of rheumatoid arthritis for ten years treated with methotrexate 22.5 mg for one year, thereafter, in 2011, switched to rituximab at a dose of 1000 mg once every six months.

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In 2017, the patient's alopecia relapsed in three months as alopecia universalis with hair loss on the scalp, eyebrows, eyelashes, and the entire body. At that time, she presented herself to our clinic. Other causes of alopecia were excluded by history taking and laboratory tests, including a thyroid function test with anti-thyroid antibodies, iron, vitamin D, vitamin B_{12}, which were all within normal limits.

In May 2018, after a discussion with the patient's rheumatologist, we decided to stop rituximab and, instead, switch her to tofacitinib 5 mg orally twice daily, targeting both rheumatoid arthritis and alopecia universalis, in addition to topical minoxidil 5% once daily.

Baseline investigation was performed prior to starting tofacitinib, including complete blood count (CBC) with a differential to measure the amount of hemoglobin and the number of lymphocytes and neutrophils. In addition, the renal panel, liver panel, lipid profile, intradermal purified protein derivative (PPD) test, chest X-ray (CXR), hepatitis screening, and antinuclear antibodies (ANA) were all within normal limits. On each visit, vital signs were taken, a thorough physical examination was performed, and laboratory monitoring for CBC with a differential was conducted. All these were unremarkable.

An examination at presentation revealed diffuse hair loss on the scalp, eyelashes, eyebrows, and the entire body (Fig. 1a). On trichoscopy, follicular ostia were seen with black and yellow dots. No perifollicular erythema or scales were found. After three months of starting tofacitinib, fine patches of hair growth were observed on the scalp, eyebrows, and eyelashes (Fig. 1b). At six months, significant hair growth was noted on the eyebrows, eyelashes, and entire body, with the complete regrowth of the scalp hair (Figs. 1c-d). At nine months, the length and density of the hair of the scalp and entire body increased (Figs. 1e-f). Eleven months after starting the treatment, the patient maintained excellent clinical improvement with an increasing hair length (Fig. 1g). At thirteen months, the patient maintained the hair growth all over the body, again with an increasing hair length (Figs. 1h-i). The patient has

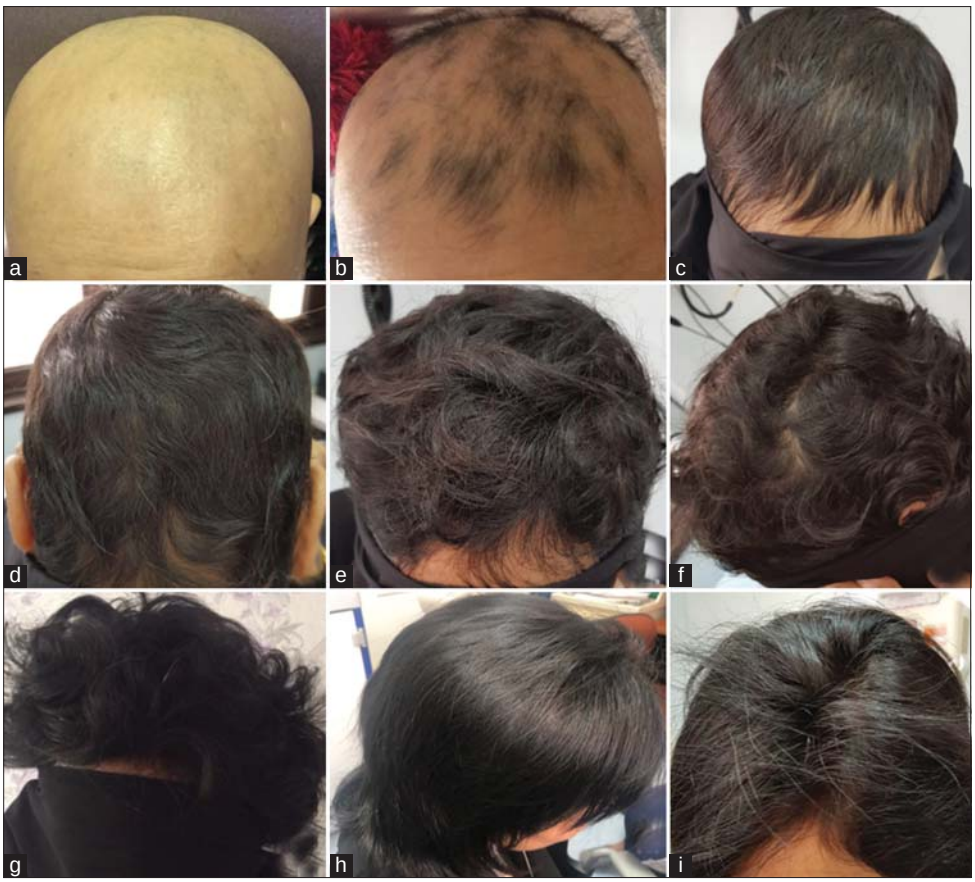

Figure 1: Clinical response to tofacitinib (a) at presentation, (b) after three months, (c-d) six months, (e-f) nine months, (g) eleven months, and (h-i) thirteen months after its first administration.

stayed on tofacitinib for the last thirteen months with a good and sustainable response and without any side effects or relapses.

DISCUSSION

Alopecia areata (AA) is a known T-helper 1 T_h1 disease involving cytokines such as interleukin-2 (IL-2), tumor necrosis factor alpha (TNF-α), and interferon gamma (IFN-γ). The contribution of IFN-γ leads to the release of a chain of cytokines IL-2, IL-7, IL-15, and IL-21, which are implicated in the signaling of the Janus kinase–STAT pathway [4,9]. JAK inhibitors interfere with the inflammatory process within the immune system, blocking a series of cytokine-mediated interactions in the JAK-STAT pathway. Tofacitinib is a targeted medication blocking JAK1–3 and has been shown in several studies to diminish or block the inflammatory cascade targeting the hair follicle in alopecia areata. Tofacitinib is now FDA approved for the treatment of rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis [4,8].

Our case report supports the results of prior reported cases. Crispin et al. published the results of a clinical trial that evaluated the efficacy of tofacitinib, and of the pan–JAK inhibitor, in the treatment of severe AA and its variants. These results suggest that tofacitinib is a safe and effective treatment for severe AA, AT, and AU [4]. Similar cases of alopecia universalis treated with tofacitinib were reported by Gupta [10]. Another case of alopecia universalis responding well to oral tofacitinib without significant side effects was reported by Hogan, who claimed that JAK inhibition may serve as an effective treatment modality for AA [11]. A comparable case reported by Ferreira et al. showed an excellent response to oral tofacitinib in an adolescent patient with alopecia areata [12].

Our patient obtained sustainable results after thirteen months of starting the treatment. Relapses were reported upon the discontinuation of the medication [10,13,14]. Relapses require longer follow-ups in addition to changing the management plan with the treating rheumatologist.

This patient had two autoimmune diseases, probably with a similar pathogenesis. Thus, treating rheumatoid arthritis might result in treating alopecia as well. Nevertheless, the pathogenesis of alopecia areata is not always that clear. Therefore, treating other types of alopecia where it is the sole presentation in the patient is necessary to evaluate the effects of tofacitinib. Moreover, the patient was on minoxidil simultaneously with tofacitinib. Thus, the results might have been due to the synergistic effect of the medications. Nonetheless, minoxidil was not applied over the body, and so the effect is to be mainly attributed to tofacitinib.

Pictures of the face and body could not be taken due to the patient's refusal. Trichoscopy pictures were not taken for the same reason.

CONCLUSION

Our case report shows significant improvement of AU with oral tofacitinib with no reported side effects. However, further clinical trials are required in order to confirm the results with longer follow-ups while on and off medication.

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.

ACKNOWLEDGMENTS

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Our Dermatology Online

Case Report

Plica polonica: Trichoscopic findings with a brief literature review

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ABSTRACT

Plica polonica is a common but rarely reported acquired condition characterized by sudden onset of irreversible entanglement of the hair. Psychological disturbance is a risk factor for plica formation. Plica polonica was considered a disease of the past caused by poor hygiene and haircare in psychiatric patients. In view of its clinical rarity, we describe the case of a 50-year-old Muslim woman of Kashmiri ethnicity presenting with plica polonica to explain the trichoscopic findings gathered in the process of medical examination. The patient had attempted the treatment of the condition with various shampoos and conditioners but without improvement. There was no history of mental illness either in the patient or the patient's family. The hair was dry, lusterless, densely adherent, but without discharge, foul odor, or lymphadenopathy. Trichoscopy revealed varying shades of brown and crisscrossing of hair shafts resembling an intertwined mesh of wires with concretions of the hair shafts. The patient was advised to cut the matted hair.

Key words: Plica polonica; Hair; Trichoscopy

INTRODUCTION

Plica polonica—also known as plica neuropathica or Polish plait—is a rare acquired disorder of the hair shafts in which groups of hair are matted, together forming a malodorous, encrusted, sticky, and moist mass [1]. Not combed or cut, long hair tangles leading to the formation of twisted masses of matted ropes of hair known as dreadlocks. Plica polonica used to be prevalent in 19th-century Poland, hence assuming the name *plica polonica* or *Polish plait*. The then habit of wearing tight fur caps and the superstitious belief that a lousy scalp was a synonym of health contributed to the prevalence of plica polonica in 19th-century Poland. Clinically, plica polonica manifests itself as a compact mass of scalp hair with irregular twists and irreversibly tangled plaits, firm-to-hard impenetrable masses of keratin concreted with dirt and exudates [1].

Its exact etiopathogenesis remains unexplained, but the risk factors include psychological disturbance, secondary scalp infection, infestation of the scalp, or the use of shampoos with cationic surfactants. Treatment involves cutting the matted hairs.

CASE REPORT

A 50-year-old Muslim female from an average urban background consulted us complaining of matted scalp hair persisting for two months prior. The patient gave a history of having had straight hair without curls, frequent application of hair oil, and washing the scalp hair once to twice a week in plain water. After the sudden death of her brother, she kept her hair locked over the vertex for a period of two weeks without washing the hair. During this period, she made no attempt to disentangle the matted scalp hair or to use shampoo or soap to wash. Since she noticed sudden tangling of the scalp hair in the hair lock on the vertex, she had attempted the treatment of the condition with various shampoos and conditioners but without improvement. There was no history of plica before this incident. She denied application of hair dye two months prior, although she had used it often in the

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past. There was no history of mental illness either in the patient or her family and no history of behavioral disturbance. The patient was not on mental health medication. There was no itching or discharge and no suggestion of scalp hair disease.

Upon examination, the hair was dry, lusterless, densely adherent to the individual hairs, but not to the scalp. There were numerous tangled bunches of long hairs, greater in number over the parietal and occipital areas of the scalp (Figs. 1 and 2). There was no evidence of discharge from the scalp and no foul smell. There was no evidence of pediculosis capitis or other primary scalp or hair disorders. There was no cervical or occipital lymphadenopathy. Trichoscopy (DermLite DL3N, USA, 10×) revealed varying shades of brown and crisscrossing of the hair shafts resembling an intertwined mesh of wires. The hair fibers showed thickening and concretions due to hair shaft damage (Figs. 3 and 4). The scalp could not be visualized in either a clinical or trichoscopic examination. Upon potassium hydroxide examination, fungal hyphae were found absent. A qualified psychiatrist conducted a psychological evaluation to reveal no abnormalities. The patient seemed to have developed the condition initially due to neglect and lack of hygiene, and then due to the weathering effect of harsh shampoos. The trichoscopic pattern also resembled that of cosmetic weathering. The patient was advised to cut the matted hair.

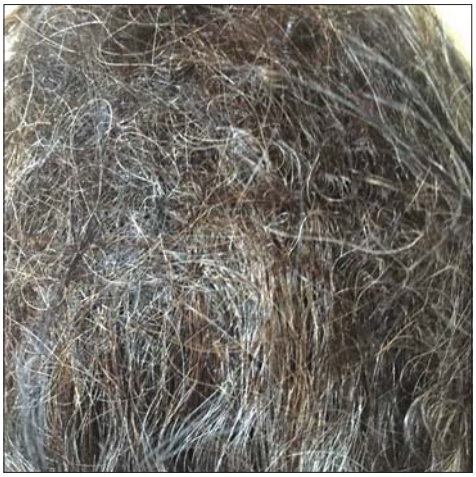

Figure 1: A compact, matted mass of dry, lusterless, tangled hair with no visualization of the scalp in the parietal area.

Figure 2: A compact mass of dry, lusterless, tangled hair in the occipital area.

DISCUSSION

The term *plica neuropathica*, an alternative designation of plica polonica, was coined by Le Page in 1884 to describe a case of sudden-onset hair entanglement in a 17-year-old female suffering from hysteria [2].

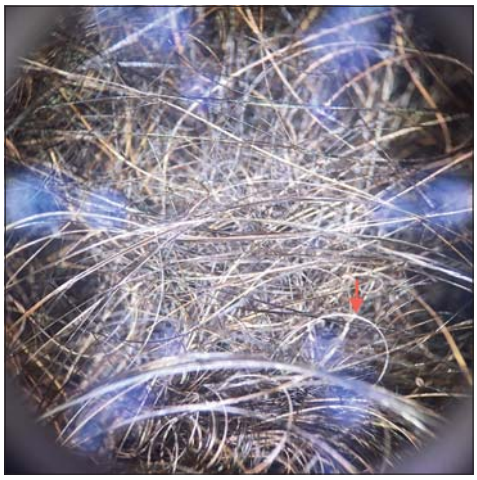

Figure 3: Trichoscopy revealing varying shades of brown and crisscrossing of the hair shafts resembling an intertwined mesh of wires; arrows pointing to the thickening of the hair shaft. (Non-polarised mode, DermLite DL3N, 10×).

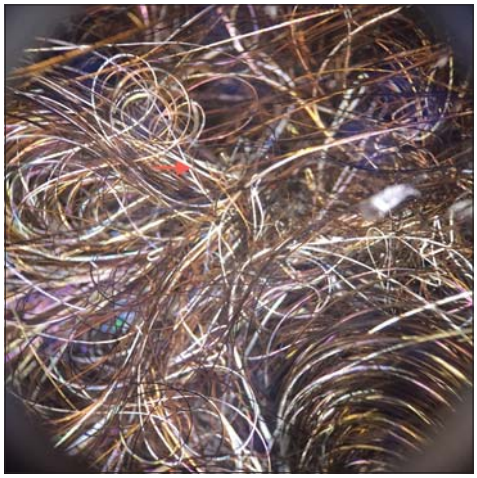

Figure 4: Similar findings in the Polarised mode (10×).

Le Page attributed this uncommon phenomenon to "nerve force," while the patient's parents believed it to be a "visitation from God" [2]. Mullin reported more instances of plica polonica. The first records of dreadlocks go back to 2500 BCE with the dreadlocked Hindu deity Shiva and his followers reported in the Vedas, Indian religious scriptures [3].

Bogaty and Dunlap first used the term *matting of hair* in 1970 and compared the condition to *felting* [4]. Felting in the textile and wool industry causes conglomeration of contiguous fibers when exposed to friction and compression in a liquid medium. The pathogenesis of plica polonica has not been fully understood and different etiopathological mechanisms have been proposed, including physical, chemical, and behavioral factors [1,5,6].

Other pathogenetic factors may include long hair and vigorous rubbing of wet hair in a rotatory manner [7]. Neglect of scalp care, constant avoidance of haircutting, and psychological disorders have also been proposed as relevant factors. Habitually uncut, the hair may begin to display areas of cuticular irregularities, which could interdigitate and enhance matting. Loss of cuticles may lead to the exposure of the sticky cortex, causing the hairs to adhere to one another [8]. Plica polonica has also been reported to follow irritant contact dermatitis of the scalp [9], and in two cases of pancytopenia following the use of azathioprine, attributed to the cuticular damage of the hair shaft in the presence of inadequate haircare habits [10,11]. Some superstitious beliefs may also encourage the application of sticky materials on the hair together with avoidance of washing and combing. A common superstitious belief maintains that such negligence helps in curing internal illnesses and that cutting hair brings poor health. Plica polonica has also been attributed to longitudinal splitting and weathering of the hair shaft due to vigorous friction and frequent use of harsh shampoos. Dermoscopy of plica polonica reveals intertwining of the hair shafts, matting, and honey-colored concretions resembling a wrangled mesh of wires [12]. Cosmetic weathering may also give rise to such concretions due to acquired trichorrhexis nodosa caused, in turn, by hair shaft splitting and frictional forces.

Plica polonica is a condition with well-defined trichoscopic findings and can as well be attributed to the haircare practices of the modern day. In any case, the treatment of plica polonica involves the cutting of the affected hair. Its early stages may be reversible and manual separation with organic solvents can be attempted, together with avoidance of rotatory rubbing, regular trimming of the hair, and avoidance of trigger factors such as those set forth earlier. The further risk of matting can be reduced by haircare measures such as regular hair cleaning with mild shampoos, gentle oiling, combing to avoid tangles, and regular hair trimming.

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

Tinea capitis mimicking alopecia areata

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ABSTRACT

Tinea capitis (TC) is the most common dermatophyte scalp infection in children and an unusual dermatophytosis in adults. The clinical appearance of tinea capitis is highly variable and depends on the causative organism, type of hair invasion, and degree of the host inflammatory response. The commonly observed features are patchy hair loss with varying degrees of scaling and erythema. The clinical signs may be subtle and diagnosis may be challenging. We report the case of an adult patient with tinea capitis mimicking alopecia areata. The patient was initially diagnosed with alopecia areata and completed one month of treatment without clinical benefits. In view of no clinical signs of tinea capitis, a biopsy was performed. A scalp punch biopsy revealed an endothrix dermatophytosis. The patient's medication was switched to 250 mg terbinafine daily for 8 weeks and 2% ketoconazole shampoo. The patient completed two months of therapy with maintenance of hair regrowth and resolution of symptoms and scales.

Key words: Tinea capitis; Alopecia areata; Dermascopy

INTRODUCTION

Tinea capitis is a common scalp condition seen primarily in the pediatric population. It has been observed in postpubertal individuals, but is far less common, and can present bizarrely, often leading to misdiagnosis [1].

Its clinical manifestations range from mild scaling with little hair loss to large, inflammatory, and pustular plaques with extensive alopecia [2].

Delayed diagnosis and treatment can result in scarring alopecia [3].

We describe a case of endothrix tinea capitis mimicking alopecia areata.

CASE REPORT

A healthy and active 39-year-old woman presented to our dermatology clinic with a 1-year history of a painless patch of alopecia associated with pruritus on the occiput of the scalp with no erythematous background.

There was no significant drug history. She was otherwise healthy, denied constitutional symptoms, and was not immunosuppressed.

A physical examination revealed a severe alopecia involvement of the occiput and vertex (Fig. 1). There was no warmth or erythema and scant scale.

Dermatoscopy showed multiple broken hairs, comma hairs, and cadaver hairs (Fig. 2).

The patient was initially diagnosed with alopecia areata and completed one month of treatment with clobetasol cream, zinc capsule, and intramuscular triamcinolone without clinical benefits. Repeated doses with intralesional injection of triamcinolone gave no response. In view of no clinical signs of tinea capitis, a biopsy was performed.

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A 4 mm scalp punch biopsy revealed an acanthotic epidermis with a dilated follicle infundibulum, containing numerous fungal elements and occasionally invading into the hair shaft, diagnosed as an endothrix dermatophytosis (Figs. 3a and 3b). Perifollicular lymphocytic and neutrophilic infiltration was also observed.

The patient's medication was switched to 250 mg terbinafine daily for 8 weeks and 2% ketoconazole shampoo. She completed two months of therapy with maintenance of hair regrowth and resolution of symptoms and scales (Figs. 4 and 5).

DISCUSSION

Tinea capitis (TC) is a common scalp dermatosis in the prepubertal population, affecting ages 3–7 years. TC is rarely seen in postpubertal individuals, but has been described in this population and is reported to be more common in women [3].

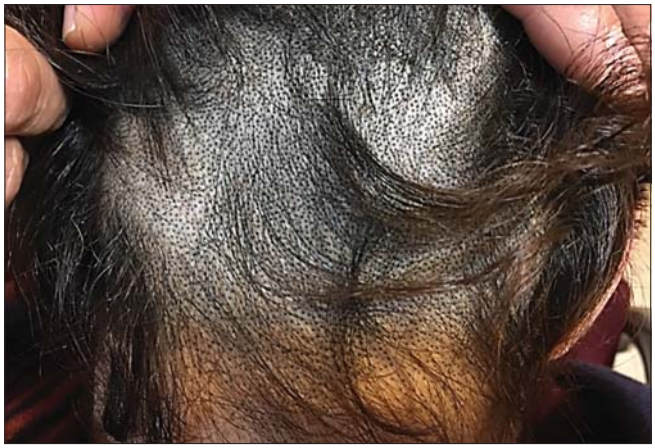

Figure 1: An alopecia involvement of the occiput and vertex.

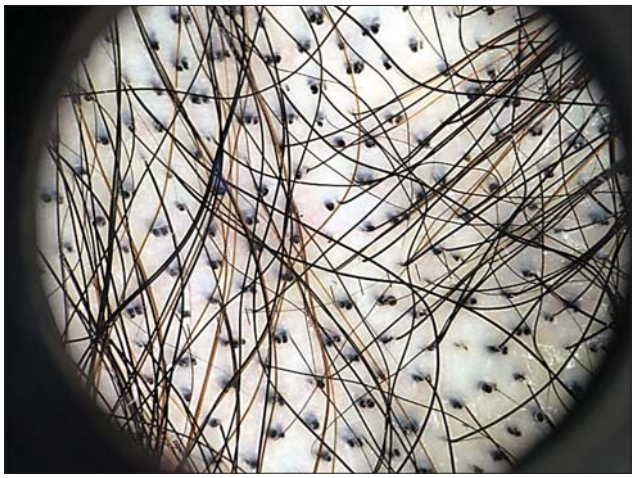

Figure 2: A dermoscopic image showing a comma sign and cadaver hairs.

TC is an unusual dermatophytosis in adults (3–11% of all cases) and is, therefore, often misdiagnosed. It mostly affects postmenopausal women and immunosuppressed individuals, and, in the majority of cases, is due to anthropophilic dermatophytes, especially *Trichophyton tonsurans* and *Trichophyton violaceum* [4].

The clinical appearance of tinea capitis is highly variable and depends on the causative organism, type of hair invasion, and degree of the host inflammatory response. The common features are patchy hair loss with varying degrees of scaling and erythema. The clinical signs may be subtle and diagnosis may be challenging [1].

The endothrix type of the infection may be caused by *T. tonsurans*, Trichophyton soudanense, African members of the Trichophyton rubrum complex, *T. violaceum, and rarely T. rubrum* (Table 1).

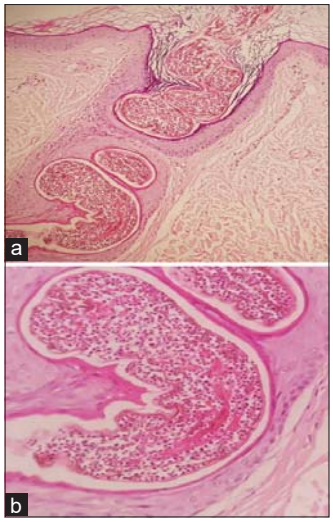

Figure 3: (a-b) Photomicrographs showing endothrix tinea capitis.

Figure 4: Hair regrowth one month after treatment.

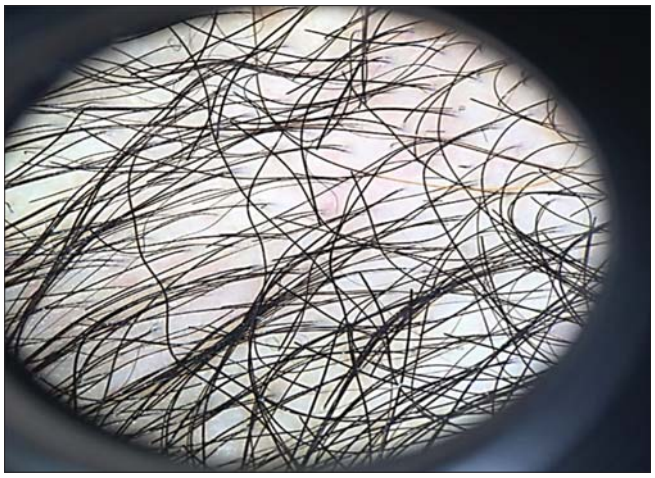

Figure 5: A dermoscopic image after treatment.

Table 1: Choice of drug depending on the organism isolated [1].

Organism	Choice of drug
Trichophyton tonsurans	Terbinafine
Trichophyton violaceum, soudanense	Terbinafine
Microsporum canis	Griseofulvin or itraconazole
Microsporum audouinii	Griseofulvin or itraconazole

This type of infection is nonfluorescent under Wood's light. Hairs often break at the scalp level, leaving swollen hair stubs within the follicles (black dot ringworm) [2].

The condition should be projected in any patient with a solitary or numerous diminutive plaques of hair loss associated with cut hairs, scales, and itching [5].

Broken hairs that resemble black dots may or may not be present, and can be scattered among normal hairs or concealed by scale. The inflammatory type of tinea capitis exhibits marked edema, redness, pustules, nodules, or sinus tracts with purulent discharge and crusting. Hair loss may be patchy or involve the entire scalp. Inflammatory lesions may be tender with marked cervical lymphadenopathy and can be associated with systemic symptoms. Diagnosis is confirmed by Wood's lamp, microscopic detection of fungal elements by a KOH test of the hair shaft, histopathological evidencing of hyphae in hair follicles with a PAS stain, or species identification by a fungal culture [6].

Alopecia areata incognita is a variety of alopecia areata characterized by acute diffuse shedding of telogen hairs without typical patches. Clinically, it has the features of telogen effluvium, but could also be misdiagnosed as alopecia androgenetica, which is the reason why a scalp biopsy is often required to confirm the clinical diagnosis [7].

The differential diagnosis of hair loss in children involves mostly TC. Slowinska et al. assert that comma hair is a distinguishing feature of TC, followed by broken and black dots (dystrophic hair). Comma hair, corkscrew hair, and pigtail hair were all observed only in patients with TC, thus embodying the characteristic features [8].

The differential diagnosis of tinea capitis is extensive and encompasses all conditions that may cause patchy hair loss, scaling, or scalp inflammation. Scalp psoriasis, seborrheic dermatitis, and atopic dermatitis may be difficult to differentiate from noninflammatory tinea capitis, although these conditions are usually more diffuse, and there may be characteristic signs elsewhere. Alopecia areata is generally non-scaly but may occasionally demonstrate erythema. Exclamation point hairs must be distinguished from the broken hairs of tinea capitis. Lupus erythematosus, lichen planopilaris, and trichotillomania, although relatively rare, should also be considered. Inflammatory tinea capitis variants may be misdiagnosed as bacterial folliculitis, folliculitis decalvans, or abscesses. Regional lymphadenopathy may be associated with the inflammatory variants of tinea capitis [1].

CONCLUSION

In conclusion, we describe a case of endothrix tinea capitis mimicking alopecia areata in dermoscopy, which showed cadaver hairs and a comma sign. Therefore, it should be kept in mind that tinea capitis can display the dermoscopic features of alopecia areata and can expand under incorrect treatment, as with corticosteroids.

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 have given 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

Desmoplastic Spitz nevus

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ABSTRACT

Desmoplastic Spitz nevus (DSN) is an uncommon variant of melanocytic nevus rarely encountered in dermatological practice. Herein, we describe a 54-year-old male who presented himself with a cutaneous tumor arising from the left arm. Histology revealed an intradermal proliferation of somewhat pleomorphic, epithelioid, spindled melanocytes in a background of desmoplastic stroma. A perineural invasion of tumor cells was found. Proliferative and mitotic rates were minimal. The tumor was diffusely positive for S-100 protein, PNL-2, and SOX-10, and only occasionally reactive for melan-A and HMB-45. The final diagnosis of DSN was established. Although DSN is a completely benign tumor, it may result in diagnostic pitfalls. Due to its unusual histopathological features, it may be confused with a malignant desmoplastic melanoma. A knowledge of the clinicopathological differences between the two prognostically distinct skin tumor entities is essential for a differential diagnosis.

Key words: Desmoplastic Spitz nevus; Desmoplastic malignant melanoma; Perineural invasion

INTRODUCTION

Desmoplastic Spitz nevus (DSN) is an uncommon variant of melanocytic nevus characterized by dermal proliferation of large epithelioid or fusiform melanocytes in a sclerotic stroma [1-5]. It occurs more frequently on the limbs of young adults, predominantly females, in the third decade of life [1-4]. Compared to the classical variants of melanocytic Spitz nevi [6], DSN exhibits some distinct microscopic features, such as the lack of dermoepidermal activity, the absence of Kamino bodies, the presence of ganglion-like epithelioid cells, and increased collagen bundles in the dermis [1-5]. From a practical point of view, DSN is particularly important as it may be confused with a desmoplastic melanoma [1-5]. Therefore, in routine biopsy practice, such cases may be diagnostically challenging. Herein, a case of a patient with DSN is described from a pathologist's perspective.

CASE REPORT

A 54-year-old male was found to have a cutaneous tumor lesion arising from the left arm. Grossly, it appeared as a light-brown, well-circumscribed, elevated nodule 6 mm in size. The presumptive clinical diagnosis was a benign skin tumor. Total surgical extirpation was done. Histology revealed an intradermal proliferation of somewhat pleomorphic, epithelioid, spindled melanocytes in a background of desmoplastic stroma. No junctional component was present. The lesion was symmetrical and had a wedge-shaped configuration, with the base beneath the epidermis and the apex in the deep dermis. The epithelioid melanocytic population was mainly located in the superficial portion of the tumor mass and exhibited abundant cytoplasm, large vesicular nuclei with conspicuous nucleoli, and occasional intranuclear pseudoinclusions (Fig. 1). The aggregations of melanocytes diminished with the depth of the lesion, where clusters of spindled cells were dispersed among thickened and hyalinized collagen bundles (Fig. 2). Interestingly, a perineural propagation was found in the reticular dermis (Fig. 3). Proliferative activity was minimal (Ki-67 index at ca. 2%) and mitoses were only sporadic (in "hot spots," two mitotic figures per 1 mm^2). Immunohistochemically, the tumor cell population was diffusely positive for S-100 protein (Fig. 4), PNL-2, and SOX-10, and only occasionally

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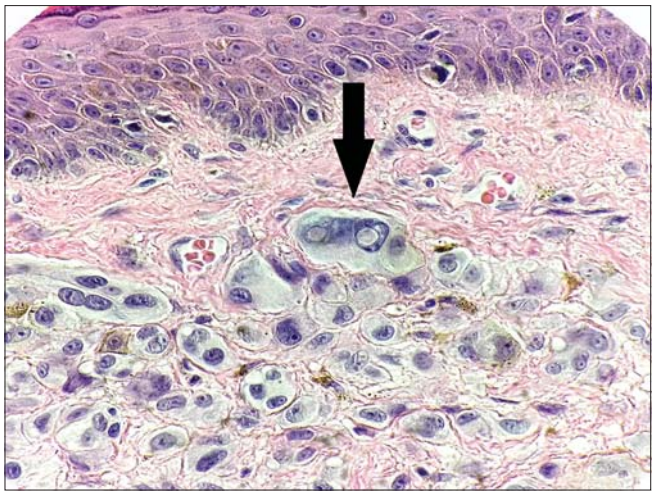

Figure 1: An epithelioid melanocytic population showing nuclear atypia with prominent nucleoli and occasional intranuclear pseudoinclusions (arrow). (H&E, 100×).

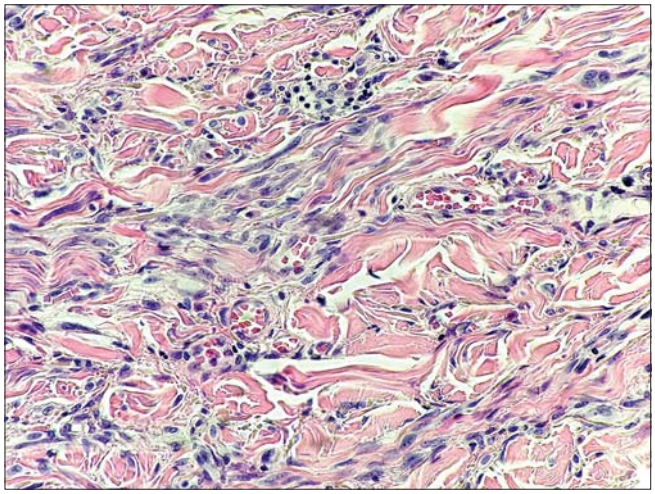

Figure 2: A spindled melanocytic population among thickened collagen bundles (H&E, 80×).

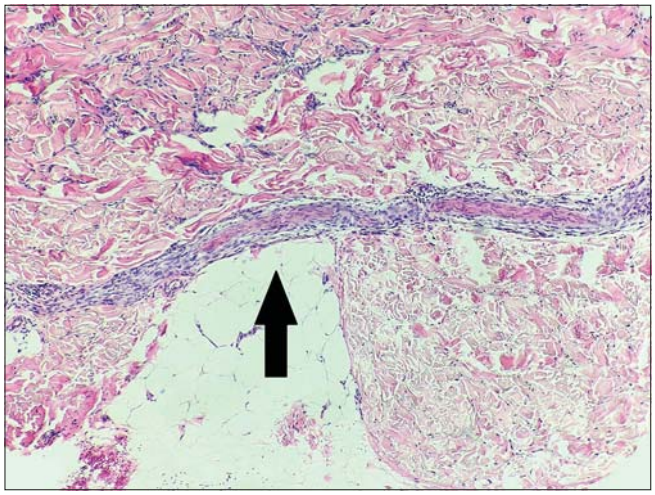

Figure 3: A perineural invasion of tumor cells (arrow) in the deep dermis (H&E, 40×).

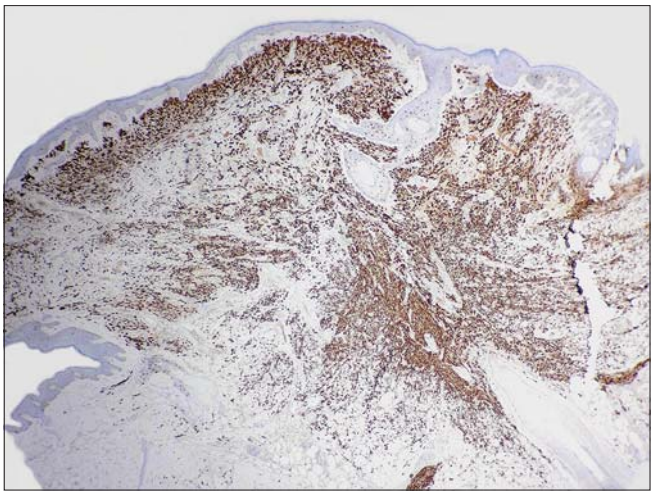

Figure 4: Diffuse immunoreactivity for S-100 protein in the tumor (10×).

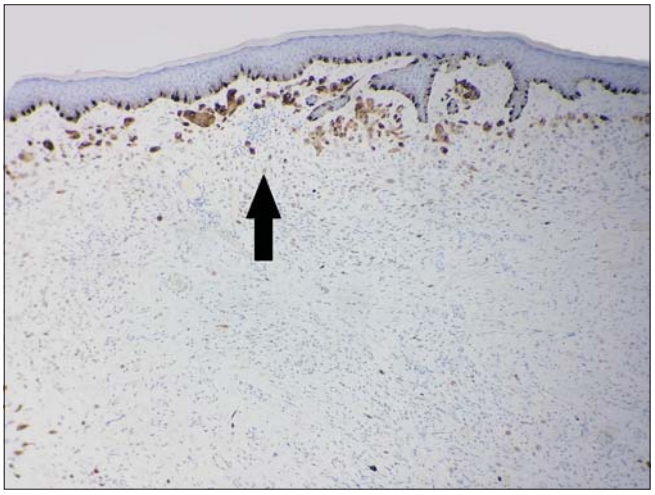

Figure 5: Focal immunoreactivity (arrow) for HMB-45 in the superficial part of the tumor (40×).

reactive for melan-A and HMB-45 (Fig. 5) in the superficial part of the lesion. Based on histomorphology and the immunophenotype, the final diagnosis of desmoplastic Spitz nevus was established. Resection margins were free of the tumor.

DISCUSSION

DSN may be a problematic diagnosis in biopsy practice. As already mentioned, it consists of somewhat pleomorphic, epithelioid, spindle-shaped melanocytes distributed among thickened, keloidal-appearing collagen fibers in the dermis [1-5]. Due to the atypia of the cells, stromal desmoplasia, and occasional neurotropism, it may be mistaken for a desmoplastic malignant melanoma (DMM) and atypical fibrous histiocytoma [1-5,7]. Because atypical fibrous histiocytoma is a benign mesenchymal tumor exhibiting a completely different

Table 1: Summary of the clinicopathological differences between desmoplastic Spitz nevus and desmoplastic melanoma [1-5,8]

	Desmoplastic Spitz nevus	Desmoplastic melanoma
Age	mean age of 28 yrs	mean age of 65–75 yrs
Sex	female predominance	male predominance
Location	usually extremities	usually head and neck
Circumscription	usually well-circumscribed	poorly circumscribed
Symmetry	present	absent
Configuration	wedge-shaped	diffusely infiltrative
Junctional component	may be present	may be present
Fascicles of melanocytes	short and discrete	at least some long
Cytologic atypia	present	present
"Spitzoid" cytomorphology	present	absent
Intranuclear pseudoinclusions	common	uncommon
Melanocytic maturation	present	absent
Ki-67 index	low	usually higher
Mitotic activity	absent or sporadic	may be low
Solar elastosis	usually absent	common
Lymphocytic aggregations	uncommon	common
Perineural spreading	may be present	common
Adnexa involvement	common	uncommon
HMB-45 and melan-A	at least focally positive	often completely negative

immunoprofile [7], a strict distinction between DSN and DMM is much more important, as the former represents a benign melanocytic lesion, while the latter is an aggressive malignancy with a poor prognosis. Accurate diagnosis of DSN requires an experienced pathologist who will take into account a combination of clinical, microarchitectural, cytological, and immunohistochemical findings. The main clinicopathological differences between DSN and DMM are summarized in Table 1 [1-5,8]. In our patient, the findings were typical of DSN. Of note was an interesting feature: an apparent perineural spreading of the tumor cells in the deep dermis. This, at first glance worrisome, histopathological finding is generally uncommon in benign tumors. Nevertheless, in accordance with our observation, some authors [9] have even described it in benign melanocytic nevi. For this reason, it may not necessarily be considered an attribute of malignancy in atypical melanocytic lesions. In any case, this is an adverse prognostic parameter that indicates a higher risk of local recurrence.

CONCLUSION

Desmoplastic Spitz nevus is rarely encountered in dermatological practice. Although a completely benign tumor, it may result in diagnostic pitfalls. Due to its unusual histopathological features, it may be confused with a desmoplastic malignant melanoma. A knowledge of the clinicopathological differences between the two prognostically distinct skin tumor entities is essential for a differential diagnosis.

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

Telangiectatic cutaneous metastasis from breast carcinoma

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ABSTRACT

Cutaneous metastasis from breast cancer has varied clinical presentations. Herein, we present the case of a middle-aged female with a large erythematous patch and an itchy bluish-red papular eruption on the left side of the breast. The patient had a history of ductal breast carcinoma at age 40. Histology from one of the red papules revealed an atrophic epidermis and emboli of carcinomatous cells in the dermal and subcutaneous blood vessels. The morphology of the tumor cells was similar to that of the primary ductal carcinoma of the breast. The diagnosis of telangiectatic metastatic breast cancer was reached.

Key words: Breast carcinoma; Intravascular tumor emboli; Telangiectatic carcinoma; Metastatic carcinoma; Ductal carcinoma

INTRODUCTION

Breast cancer is the most common cause of cutaneous metastasis in women. The clinical presentations of cutaneous metastasis vary, but infiltrative nodules are the most common feature. Telangiectatic cutaneous metastasis is rare. Herein, we report a new case of angiokeratoma-like lesions.

CASE REPORT

A 42-year-old female presented herself to our department with a three-month history of a large erythematous patch and an itchy bluish-red papular eruption on the left side of the breast. Two years before, the patient was successfully treated by mastectomy and axillary lymph node clearance followed by adjuvant chemotherapy and local radiotherapy for infiltrating stage IIIB ductal breast carcinoma. A physical examination revealed an erythematous skin patch associated with multiple bluish-red and violaceous dark papules on the left chest (Figs. 1a and 1b). The patient had no hepatosplenomegaly or ipsilateral lymphedema. Considering the medical history, cutaneous breast carcinoma metastasis was suspected. A skin biopsy obtained from one of the red papules revealed an atrophic epidermis and emboli of carcinomatous cells in the dermal and subcutaneous blood vessels (Fig. 2a). The morphology of the tumor cells was similar to that of the primary ductal carcinoma of the breast and was of the same histological grade

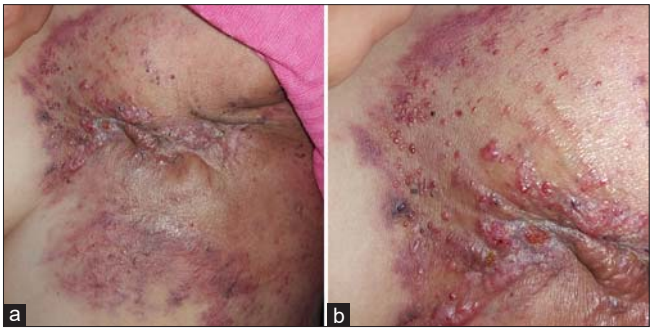

Figure 1: (a) A large erythematous skin patch associated with multiple bluish-red and violaceous dark papules on the left chest. (b) A high-power view of the angiokeratoma-like lesions.

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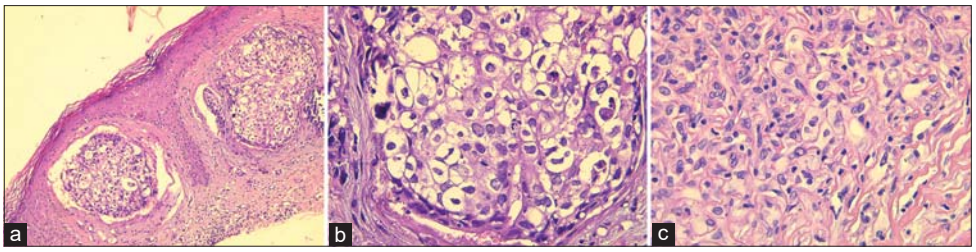

Figure 2: (a) The skin biopsy showing invasive carcinomatous proliferation in the dermis with vascular emboli. (b) Tumor cells showing nuclear atypia with numerous mitoses. (c) A high-power view of foamy histiocytes with abundant, clear cytoplasm. (H&E; original magnification: (a) 100×, (b-c) 400×).

(Figs. 2a and 2b). The receptor status was unchanged. A further work-up revealed bone metastasis. We referred the patient to a specialized oncology center, where she received sequential treatment with chemotherapy. Unfortunately, the patient passed away while on the chemotherapy, five months after the initial diagnosis of cutaneous metastasis.

DISCUSSION

Breast carcinoma is the most common tumor that causes cutaneous metastasis after melanoma. In the largest case series published, cutaneous involvement was observed in 23.9% of patients with breast cancer [1]. The clinical presentations of cutaneous metastasis from breast cancer vary. The lesions are located mostly on the chest and abdominal wall, close to the mastectomy scar. Solitary and multiple papules and nodules are more common. Less frequently, other patterns have been described in the literature [2]. These include telangiectatic carcinoma, erysipeloid carcinoma, carcinoma *en cuirasse*, neoplastic alopecia, and zosteriform patterns. Telangiectatic carcinoma (TC) manifests itself with prominent telangiectasia and/or pseudovesicles that resemble lymphangioma circumscriptum. It is habitually located on the chest and may appear on the face. In a series of 164 cases with breast cancer, 131 displayed papular and/or nodular lesions, and only 19 had TC [2]. It has also been associated with breast carcinoma, ductal carcinoma of the parotid gland, apocrine carcinoma of the vulva, and carcinoma of the prostate [3,4].

TC occurs due to malignant spread via dermal lymphatics [5]. Cutaneous biopsies reveal infiltration of tumor aggregates predominantly in the dermal lymphatic and blood vessels by neoplastic cells, causing their obstruction [6,7]. Immunohistochemical techniques, such as cytokeratin-7 and cytokeratin-20, contribute to the elucidation of the diagnosis. BRST-2 antigen as well as estrogen and progesterone receptors may also be useful for the diagnosis [8].

Although the prognosis of cutaneous metastasis depends on the type and character of the primary tumor as well as the response to treatment, it is generally considered severe as it accompanies advanced-stage tumors [7]. Cutaneous metastasis from breast cancer is usually evaluated as a severe prognostic factor in which life expectancy is several months, with only a few patients surviving for a year. It is also poorly amenable to treatment [9].

CONCLUSION

Breast cancer is one of the most common types of cancer that presents skin metastases. Telangiectatic carcinoma with angiokeratoma-like lesions is a rarity in clinical practice and may be easily overlooked. It is important to recognize this rare variant of cutaneous metastasis to avoid delay in accurate diagnosis. Despite having received the recommended treatment, the poor prognosis of our patient was corroborated by the quick progression to death.

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 have given 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

An extraordinary case of oral leukocytoclastic vasculitis demonstrating IgD deposition around dermal vessels and within mucosal keratinocytes

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ABSTRACT

Cutaneous vasculitides include a widespread and heterogeneous cluster of diseases affecting the blood vessels that are clinically characterized by polymorphic skin lesions, including palpable purpura, urticarial and/or necrotic-ulcerative lesions. Often, they can be manifestations of a systemic disease. Selected cases occur in the mouth. A 75-year-old female presented to her physician for the sudden appearance of blisters in her mouth, with severe orodynia and no history of other diseases or medication intake. A skin biopsy of the oral mucosa yielded a diagnosis of leukocytoclastic vasculitis. The direct immunofluorescence and immunohistochemistry stains demonstrated deposits of IgD, IgG, IgA, IgM, kappa, lambda, C1q, C3c, albumin and fibrinogen at the upper dermal neurovascular plexus. IgD also demonstrated positive nucleolar staining of the keratinocytes. Our case involves a rare presentation of oral cutaneous vasculitis with immune deposits of several immunoglobulins, complement, albumin and fibrinogen. Our case adds importance to studies of the IgD role in antigenic complex immune responses, especially in the mouth.

Key words: Leukocytoclastic vasculitis; IgD; Nucleolar autoantibodies

Abbreviations: Leukocytoclastic vasculitis (LV); Hematoxylin and eosin (H&E); Periodic acid–Schiff (PAS); Immunohistochemistry (IHC); Direct immunofluorescence (DIF); Fluorescein isothiocyanate (FITC); 4',6-diamidino-2-phenylindole (DAPI); *Ulex europaeus* agglutinin (ULEX).

INTRODUCTION

Cutaneous vasculitides include an extensive and diverse cluster of diseases affecting the tegumentary blood vessels; these are clinically manifested as polymorphic skin lesions, including palpable purpura, as well as urticarial and necrotic-ulcerative lesions. Sometimes extracutaneous involvement occurs [1]. Leukocytoclastic vasculitis (LV) was formerly known as hypersensitivity vasculitis. LV can have an acute form and a chronic presentation [2]. Cutaneous leukocytoclastic angiitis and urticarial vasculitis, which are the two most common variations of this disease cluster, are frequently idiopathic but may also be triggered by diverse agents, including drugs and infections, or may be as part of systemic disorders, predominantly systemic lupus erythematosus (SLE) [1]. Vasculitic skin lesions can also occur during the chronic-relapsing course of systemic vasculitides, including Wegener's granulomatosis (WG). These vasculitides often share clinical and immunohistopathologic features [1,2]. The vasculitides are associated with blood vessel inflammation that can cause internal organ damage [1-3].

The American College of Rheumatology (ACR) recommends standards for cataloging the primary vasculitides, established via a compilation of clinical

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and immunological characteristics of multiple patients. The following are types of characterized vasculitis: Takayasu arteritis, polyarteritis nodosa (PAN), WG, giant cell arteritis, and Henoch–Schönlein purpura (currently known as IgA vasculitis) [3-11].

STATEMENT OF ETHICS

Our patient gave informed consent. Although Institutional Review Board (IRB) approval for a case report is not needed, the US Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule restricts how protected health information (individually identifiable health information) on any patient may be utilized. Compliance with patient privacy, institutional rules, and federal regulations were followed. No photos or illustrations that contain identifiable features are included in the case report, and the case(s) described in the report are not so unique or unusual that it might be possible for others to identify the patients.

CASE REPORT

A 75-year-old woman presented to her doctor for the presence of small blisters, erythematous areas, and purpuric patches in the oral mucosa with severe orodynia. Lesional oral skin biopsies for hematoxylin and eosin (H&E), for direct immunofluorescence (DIF) and for periodic acid–Schiff (PAS) stains were taken. The staining techniques were performed as previously described [11,12]. Additional systemic testing for an underlying disease was performed, including a complete blood count, and liver panel assays and kidney function testing; urinalysis was also performed. Other tests included an anti-streptococcal antibody titer, and HIV testing. Further testing for rheumatologic diseases included testing for systemic lupus erythematosus (SLE), Sjogren's syndrome, antinuclear antibodies (mostly via IgG), anti-ceruloplasmin antibodies and anti-rheumatoid factor. Additional testing included serum protein electrophoresis, serum complement levels, and testing for the presence of cryoglobulins. The test results were all non-contributory, and essentially ruled out any systemic involvement. For DIF, we classified our findings as previously documented [12-14]. IHC staining was performed utilizing a Leica Bond MAX IHC automatized platform (Buffalo Grove, Illinois, USA) and a Novolink™ detection with Compact Polymer™ technology. For red staining, the Bond Max platform autostainer utilized red detection DS9390, an alkaline phosphatase linker and a fast-red chromogen. For brown staining, we used DS9800 as reported before [8-11]. We also ran negative and positive controls. We used anti-human monoclonal antibody to HLA-ABC antigen, clone W6/32, polyclonal rabbit anti-human IgD (code IR517), and C5b-9 (code M077), all from Dako (Carpinteria, California, USA).

The mouth lesions are shown in Fig. 1a. The microscopic examination of the H&E stains revealed an inflammatory process involving capillaries and small blood vessels of the dermis. Fibrinoid deposits were identified within the blood vessels walls. Leukocytoclasis, swelling of endothelial cells, occlusion of blood vessels, accumulation of fibrin and fibrinoid degeneration were all observed (Fig. 1b). Some red blood cells were seen outside the vessel walls, situated in the dermal interstitial tissue. The diagnosis of leukocytoclastic vasculitis (LV) was rendered based upon the histologic changes. The PAS stain demonstrated positivity (+++) in the same pattern of deposits as the polyclonal auto-antibody response. The DIF displayed positive staining around the upper dermal vessels with IgG (+++), IgA (++), IgM (++), IgD (+++), IgE (+), kappa (++), lambda (++), C1q (++), C3c (++), albumin (++) and fibrinogen (++++) (Fig. 1c). Of interest, nucleolar staining in epidermal keratinocytes was seen with the anti-IgD antibody (Fig. 1d). In addition, the mucosal stratum

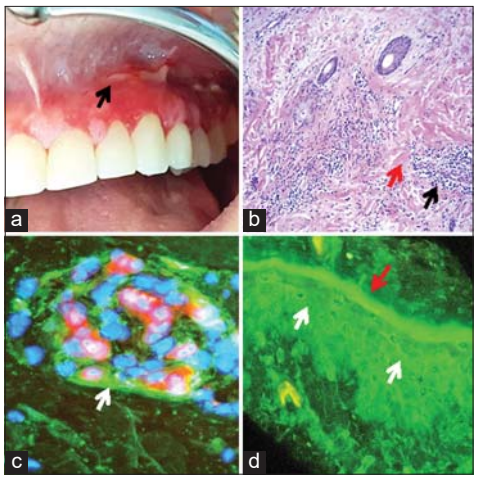

Figure 1: (a) Small blisters, erythematous areas and purpuric patches on the oral mucosa (black arrow) (b) H&E staining demonstrating affected dermal vessels, surrounded by a strong lymphohistiocytic inflammatory infiltrate (black arrow) and fibrinoid deposits (red arrow) (100X). (c) DIF positive staining on dermal blood vessels with FITC conjugated fibrinogen (++++) (green staining, white arrow) (400X). The vessels were also positive for ULEX (red staining). The nuclei of the cells were counterstained with DAPI (blue staining). (d) DIF using FITC conjugated anti-human IgD, positive in the mucosal corneal layer(yellow staining; red arrow) as well as nucleolar staining on the keratinocytes (punctate yellow staining; white arrows) (400X).

corneum demonstrated thick linear staining with the same antibody (++). The purely nucleolar staining may be seen in selected patients with systemic sclerosis. Our patient was evaluated for systemic sclerosis and this disease was excluded by negative studies, specifically with the anti-RNA polymerase I, anti-U3 ribonucleoprotein antibody, anti-topoisomerase 1, anti-centromere, and anti-RNA polymerase III, PM-Scl (anti-topo 1, Ribosomal P), and polymyositis/dermatomyositis (PM/DM) (PM-Scl, anti-RNAP III).

DISCUSSION

Vasculitis may be categorized based on the size of the affected vessels, specifically small, medium, or large vessel [1]. Alternatively, classification may reflect the etiology: idiopathic or linked with an underlying pathology/disease. Confirming the diagnosis of a vasculitis ideally requires characteristic mucosal/cutaneous lesions, an appropriate clinical history, the histologic and immune pathologic patterns, [12] pertinent laboratory data and possible extracutaneous manifestations due to the complexity of these disorders [1]. Leukocytoclastic vasculitis was previously also called anaphylactoid purpura [15] and has been considered an immune complex disorder (Gell Coombs Type III) [2]. The histologic findings are of paramount importance in reaching the diagnosis of vasculitis, and it is imperative to consider the timing of the biopsies for H&E, PAS [12] and DIF and IHC staining. DIF is highly recommended in cases of suspected leukocytoclastic vasculitis. Routinely, most laboratories test DIF antibodies against IgM, IgG, complement C3, albumin and fibrinogen in cases of suspected vasculitis. Because of our extended experience with DIF testing, we tested for all the immunoglobulins (including IgD and IgE), complement factors C1q, C3c and C4, plus albumin and fibrinogen. We had noticed that most vasculitis and autoimmune blistering diseases, as well as rheumatologic diseases affecting the skin and oral mucosa demonstrate some reactivity via IgD (publication in preparation). In the current case, we utilized our routine panel of autoantibodies and markers. Thus, we tested for the presence of IgD and noted positive findings. It is known that mature B cells express immunoglobulin M (IgM) and IgD-isotype B cell antigen receptors (BCRs). It has further been shown that polyvalent antigens activate both IgM and IgD receptors, indicating a more complex immunologic response [16]. For many years, the role of IgD has been poorly understood. In our case, we note that many autoantibodies were positive including IgM and IgD; their role *vis-a-vis* BCRs not only establishes a novel concept for immune regulation, but also might open new opportunities for improving vaccination approaches. These approaches could be aimed at protection from autoimmune disorders or pathogens in light of the B cell antigen receptors. In this rare case of oral leukocytoclastic vasculitis, the presence of IgD antibodies deposits is quite intriguing. Some authors have speculated that in renal vasculitis an IgD response may be formed to a variety of illnesses, including autoimmune disorders. Again, in our experience the role of autoantibodies against IgD are important in the context of current reports in the medical literature [17,18]. Moreover, these authors state that glomerular deposits of IgD suggest that immunoglobulins of this class may be present in association with some immunologically induced systemic processes [17].

We conclude that in our case of oral leukocytoclastic vasculitis with polyclonal autoantibody deposition, the response of IgD antibodies is uncommon. Indeed, oral manifestations of a leukocytoclastic vasculitis are infrequent, although a few cases have been described [2]. Thus, we document a combination of rare leukocytoclastic vasculitis oral mucosal involvement with a rare LV autoantibody deposition.

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Our Dermatology Online

Case Report

Post-surgical pyoderma gangrenosum following electrosurgery and elliptical excision: A rare disease following common procedures

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis with an estimated annual incidence of 3–10 cases per million per year. Post-surgical pyoderma gangrenosum (PSPG) refers to the development of pyoderma gangrenosum at surgical sites in the postoperative period. A 55-year-old female was admitted with two acute and enlarging painful breast ulcerations resistant to antibiotic treatment following surgical resection and electrofulguration by her dermatologist. Multiple wound cultures were negative. A skin biopsy was consistent with PG and the wounds improved after adequate oral immunosuppressive therapy. A high index of suspicion, exclusion of other differential diagnoses, and previous experience with this disease ensured an early diagnosis, prevented injury to life and unnecessary debridement, and resulted in an excellent outcome for the patient.

Key words: Pyoderma gangrenosum; Breast; Elliptical excision; Electrosurgery

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis characterized by a well-defined painful ulcer with a red-violaceus border. The annual incidence is estimated at 3–10 cases per million per year [1]. The peak incidence occurs between the ages of 20–50 years, with a possible slight female preponderance and with approximately 4% of patients being children [2]. There are immunological alterations involved and various well-recognized associations, such as rheumatological diseases, inflammatory bowel disease, and hematological neoplasms, present in 50–70% of cases [3]. Post-surgical pyoderma gangrenosum (PSPG) refers to the development of pyoderma gangrenosum at surgical sites in the postoperative period. Compared to PG, PSPG occurs in uncommon locations and is less likely to be associated with systemic disease. Herein, we present a case of PSPG triggered by common dermatologic procedures.

CASE REPORT

A 55-year-old female presented herself to our clinic with two acute and enlarging painful breast ulcerations. The past medical history was unremarkable. No evidence of rheumatologic disease or malignancy was found. A physical examination revealed two undermined ulcers, 3 cm × 1.5 cm and 3 cm × 2 cm in size, respectively, with well-defined purplish erythematous edges and seropurulent discharge, and were located on the right breast in the inframammary area (Fig. 1) and on the lower outer quadrant of the left breast (Fig. 2). Three weeks ago, she had a surgical resection of an atypical melanocytic nevus in the left mammary region and electrofulguration of a seborrheic keratosis in the

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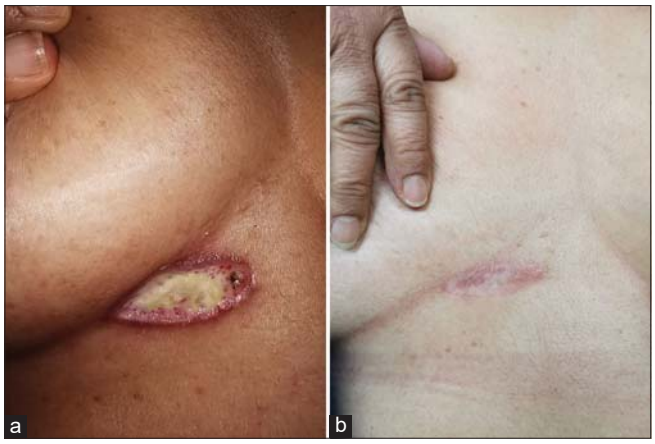

Figure 1: (a) The initial lesion located in the right inframammary area consisting of a purulent ulcer with well-demarcated violaceous edges. (b) The lesion after four months of treatment (ulcer resolution with a cribriform scar).

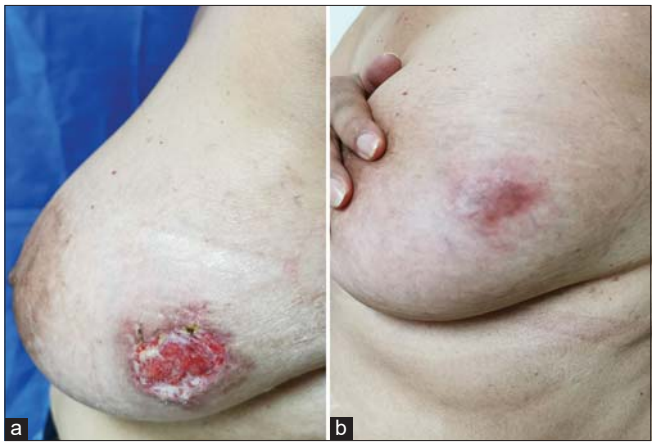

Figure 2: (a) The initial lesion located in the left mammary area consisting of a purulent ulcer with central exudate and violaceous edges on an erythematous background. (b) The lesion after four months of treatment (ulcer resolution with residual scar).

right inframammary area. Postoperative infection was suspected, and the patient was started on topical and systemic antibiotics with no improvement and progressive worsening of the ulcers. Cultures from the ulceration discharge grew no bacteria, acid-fast bacilli, or fungi. A punch biopsy revealed ulceration and a superficial neutrophilic inflammatory infiltrate in the dermis, compatible with the diagnosis of early PG (Fig. 3). Treatment was started with prednisone 60 mg/day and azathioprine 100 mg/day with an excellent response at 2 months and a subsequent tapering regimen with no relapse at 18 months.

DISCUSSION

PG was first described by French dermatologist Brocq in 1916, although it was not until 1930 that it was given its present name by Burnsting at the Mayo Clinic under the assumption that it was an infectious disease [4]. The pathogenesis of the disease is unknown, but the proposed causes include immune-complex mediated neutrophilic vascular reactions.

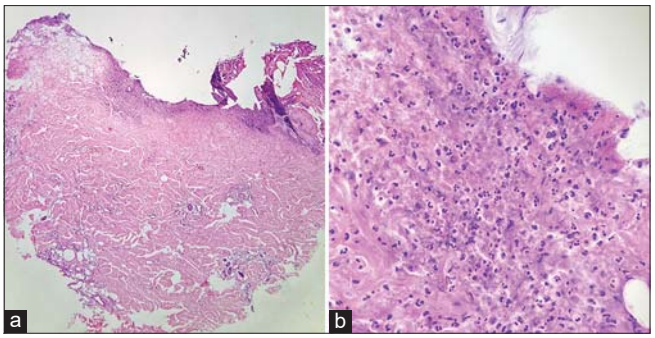

Figure 3: (a) Necrosis with ulceration of the epidermis (H&E, 40×). (b) High-power examination revealing dense neutrophilic infiltrate in the dermis; no bacterial components or tumor cells were observed (H&E, 200×).

Currently, three factors are considered to be involved—neutrophilic dysfunction, genetic susceptibility, and systemic inflammation—all of which favor an important immunological alteration in the host. This systemic inflammation has been demonstrated with a high presence of IL-8, IL-23, and TNF-alpha. Unquestionably, the most significant triggering factor is pathergy (Koebner phenomenon), reported in 20–30% of patients affected by PG. Any kind of skin trauma due to surgery, injections, prick tests, or insect bites may induce the appearance of a new lesion or worsen preexisting ones [4].

Around 50% of patients with PG have an associated underlying disease. This was confirmed by a cohort study on 356 patients, 45% of which had preexisting conditions; 41% with inflammatory bowel disease, 21% with inflammatory arthritis, 11% with hematological alterations ranging from different types of leukemias, monoclonal gammopathies, and myelodysplastic syndrome, and finally 7% with solid organ neoplasms [5].

PSPG is also known as postoperative PG or pathergic PG. Clinical presentation usually begins as multiple small areas of dehiscence or ulceration several days to weeks after the procedure. They exhibit erythema and severe pain, followed by wound dehiscence and the formation of an aggressive ulcer. The trauma caused by surgery, and consequent cytokine release, is likely the initiating factor of pathergy in PG [6]. Compared to classic PG, PSPG is associated with systemic disease in only 22–35% of cases, with the most common

comorbidity being myeloproliferative disorders [7]. This leaves most patients with no predisposing comorbidity other than surgery.

Although cases of PSPG reported in the literature remain rare, several locations have been reported, following surgical incisions almost anywhere on the body. In a study of 220 patients identified with PSPG, the most common procedures were breast (25%), cardiothoracic (14%), abdominal (14%), and obstetric (13%) surgeries. The most common breast procedures in which post-surgical pyoderma gangrenosum was reported were bilateral reduction mammoplasty (45%), breast reconstruction (25%), and other procedures (12.5%), such as excision or biopsy, as in our case [6].

In a clinical scenario of PSPG, the major and minor diagnostic criteria for PG [8] are scarcely useful. The rapid progression of lesions and severe pain are inconstant in PSPG. Only some patients experience severe pain and breast tenderness after breast surgery in the early phase of PSPG. Moreover, there may be no previous history of PG, both as in our case and as in those reported in the literature [9,10].

Due to its similar presentation to wound infection, PSPG is a complex diagnosis that may be challenging to identify in a context of recent surgery. Therefore, as our case illustrates, PG should be considered in the setting of non-healing postoperative wounds refractory to antibiotics. Misdiagnosis of PSPG may lead to ineffective treatment with antibacterial agents and debridement, which may accelerate the progression of the disease. Thus, it is imperative to make a prompt diagnosis to reduce its destructive course.

In the initial phase, histological examination may show perivascular lymphocytic infiltrate and intradermal abscess formation. As the disease progresses, significant edema, intense neutrophilic infiltrate, necrosis, and granuloma formation are found in the dermis, as well as vasculitis with or without leukocytoclasia. However, none of these findings are pathognomonic [11]. Differential diagnoses are diverse since many diseases produce ulcers, mainly of infectious, neoplastic, and vascular etiologies.

A review of the literature demonstrated no consensus for the treatment of PSPG. The most commonly employed protocol involves high-dose systemic corticosteroids, such as oral prednisone, prednisolone, and intravenous methylprednisolone. Since the complete resolution of an ulcer takes months, in order to maintain the response once the glucocorticoid is stopped, it is recommended to associate a steroid-sparing agent with the treatment; these include mycophenolate mofetil 2–3 g/day, azathioprine 100–300 mg/day, or methotrexate 10–25 mg/week [12]. In our case, we observed an excellent response with a combination of prednisone and azathioprine.

Systemic cyclosporine is an alternative first-line treatment for patients who cannot tolerate systemic glucocorticoid therapy [13]. The second-line treatment is biological therapy with infliximab, etanercept, and adalimumab, the latter with a better clinical response, mainly in patients with rheumatoid arthritis [12]. Other therapies described are dapsone 50–200 mg/day or minocycline 200 mg/day in a context of limited disease without corticosteroids or adjuvant to them. With refractory disease, starting treatment with intravenous immunoglobulin or cyclophosphamide should be considered [14].

The course of the disease is chronic, with frequent relapses and exacerbations, for which close follow-up must be observed and paraclinical monitoring and systemic therapy should be adjusted if necessary.

CONCLUSION

PSPG must be considered in any patient undergoing surgery who afterward manifests characteristic necrotic lesions with delayed wound healing, fever, and severe localized pain.

Considering pyoderma gangrenosum as an underdiagnosed disease, clinical suspicion aids a timely diagnosis and completes the diagnostic approach that may unmask this pathology. In our case, timely diagnosis avoided detrimental procedures for the patient, such as surgical debridement, and prevented further disease progression.

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

Giant idiopathic pyoderma gangrenosum at an unusual site with highly elevated c-ANCA levels: A rare association

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare neutrophilic disorder with an incidence rate of 3–10 cases per million per year, characterized by classically painful and aseptic ulcers, which may be associated with underlying systemic diseases. The pathergy reaction is seen in one-fourth of patients with PG. Accurate and timely diagnosis is crucial, as PG is known for its rapid progression. The management of PG is challenging and depends on its severity and rate of progression. An underlying systemic involvement should be sought even in spite of no symptoms. Herein, we report a case of giant pyoderma gangrenosum involving almost the entire left buttock with exceptionally raised c-ANCA levels, but no underlying systemic abnormality. The patient reported intense pain, rapid progression of the ulcers, an inability to perform daily activities, was significantly morbid and pathergy-positive. Aggressive and early management is required in cases such as this. A dramatic response was achieved with a combination of cyclosporine, dapsone, and methylprednisolone pulses.

Key words: Pyoderma gangrenosum; Neutrophilic dermatoses; ANCA; Pathergy

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis characterized by noninfectious ulcers, usually involving the lower extremities, with an estimated incidence rate of 3–10 cases per million per year [1]. PG is associated with underlying systemic diseases in around 50% of cases [2]. Modified immunological response and altered neutrophilic chemotaxis have been proposed as the underlying mechanism of pathogenesis. Pathergy is seen in one-fourth of cases of PG [3]. Herein, we report a case of giant pyoderma gangrenosum on an atypical site—the left buttock—with highly elevated c-ANCA levels, treated with multidrug therapy.

CASE REPORT

A 28-year-old female presented herself to our dermatology outpatient department with a history of recurrent progressive ulcerations involving the lower extremities and left buttock. The ulcerations had shown two years prior as a single nodular abscess over the right ankle, which had been incised and drained by a surgeon. Pathergy developed at the incision site to form a painful nonhealing ulcer. As the ulcer expanded, the patient noted simultaneous development of new ulcers bilaterally on the shins, ankles, and the dorsum of both feet within several days. While some of the ulcers healed with scarring, others progressively enlarged despite continuous treatment with oral steroids, doxycycline, and azathioprine elsewhere. Intermittent remissions and relapses of the lesions occurred during these two years.

Later, the patient developed three small ulcers on the left buttock while on treatment with azathioprine, oral steroids, and minocycline for two consecutive months. The edge of one ulcer was biopsied, after which the ulcers

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enlarged and coalesced to form a large necrotic ulcer within a period of three days, thus, again, demonstrating the presence of a pathergy reaction. No further medical or surgical history of significance was recorded.

An examination revealed a giant oval ulcer 23 × 17 cm in size covered with a necrotic brown crust on the left buttock (Figs. 1a and 1b). Manipulation produced purulent exudate and oozing of the blood. Another deep-seated ulcer, 2 × 3 cm in size and adjacent to the initial, was present medially. Its base was not fixed to the underlying structures. Multiple discrete erythematous-to-violaceous warm and tender nodules—several with central suppuration—were present over both lower limbs, predominantly over the thighs, indicating primary lesions. A single left inguinal lymph node 2 × 2 cm in size was present. Multiple healed atrophic cribriform scars were evident on both the shins and the dorsum of the feet (Figs. 2a and 2b). A systemic examination was unremarkable.

Routine and specific investigations revealed hemoglobin at 6.6 g/dL, a total leukocyte count of 13,000 with neutrophilia (90%), ESR at 102, C-reactive protein at 49.4, and rheumatoid factor at 298.7. c-ANCA (antineutrophil cytoplasmic antibody) levels were as high as 76.0 units/mL. ANA (antinuclear antibody), anti-CCP (anti-cyclic citrullinated peptide), p-ASCA (anti-saccharomyces cerevisiae antibody), and p-ANCA (perinuclear-staining ANCA) were normal. Fecal occult blood was absent. Colonoscopy was inconclusive of inflammatory bowel disease (IBD), showing several tiny ileal ulcerations with the rest of the intestinal mucosa completely normal. A pus culture revealed growth of *Escherichia coli*. Tubercular and fungal cultures revealed no growth. A deep skin biopsy from the edge of the ulcer revealed partially treated vasculitis, endothelial swelling, intravascular thrombi, and large neutrophilic aggregates in the subcutaneous tissue, consistent with the diagnosis of PG (Figs. 3a and 3b). No grains or AFB were seen.

The patient was given a blood transfusion and IV antibiotics. Once the secondary infection was controlled, methylprednisolone pulses for five days, oral cyclosporine 200 mg/day, and dapsone 100 mg/day were initiated. Anticipating the risk of pathergy, surgical debridement was discouraged. Desloughing with hydrogen peroxide and daily sterile dressings were performed. Within two weeks of initiating treatment, the purulent exudate reduced markedly and the ulcer began re-epithelizing with healthy granulation tissue at the floor (Fig. 4). Complete healing was observed

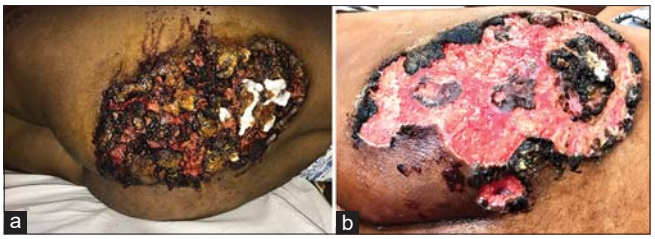

Figure 1: (a) The initial presentation as a giant necrotic crusted lesion covering almost the entire left buttock (day 1). (b) The ulcer covered with frank purulent exudate after desloughing (day 3).

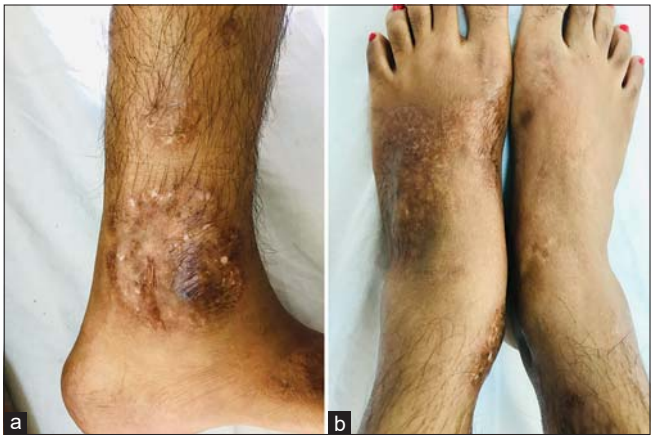

Figure 2: (a) Atrophic cribriform-like scarring on the lateral aspect of the right foot and the right lower leg. (b) The dorsum of the left foot and the medial aspect of the left ankle.

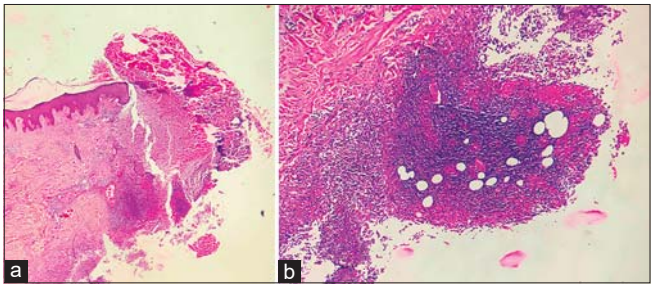

Figure 3: (a) A photomicrograph of the edge of the ulcer (gross view) (H&E, scanner view). (b) Intravascular thrombi and large neutrophilic aggregates in the subcutaneous tissue (H&E, 10×).

in two months, although the atrophic hyperpigmented scar was still present (Fig. 5). The patient was, however, fully satisfied. Drugs were gradually tapered and stopped after six months. Currently, the patient is off cyclosporine and dapsone, and has had no recurrence after nine months of continuous follow-ups. The levels of ESR, CRP, and c-ANCA (4.0 units/mL) have returned to normal.

DISCUSSION

Pyoderma gangrenosum ulcers are classically painful and aseptic, although superinfection may eventually

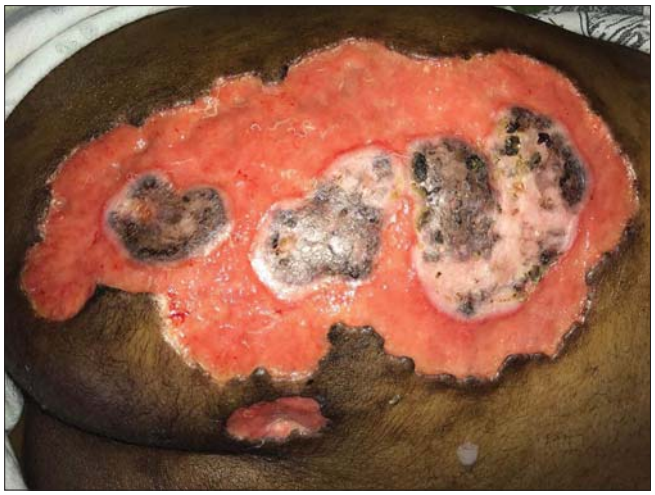

Figure 4: A response two weeks after therapy, with epithelization evident in the center and healthy granulation tissue at the floor of the ulcer.

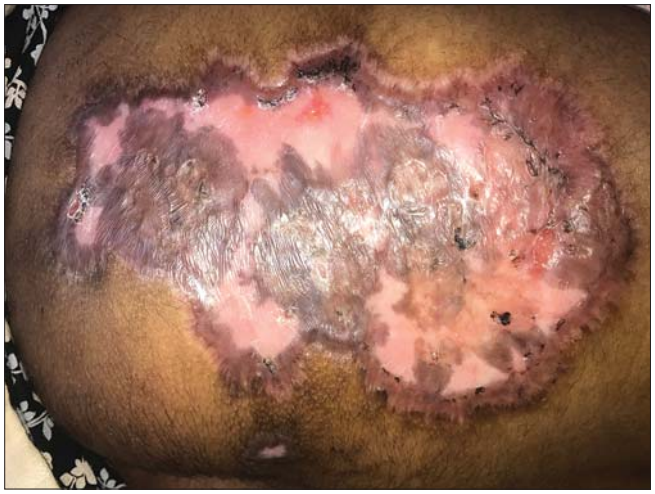

Figure 5: The nearly complete resolution of the ulcer after two months of therapy.

occur, probably, as in our case, because of an odd anatomical site. This ulcer, on removal of the necrotic crust, showed a purulent base with undermined asymmetrical borders. Extension of the lesion on surgical incision was observed twice, indicating a pathergy reaction. Multiple old healed cribriform scars again favored the diagnosis of PG. Systemic associations of ulcerative colitis, Crohn's disease, rheumatoid arthritis, hematological malignancies, and monoclonal gammopathy have been reported [2].

Skin manifestations in both classical and localized Wegener's granulomatosis (WG) have been reported in around 50% of cases [4]. They may present themselves as papulonecrotic, urticarial, vesicular lesions, palpable purpura or necrotizing ulcers resembling pyoderma gangrenosum [5]. It must be noted that initial presentations in the form of PG-like lesions have been reported in 10% of cases of WG [4]. Although c-ANCA levels were severely raised, no manifestation suggestive of upper and lower airway and renal involvement were found in this case to fulfil the classical triad of Wegener's granulomatosis (WG).

Other than the former, ANCA-associated vasculitis (AAV) has been reported with neutrophilic dermatoses (ND). Indeed, several clinical conditions, such as inflammatory bowel diseases (IBDs), can exhibit both ND and ANCA, especially their anti-MPO subtypes [6]. However, the specific targets of these antibodies, as of now, have not been identified. One study suggests that, in cases of neutrophilic dermatosis, the patient may be tested for ANCA and, if positive, careful attention should be paid to observe signs suggestive of systemic vasculitis [7]. Another study, conducted by Kawakami et al., proves the pathologic role of ANCA beyond vasculitis and suggests that c-ANCA may be directly or indirectly pathogenic in PG and/or may be produced because of neutrophilic activation and apoptosis in cases with PG, resulting in a self-amplifying loop [8]. Our patient displayed highly elevated c-ANCA levels, but no sign of WG or IBD was discovered.

Therapy in cases with PG is a matter of debate, as there is no uniformly effective treatment. The aim is to treat the underlying cause. In a rapidly progressive disease with significant morbidity, an aggressive treatment approach to halt the immunological process is crucial. Hence, methylprednisolone pulses, followed by cyclosporine, for its quick onset of action, and dapsone, for its antineutrophilic and steroid-sparing effects are preferred in rapidly progressing cases such as ours, in which such a regimen dramatically improved the outcome and expedited recovery in two months with sustained remission. However, regular follow-ups are necessary to detect signs of recurrence; otherwise, rare cases may display this as an early manifestation of Wegener's granulomatosis or ulcerative colitis.

CONCLUSION

Pyoderma gangrenosum, a type of neutrophilic dermatosis, oftentimes causes significant agony to the patient. PG is typically noninfectious, painful, and rapidly progressive, and so demands aggressive management with immunosuppressants, as in our case. Surgical maneuvers should be discouraged because of the high risk of pathergy. Common sites are the

lower limbs, but PG may present itself at any site, making diagnosis problematic. A thorough systemic examination and a battery of investigations should be performed in search for an underlying systemic abnormality. c-ANCA, although considered highly specific to Wegener's granulomatosis, may also be a possible marker for ulcerative colitis or AAV associated with PG; hence, long-term follow-ups are obligatory because pyoderma gangrenosum may be an initial presentation of either of these underlying disorders.

Consent

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

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

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Our Dermatology Online

Case Report

Skin endometriosis at the caesarean section scar: A case report

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ABSTRACT

Endometriosis is a pathology little referenced in the dermatological literature and is defined as the presence of endometrial tissue outside the uterus. When it is a well-defined mass of endometriosis it is called endometrioma. Cutaneous endometriosis is one of the rare gynecological conditions. Cutaneous endometriosis is a disorder that primarily affects women of reproductive age. The disorder is most commonly associated with cyclical pain during menses, but it can be difficult to diagnose in the absence of these symptoms and requires biopsy testing for a definitive diagnosis. We report on a case of a 39-year-old patient who presented with pain at the cearean section scar. She was ultimately diagnosed with cutaneous endometriosis and underwent surgical excision.

Key words: Scar endometriosis; Cutaneous endometriosis

INTRODUCTION

Endometriosis represents the presence of non-neoplastic endometrial tissue outside the uterus. The disease is relatively common and typically affects the ovaries and presents with deep pelvic pain, dyspareunia, and dysmenorrhea.

The usually presentation location is usually the intrapelvic location and among them the most frequent ovarian form. However, extra-pelvic location may occur in more than 12% of women with endometriosis [1,2] and affect any part of the body, even the skin [3].

Cutaneous endometriosis is relatively uncommon and occurs when endometrial glands and stroma reside in the skin.

Cutaneous endometriosis can be divided into primary and secondary endometriosis.

Endometriosis usually occurs in the form of diffuse involvement, in plaques, although sometimes it does so by adopting cystic or tumor morphology. When endometriosis occurs as a well-defined mass, it called endometrioma [4].

The pathogenesis for primary cutaneous endometriosis remains unclear, but secondary cutaneous endometriosis is believed to occur due to seeding after abdominal or pelvic surgery.

Because the condition is rare and can mimic presentations of other diseases, such as keloid or dermatofibroma, cutaneous endometriosis can be difficult to diagnose.

Punch biopsy can be performed to obtain tissue for histopathologic testing, but physicians must take care to obtain abdominal ultrasound if there is potential for uterocutaneous fistula. Once the diagnosis has been established, treatment options include hormonal agents and surgical excision with wide margins.

CASE REPORT

A 39-year-old patient with no family or personal history of interest, with a gynecological history of cesarean

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delivery 7 years ago without complications, without other valuable gynecological records.

Three years after the surgical history, she noticed a tumor of approximately 10 mm in diameter in the left lateral third of Pfannenstiel's scar. This tumor 1 year ago undergoes progressive growth, accompanied by stabbing pain related to the menstrual cycle, with local color change.

Physical Examination

A tumor of 50 mm in diameter, of elastic solid consistency, mobile that does not impress being adhered to deep planes, is observed.

According to the patient's clinic, the presumptive diagnosis of soft tissue endometriosis is made and it is decided to perform surgical excision with loco regional anesthesia.

Losangic incision is made on the tumor with a 20 mm window, being removed in block, it reaches an aponeurotic plane without exceeding it, a piece is sent to a pathological anatomy. There was a satisfactory evolution in the postoperative period.

Pathological Anatomy

A surgical piece that measures 55 x 25 x 45 mm of major axes, upholstered by a skin losange, is remitted.

The cut shows a poorly defined and non-encapsulated nodular formation of 20 mm of major axes. On the periphery of the same, multiple small cystic cavities full of hematic material are observed and in the center a yellow white tissue, of solid elastic consistency.

Serial cuts are made and the sample is processed routinely (Fig. 1).

At the histopathological examine there are multiple endometrial glands with surrounding endometrial stroma (Fig. 2). Decidualization of the stroma is not. Smooth muscle metaplasia is found. The glands show variable cystic dilatation and may contain blood and debris. There is not hemosiderin pigment There is dense fibrosis between the endometriotic foci.

Final Diagnosis

Cutaneous endometriosis.

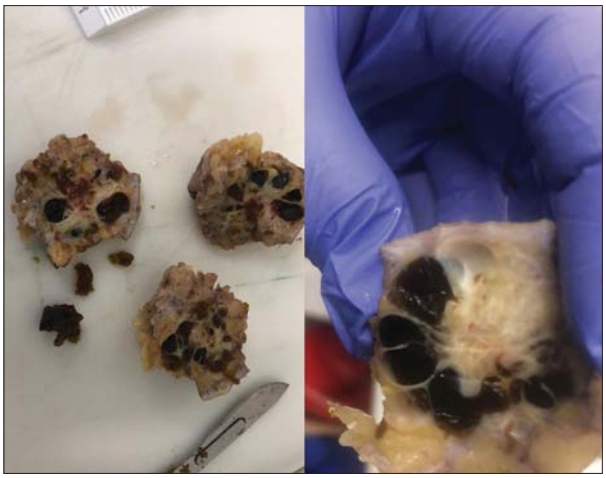

Figure 1: Gross pathology. The surface cut shows a poorly defined and non-encapsulated nodular formation of 20 mm of major axes with multiple small cystic cavities full of hematic material at the perifery.

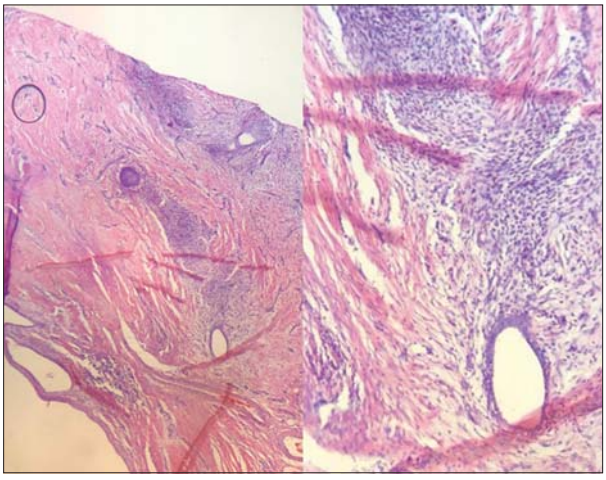

Figure 2: Histopathology. Endometrial glands with surrounding endometrial stroma (HE4X; HE20X).

DISCUSSION

Endometriosis is a chronic inflammatory reaction characterized by the presence of endometriomas outside the uterine cavity. It mainly causes painful symptoms and infertility while some women don't experience symptoms at all. The prevalence in the general female population is 2% to 10% but reaches up to 50% in infertile women [5].

The main etiology of endometriosis is not clear, but many studies suggest the hematogenous or lymphatic spread of stem cells from bone marrow or coelomic metaplasia [6].

Classically presents as a firm subcutaneous papule or nodule that averages 2 cm in diameter [7]. Its color can range from blue or violaceous to brown or skin-

colored. Patients frequently experience cyclical pain, swelling, and even bleeding that corresponds with their menstrual cycle [8].

A diagnosis of cutaneous endometriosis can be made once the presence of endometrial glands and stroma in the skin is established. Notably, an ultrasound should be completed prior to performing a punch biopsy of the lesion to rule out the presence of uterocutaneous fistula.

The skin is an uncommon location for endometriosis, and cutaneous endometriosis cases comprise <1% of all cases in large series (8). One review demonstrated that only 109 cases of cutaneous endometriosis had been described in the literature up to that point in time [9].

Cutaneous endometriosis is subdivided into two categories depending on patients' surgical history. Primary cutaneous endometriosis refers to cases in which the endometriosis develops spontaneously without any history of local surgery. It is the less common of the two (only 30% of patients present without a surgical history that could explain their cutaneous manifestations). Secondary cutaneous endometriosis, also called scar endometriosis, is associated with prior abdominal or pelvic surgery [7].

Our patient was diagnosed with cutaneous endometriosis based on the cyclical nature of her pain and the dermatopathologist diagnosis is in bad order. Identifying the patient's surgical history was crucial to subclassifying our patient's involvement as most likely being secondary in nature.

The most common location for both primary and secondary cutaneous endometriosis is the umbilicus. Umbilical cutaneous endometriosis comprises 30% to 40% of all cutaneous endometriosis cases, but other locations such as the groin, arm, episiotomy wounds, appendectomy scars, and cesarean scars have also been described [7].

Secondary cutaneous endometriosis is perhaps easier to conceptualize, and the prevailing hypothesis remains that endometrial cells dislodged during surgery seed the wound within and adjacent to the incision sites. In cases of primary cutaneous endometriosis, some postulate that seeding occurs hematogenously or via lymphatics [7].

Cutaneous endometriosis can mimic variable number of pathologies and also can mimic malignancy.

The most effective treatment of cutaneous endometriosis It is the surgical one. In the exeresis the focus of endometriosis with wide margins of 5-10 mm may be done with the intention of avoiding recurrence [3,10,11].

The incidence of cancer on an ovarian endometriosis site is 1%. The incidence of cancer in a focus of extrapelvic endometriosis is unknown [12]. Few cases of cancers of endometriosis on the abdominal wall have been described [13].

Consent

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

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Elephantiasis nostras verrucosa in a patient with lipedema and lipolymphedema

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ABSTRACT

Elephantiasis nostras verrucosa is a group of rare cutaneous changes comprising dermal fibrosis, hyperkeratotic, and verrucous and papillomatous lesions secondary to chronic non-filarial lymphedema. The following study reports a case associated with lipedema and lymphedema, several episodes of erysipelas unfolding over the previous years, and warty lesions appearing in the transitional region between the right ankle and foot. Several episodes of erysipelas in patients with lipolymphedema can evolve into elephantiasis nostras verrucosa (ENV).

Key words: Elephantiasis nostras verrucosa; Lipedema; Lymphedema

INTRODUCTION

Elephantiasis nostras verrucosa (ENV) is a group of rare cutaneous changes comprising dermal fibrosis, hyperkeratotic, and verrucous and papillomatous lesions secondary to chronic non-filarial lymphedema [1]. It is a peculiar clinical stage of lymphedema resulting from infectious processes in the limbs and leading to their fibrosis. It is also a progressive condition that, without intervention, leads to continuing deformity and disability [2]. However, there is no standard treatment for ENV, and surgery may not always be its best treatment since it does not treat its cause, only its cutaneous symptoms. Nevertheless, debridement is a quick and aesthetically adequate form of treatment [3].

Lipedema is a clinical syndrome first described by Allen and Hines in 1940 [1] that is characterized by a bilateral and symmetrical increase in the size of the lower limbs, but not the feet. Its physical features are characterized by a more pronounced deposition of fat tissue in the extremities. Stemmer's sign is negative. Its signs and symptoms may include, among other conditions, cutaneous hypothermia, alterations in the plantar support, and hyperalgesia [4,5]. It is important to understand that the concept of lipolymphedema is a progression of lipedema to lymphedema [6]. The aim of this study is to report on the association of lipedema with elephantiasis, the most advanced clinical stage of lymphedema, and elephantiasis nostra verrucosa.

CASE REPORT

The patient reported that the swelling had been persistent for around five years without diminishing upon rest and was, therefore, diagnosed as lipolymphedema. The warty lesions on the right ankle and foot (Fig. 1) were diagnosed as elephantiasis nostras verrucosa, the advanced clinical stage of lymphedema. There were no obvious clinical signs of lymphedema of the left foot at the time of the physical examination (Fig. 2), but there was an ulcerated lesion due to infection. Lesions were also observed in the middle third of the right leg, suggestive of grade II lipedema. The case received approval from the Human Research Ethics

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DOI: 10.7241/ourd.20211.17

Committee of São José do Rio Preto School of Medicine (#2.336.797).

DISCUSSION

This report describes elephantiasis nostras verrucosa in a patient with an evolution of lipedema into lipolymphedema. This type of presentation of lipedema has not been described in the literature. The term 'nostras' was introduced by Castellani in order to distinguish tropical filarial elephantiasis from lymphedematous disorders in the temperate regions. One suggested hypothesis for the etiology and pathogenesis of the disease is lymphangitis and localized lymphatic lesions caused by streptococcal infection [7].

In this study, the patient reported several outbreaks of erysipelas, which had probably contributed to the aggravation of the lipedema. Initially, these outbreaks were localized and led to the development of elephantiasis nostra. Subsequently observed was evolution of lipolymphedema. This finding highlights the consequences of chronic infection in the evolution of this type of disease.

Lipedema is a common condition that involves the distribution of fat tissue and leads to changes in the lymphatic system [8]. The possibility that prior lymph injury or recurrent infection may be its cause should, however, be questioned.

As for treatment, the use of bandages is inadvisable because the friction on the verrucosities may cause injury and infection. The patient reported that this change occurred during one of the treatments. Clinical management does not, therefore, appear to be effective in more advanced cases of the disease, and surgical resection of the lesions to permit the use of bandages seems, currently, to be the best option. In this case, prophylaxis with benzathine penicillin reduced the outbreaks of infection, but, on cessation, the infections restarted.

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 have given consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

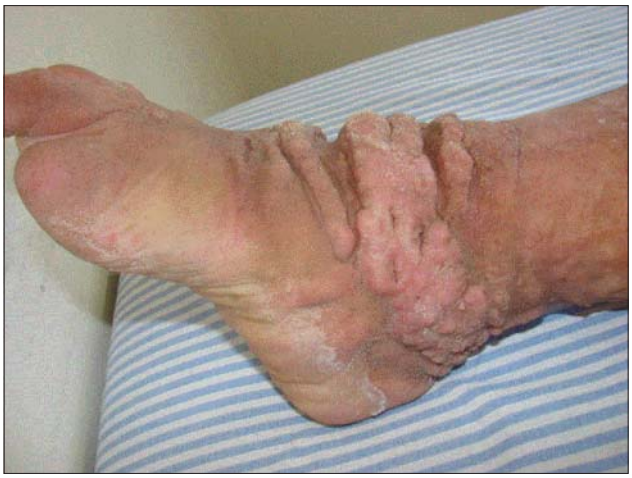

Figure 1: The right ankle and foot with lipolymphedema and elephantiasis nostras verrucosa; advanced fibrosis and nodules on the lower third of the leg, suggestive of grade II lipedema.

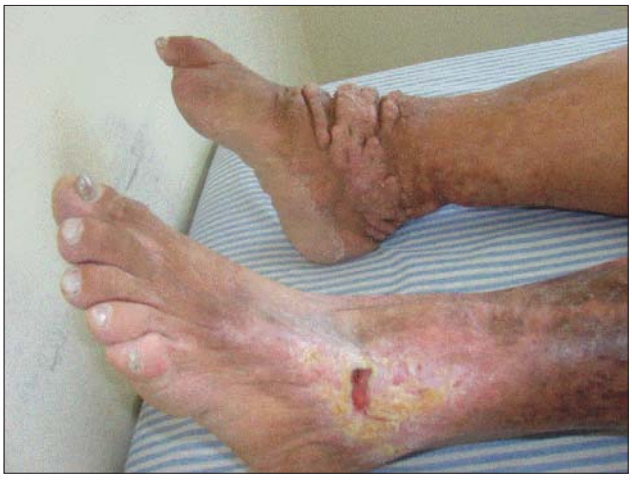

Figure 2: The lower limbs with lipolymphedema, advanced elephantiasis nostras verrucosa on the right leg, and an ulcerated lesion on the left leg.

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Our Dermatology Online

Case Report

Disseminated superficial actinic porokeratosis in a patient with generalized vitiligo: A case report

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ABSTRACT

Disseminated superficial actinic porokeratosis (DSAP) is the most common type of porokeratosis, occurring mainly on sun-exposed skin. Chronic sun exposure is one of the main risk factors, in addition to genetic susceptibility. Most published data concerning the relationship between vitiligo and its predisposition to nonmelanoma skin cancer suggests that patients with vitiligo show the same or even a lower incidence than other populations. Herein, we report a case of disseminated superficial actinic porokeratosis occurring in vitiligo in which chronic sun exposure was the main risk factor.

Key words: Porokeratosis; Vitiligo; Sunlight; Ultraviolet radiation

INTRODUCTION

Porokeratosis is a keratinization skin disorder inherited as an autosomal dominant [1]. Disseminated superficial actinic porokeratosis (DSAP) is characterized by annular keratotic papules or plaques with a characteristic thread-like ridge and central atrophy that expand peripherally on sun-exposed skin [2]. A cornoid lamella is a distinctive histopathological feature of all its types [3]. Certain stimuli can hasten the appearance of porokeratosis, such as immunosuppression, radiation therapy, artificial ultraviolet radiation, and chronic sun exposure [4,5]. Herein, we present the case of a patient with generalized vitiligo in whom DSAP occurred mainly in a sun-exposed depigmented patch.

CASE REPORT

A 65-year-old male farmer presented to our dermatology clinic complaining of pruritic and hyperkeratotic skin on the back of the hands and fingers persistent for five years prior. He had had generalized vitiligo for the last twenty years with no special treatment and no history of treatment with phototherapy or immunosuppressive drugs. Upon examination, the patient looked healthy, apart from the vitiligo, which involved more than 70% of the body, including the face, extremities, and trunk. There were multiple annular plaques with sharply-defined thin edges and atrophic centers distributed bilaterally and symmetrically on the back of both hands, limited mostly to the depigmented skin (Figs. 1a and 1b). A punch biopsy was taken to show a cornoid lamella, the characteristic histopathological feature of porokeratosis (Fig. 1c). General laboratory investigations were within normal limits. The patient was advised to avoid sun exposure, apply sunscreen regularly in the daytime and topical retinoid at night, and attend regular follow-ups. Informed consent was taken from the patient and approval for the study was obtained from our institution.

DISCUSSION

Vitiligo is a common acquired pigmentary disorder that results from loss of melanin-producing cells.

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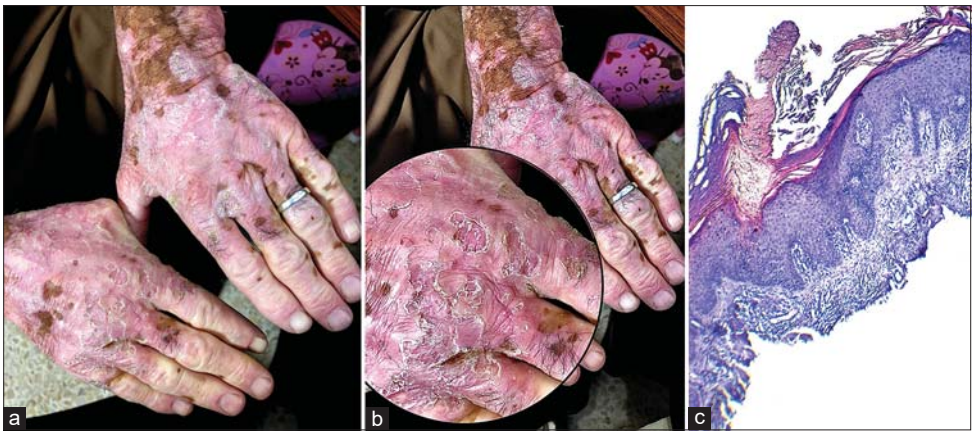

Figure 1: (a) Multiple hyperkeratotic plaques on the back of the hands. (b) A close-up view of the affected skin showing the elevated ridges and central atrophy of the plaques. (c) Histopathological findings of the punch biopsy showing a cornoid lamella (H&E, 10×).

Melanin protects the skin from the harmful effects of the ultraviolet radiation (UVR) in sunlight [6]. UVR is the main factor in chronic sun exposure that induces nonmelanoma skin cancer (NMSC) by mutation of the TP53 gene [7]. Accordingly, vitiliginous skin is more vulnerable to these influences in comparison with normally pigmented skin. People with vitiligo show the same and even a lower incidence of cutaneous malignancies than other populations [1,8,9]. Some ascribe this to the increased expression of the tumor-suppressing gene TP53 in vitiligo [10,11]. Others point to the increase in certain cytokines and decrease in others acting as protective factors in vitiligo skin [10]. Photoadaptation, thickening of the stratum corneum, and the altered activity of the immune system are other explanations [11,12].

In contrast, there were several cases mentioned in the literature in which NMSC arose on depigmented skin, whether protected from the sun [2,11] or sun-exposed [13,14]. In our case, DSAP developed on sun-exposed vitiliginous skin, and this may be the first such case published in the literature so far. In our case, there were no specific risk factors apart from chronic sun exposure and a 30-year absence of photoprotection.

CONCLUSION

Although sun-exposed vitiliginous skin may have a lower chance to become affected by NMSC for different reasons, certain factors may increase this possibility, such as the age of the patient, the duration and extent of the vitiligo, the chronicity of sun exposure, the presence of immunosuppression, and a family history of other genetic diseases.

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

Destombes and Rosai-Dorfman disease of the anterior abdominal wall - Extra nodal sinus histiocytosis with massive lymphadenopathy

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ABSTRACT

Destombes–Rosai–Dorfman disease—often simply referred to, in the literature, as Rosai–Dorfman disease (RDD)—is a rare, nonmalignant disorder of histiocyte proliferation typically involving the cervical lymph nodes. A subset of patients with RDD, however, display extranodal manifestations highly variable in presentation, more challenging to diagnose, and less likely to spontaneously regress when compared to the nodal manifestations. This study describes the case of a young African male presenting himself with multiple nodules involving the anterior abdominal wall, who was found to have extranodal RDD. The current mode of diagnosis and the clinical management of RDD are reviewed.

Key words: Destombes–Rosai–Dorfman disease; Extranodal; Histiocytic proliferation

INTRODUCTION

Sinus histiocytosis with massive cervical lymphadenopathy is a non-neoplastic proliferative disease of histiocytes of unknown etiology. It is commonly referred to as Rosai–Dorfman disease (RDD), although it was Destombes who first reported it [1]. The nodal presentation of RDD is fairly common and poses little difficulty in diagnosis. However, the extranodal presentation is uncommon and often presents a diagnostic challenge to pathologists. We report a case and present the modern tools available to aid in such diagnosis.

CASE REPORT

A 29-year-old African male presented himself to the Accident and Emergency department with a two-year history of an initial pustule on the left upper abdomen. During that period, however, the pustule resolved and was replaced by multiple, small, nonfluid-filled, erythematous papules in a hyperpigmented area. The lesions were nonpruritic. There were no constitutional symptoms.

An examination revealed a 3 × 2.5 cm area of hyperpigmented skin on the left upper abdomen with multiple nontender, firm papules. There was no lymphadenopathy.

Laboratory investigations performed showed a complete blood count with normal parameters. Liver and renal function tests were essentially normal, except for hypoglobulinemia of 2.74 g/dL (range: 3.2–3.9 g/dL) (Table 1).

An excision biopsy of the lesion was done and sent for histological examination.

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Table 1: The hematological and biochemical profile of the patient

	Value	Units
WBC	7.57 (4-11)	10^3/uL
HB	14.6 (11-17)	g/dL
RBC	5.33 (3.8-5.5)	10^6/uL
HCT	43.2 (36-50)	%
MCV	81.1 (83-101)	fL
Platelets	224 (150-410)	10^3/uL
BUN	12 (6-20)	mg/dL
Creatinine	1.2 (0.7-1.2)	mg/dL
Potassium	4.39 (3.5-5.1)	mmol/L
Sodium	135 (136-145)	mmol/L
Chloride	98.7 (98-107)	mmol/L
Indirect Bilirubin	0.21 (0.01-0.8)	mg/dL
Direct Bilirubin	0.20 (0.00-0.20)	mg/dL
ALT	39 (0-41)	U/L
AST	26 (0-40)	U/L
ALP	94 (40-129)	U/L
GGT	29.3 (0-60)	U/L
Albumin	4.61 (3.5-5.2)	g/dL
Total Protein	7.35 (6.6-8.7)	g/dL
** Globulin	2.74 (3.2-3.9)	g/dL
Total Bilirubin	0.41	(0.0-1.2) mg/dL

Histology

Received for histology was a 3.5 × 3 × 2.4 cm ellipse of skin with multiple firm tan papules. The cut sections revealed firm, rubbery, faint-pink tissue (Fig. 1).

The histopathology of the skin lesion mimicked those seen in lymph nodes with sinus histiocytosis with massive lymphadenopathy.

The lesion was composed mainly of a well-circumscribed lymphohistiocytic infiltrate involving the dermis and subcutaneous tissue (Fig. 2a). The lesional histiocytes constituted a large central hyperchromatic nucleus set in abundant, pale, water-clear cytoplasm and single distinct nucleoli. Within the lesional histiocytes, emperipolesis was evident, which constituted intact lymphocytes and neutrophils in the cytoplasm (Figs. 2b and 2c). Mature lymphocytes and numerous plasma cells and neutrophils were also present between histiocytes. Mitosis was rare and necrosis was absent. The overlying epidermis showed hyperkeratosis, parakeratosis, and atrophy of rete ridges. Several binucleated histiocytes resembling Reed–Sternberg (RS) cells were seen, but there was a complete lack of expression of the markers CD15 and CD30, which made Hodgkin lymphoma quite unlikely.

Immunohistochemical stains confirmed the diagnosis of extranodal RDD by showing positivity for CD68 and S100 (Figs. 2d and 2e).

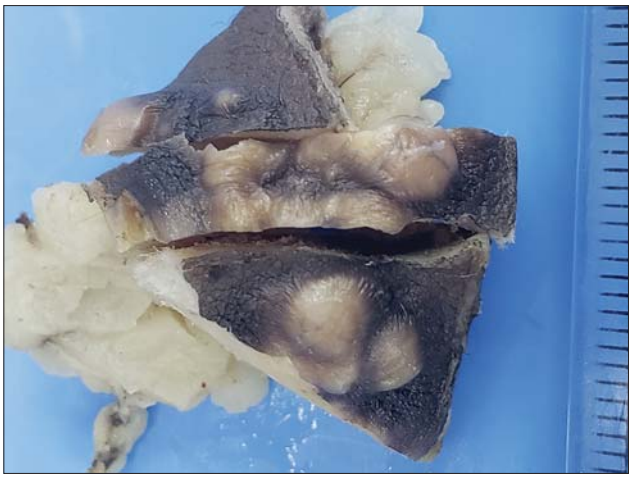

Figure 1: The excised lesion from the abdominal wall.

A few binucleated histiocytes resembled those of Reed-Sternberg cells (RS cells) were seen, however there was a complete lack of expression of the markers CD15 (Fig. 2f) and CD30, which makes Hodgkin Lymphoma quite unlikely.

The overall histological picture of the abdominal lesion was that described by Rosai and Dorfman in lymph nodes with sinus histiocytosis with massive lymphadenopathy.

DISCUSSION

The disease entity first reported in French by Destombes in 1965 [1] was further characterized by Rosai and Dorfman in 1969 [2]. Hence, it would be fitting for the disease to bear the name of the original researcher. Destombes–Rosai–Dorfman disease is seen in all ages and ethnicities, but with a slight predominance in young males.

The classic presentation includes fever and painless massive cervical lymphadenopathy, the latter showing sinus histiocytosis with emperipolesis as the hallmark of the disease [3]. Other lymph node groups may be involved.

RDD is a benign proliferative histiocytic disorder of unknown etiology, self-limiting in most instances. The extranodal manifestations may present themselves in any site, with cases reported in the bone, eyelid, skin, central nervous system, lungs, and other sites with or without nodal involvement [4-8].

The extranodal lesions often present a challenge to histopathologists because of the broad differentials for

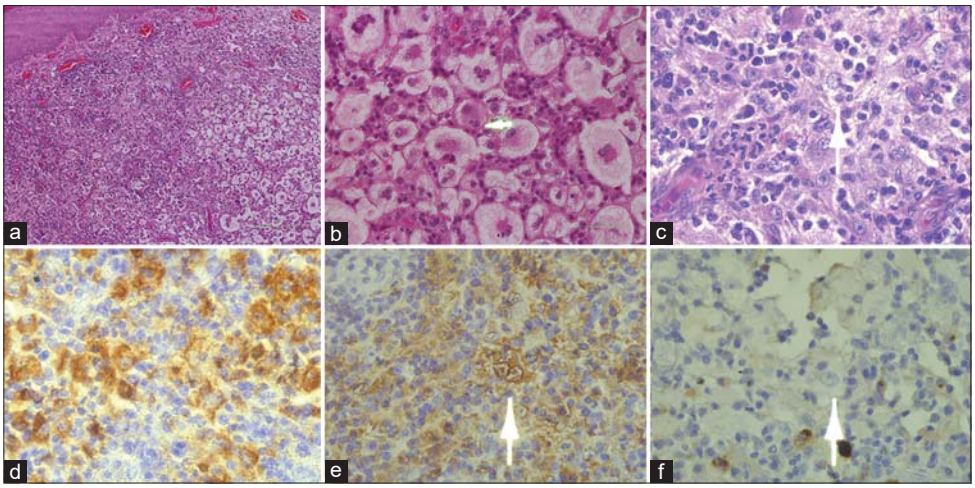

Figure 2: (a) The lymphohistiocytic infiltrate in the dermis. (b) Emperipolesis of lymphocytes and neutrophils in a histiocyte. (c) Emperipolesis (H&E, 40×). (d) CD68 positivity (40×). (e) An S100-positive binucleated histiocyte of Destombes–Rosai–Dorfman disease. (f) A CD15-negative histiocyte demonstrating that the histiocyte is not a lacunar cell of Hodgkin lymphoma.

lymphohistiocytosis, and all these histiocytic disorders share the common pathological findings of abnormal proliferation of histiocytes.

Disorders warranting a differential diagnosis with RDD include lipogranulomatosis, Langerhans cell histiocytosis, Hodgkin disease, metastatic carcinoma, malignant melanoma, and Erdheim–Chester disease.

A lack of Touton giant cells eliminates the diagnosis of lipogranuloma. Langerhans cell histiocytosis, similarly to RDD, demonstrates lymphohistiocytic proliferation and positive expression of S100 and CD1a. However, cells of Langerhans cell histiocytosis lack lymphophagocytosis and, ultrastructurally, reveal the presence of the characteristic rod-shaped Birbeck granules. Lacunar cells of nodular sclerosis, a form of Hodgkin disease, may on occasion be confused with RDD cells. However, Reed–Sternberg cells and their variants do not exhibit emperipolesis. They are S100-protein-negative, CD15-positive, and CD30-positive. Negative staining for HMB-45 and pankeratin differentiate RDD from melanoma and metastatic carcinoma [9].

Erdheim–Chester disease is a rare non-Langerhans cell histiocytosis and a true histiocytic neoplasm characterized by multisystemic proliferation of mature histiocytes in a background of inflammatory cells [10]. Cutaneous infiltrates in Erdheim–Chester disease contain xanthogranulomata with large Touton giant cells, which are not reactive cells, but part of the neoplastic process. In addition, there is the common background of inflammatory cells of foamy histiocytes, lymphocytes, and neutrophils, as observed in RDD. Emperipolesis is not a feature of Erdheim–Chester disease.

The clinical and pathological features in our case fit those described by Destombes, Rosai, and Dorfman, with emperipolesis being the hallmark and the distinguishing feature [3].

Surgical excision of these lesions in extranodal sites is the treatment of choice, although there have been reports of recurrence after excision [11]. Therapy with acitretin, thalidomide, methotrexate, and steroids has shown promising results in cases that recurred after surgical excision [12,13]. Complete resolution of the disease has been reported with siltuximab therapy [14]. Further research needs to be done to better understand the underlying pathophysiology of RDD. In doing so, clinical management would become less problematic.

CONCLUSION

The extranodal manifestations of Destombes–Rosai–Dorfman disease (RDD) present numerous diagnostic and therapeutic challenges, as it may occur in any organ or site. However, the use of immunotyping aids the pathologist in making the diagnosis. There is much to learn about the etiology of RDD for effective therapy to be possible.

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

Clinical Image

Degeneration of chronic intertrigo into squamous cell carcinoma

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Squamous cell carcinoma is the second carcinoma of the skin after basal cell carcinoma, which is known to have a poorer prognosis due to its lymphophilic character with frequent lymph node and visceral metastases [1,2]. Several precancerous lesions, genetic and acquired, are providers, including irritations and inflammatory chronic mucocutaneous conditions, as shown by the clinical case of a 65-year-old woman, diabetic on oral antidiabetics, with a history of recurrent mycotic intertrigo, who consulted for a swelling of the fourth and fifth toes evolving for more than 3 months and resistant to usual treatment. A dermatological examination found a tumefied, ulcerated, slightly necrotic and bleeding intertrigo in contact with the fifth right inter-toe space, and an onychodystrophy of a mycotic appearance (Figs. 1a and 1b). Popliteal and inguinal lymph nodes were free. A histological study of a cutaneous biopsy favored moderately differentiated squamous cell carcinoma. A paraclinical extension assessment was reassuring. The patient was subsequently referred for plastic surgery. In conclusion, the prevention of this type of cancer involves the treatment and correct and early management of precancerous conditions, including chronic inflammatory conditions of the skin.

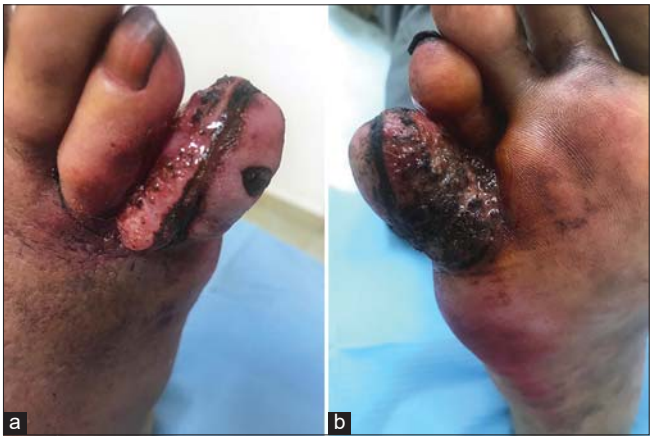

Figure 1: (a-b) An ulcer-budding tumor of the fifth right toe complicated by a chronic mycotic intertrigo.

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 have given 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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Clinical Image

Crack hands and crack thumbs in chronic cocaine abuse

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Cocaine, a substance very commonly abused around the world, is a stimulant that increases dopamine concentrations in the brain reward system, producing a dose-dependent feeling of euphoria, which leads to long-term alterations in neuronal pathways, ultimately giving rise to addiction [1].

Crack cocaine is a cheaper and more potent version of cocaine prevalent in lower socioeconomic classes. Numerous dermatological manifestations of cocaine abuse have recently been mentioned, including pyoderma gangrenosum and Raynaud's phenomenon, to name a few [1-3]. We report the case of a 38-year-old male chronically abusing crack cocaine for the past 5 years, displaying blackened punctiform hyperkeratotic lesions on the palms and the ventral surfaces of the fingers, a condition known as crack hands [2]. These lesions are more evident in the dominant hand, which, in this case, is the left hand (Fig. 1). Burns on the hands along with callus or blister formations on the thumb are due to the act of igniting cocaine pipe lighters, the latter known as a crack thumb [3]. Such blister formation can, indeed, be seen in this case of chronic cocaine abuse (Fig. 2).

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 have given consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

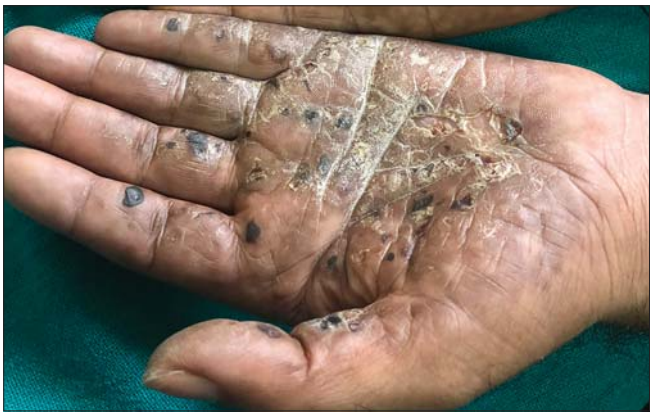

Figure 1: Blackened punctiform hyperkeratotic lesions located on the palms and the ventral surfaces of the fingers known as crack hands.

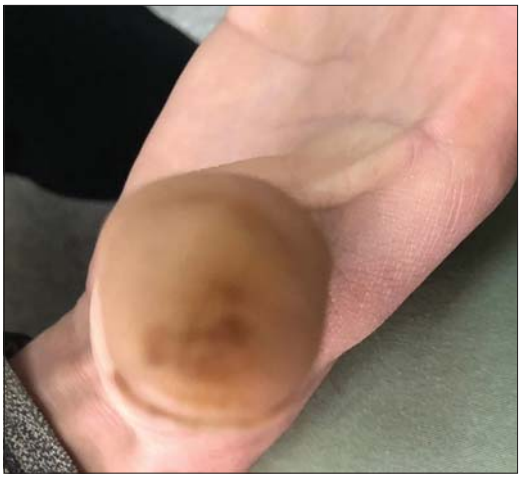

Figure 2: A blister on the thumb known as a crack thumb.

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Letter to the Editor

Sculpt plaster therapy for abdominal circumference reduction

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Sir,

Research demonstrates that the pattern of one's fat distribution has a profound impact on cardiometabolic risk [1].

Sculpt plaster therapy is a beauty treatment that allows quick elimination or reduction of cellulite, flaccid skin, and localized fat. Plaster helps to eliminate liquid from the body, producing improvements that are not only aesthetic in nature but also health-wise, for instance, by maximizing abdominal fat loss.

In practice, the procedure begins with the preparation of the skin. During the preparation process, the area is cleansed and exfoliated for better absorption of the ingredients. During the treatment, the plaster absorbs heat released by the body, which increases blood circulation and facilitates the penetration of the active ingredients into the skin.

To complement sculpt plaster therapy, green clay has also been used. Green clay contains minerals such as iron and magnesium, which facilitate lipolysis. Iron increases the rate of lipolysis in adipocytes [2]. Magnesium is gathered by adipocytes during lipolysis [3].

The purpose of this study was to analyze the effect of sculpt plaster therapy in the reduction of abdominal circumference.

The initial consultations and subsequent treatments were developed in Clínica Áurea (Aesthetic Biomedicine Clinic, Portugal). A total of nine patients were submitted to the treatment. During the initial consultation, all the procedures, side effects, expected results, and contraindications were explained. The patients signed an informed consent. Also, during the initial consultation, initial measurements were taken. The aim of this procedure was to measure the reduction in abdominal circumference.

Instruments

A nonstretchable measuring tape was used to measure height and circumference. Tanita UM-076 with bioelectrical impedance was used to measure weight, muscle mass, and fat mass.

The following components were used: green clay (from lot 00301, Seara, Portugal, smectite clay with the following chemical composition: SiO_2 (27.8%), CaO (25.5%), Al_2O_3 (11.2%), MgO (4.6%), Fe_2O_3 (2.3%), K_2O (1.57%), TiO_2 (0.37%), Na_2O (0.05%); loss on ignition (26.0%)), magnesium sulfate, distilled water, Exfoliating Cherry and Nutshell Gel (Paraíso, Portugal), plastic film, sculpt plaster (from lot 010824, Body Secrets by SB Nails: calcium sulfate, bentonite, vanillin, ascorbic acid, and Cl 77007), and massage oil (Quickepil, Portugal).

Procedures

The treatments were applied once a week for five weeks. With every session, the patients' measurements were collected. Abdominal circumference was measured by finding the middle point between the last rib cage and the iliac crest. Height, fat mass, muscle mass, and weight were also measured.

During the first session, green clay therapy was given. Green clay was prepared with the following components: 30 g of green clay, 30 g of magnesium sulfate, and 50 mL of distilled water. The components

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were mixed and then applied. The patients were wrapped with a plastic film in the abdominal region for twenty minutes. Green clay was removed with water.

During sessions two to five, sculpt plaster therapy was given. The abdominal area was exfoliated with an exfoliating gel. The patients were wrapped in a plastic film for fifteen minutes. Afterward, the exfoliating gel was removed with water. Sculpt plaster was prepared with the following components: 30 g of sculpt plaster and 30 g of distilled water. The components were mixed and applied in the abdominal area. The patients were wrapped in bandages and a plastic film to keep the area moist and to maintain body temperature for fifty-five minutes. After this, the sculpt plaster was removed with water and shaping massage with a massage oil was given for thirty minutes.

Table 1 shows a decrease in abdominal circumference, weight, and fat mass and an increase in muscle mass (Fig. 1).

The results of sculpt plaster therapy are due to the individual action of each of the components after topical application. Magnesium is gathered by adipocytes during lipolysis and, as fatty acids are mobilized, its concentration decreases. This is the reason why the administration of sculpt plaster therapy may intensify the lipolysis process. There is, nonetheless, a lack of studies on the action of these components through topical absorption.

Taking into account the results of this study, it seems that sculpt plaster therapy may enhance the reduction in abdominal circumference [4,5]. It should, however, be a complement to physical exercise and an optimal diet [6]. One study shows that complement sculpt plaster therapy coupled with aerobic exercise reduces abdominal fat [2].

Further investigation could be conducted in order to study the influence of temperature increase, abdominal lymphatic drainage, differences between sculpt plaster in powder—as used in this study and plaster bandage, and the type of exercise performed while using the sculpt plaster. Separate studies should be conducted to better understand each of the factors.

It would also be meaningful to study the effects of sculpt plaster therapy in the gluteal–femoral area, especially in females, as, in females, fat deposits are located preferentially in this region [5,7].

Table 1: The means of weight, fat mass, and abdominal circumference loss and muscle mass gain

	Weight (kg)	Fat mass (%)	Abdominal circumference (cm)	Muscle mass (kg)
Mean	-0,24	-1,13	-3,59	+0,54

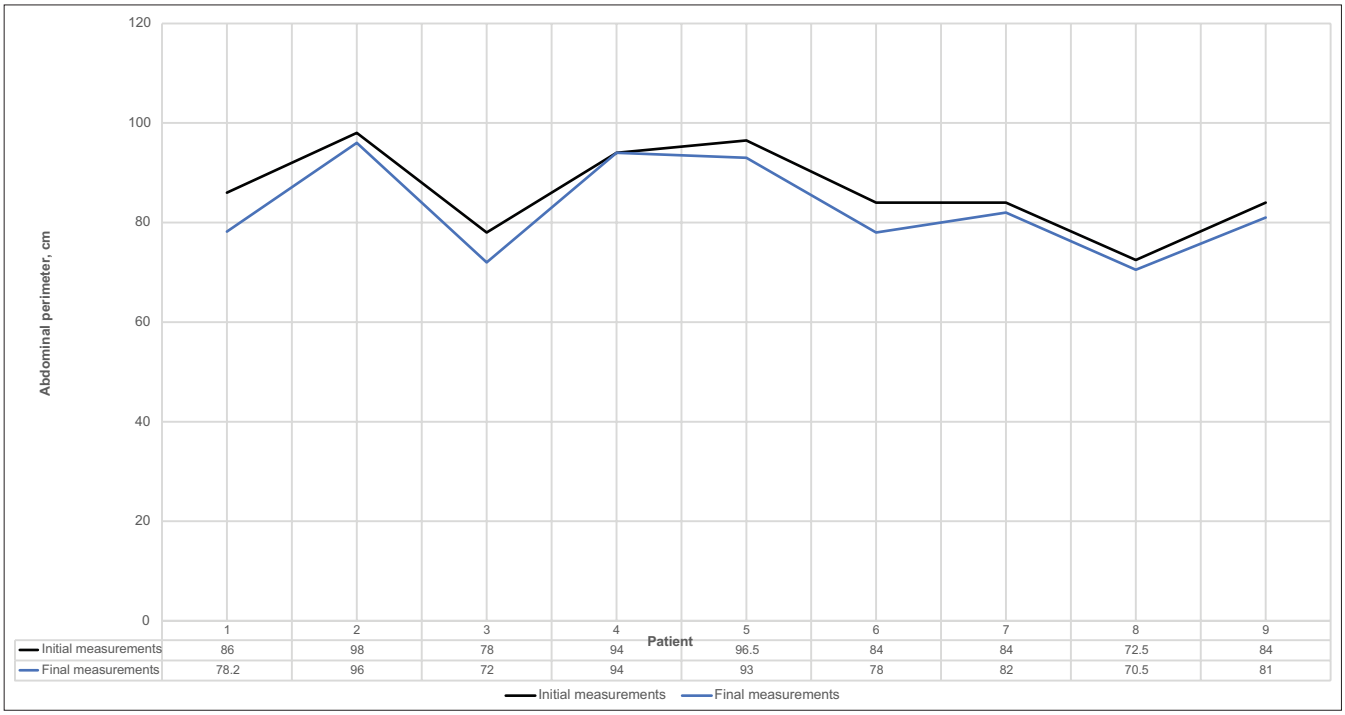

Figure 1: Initial and final abdominal circumference measurements.

It is important to highlight the results of this study so that aesthetic biomedicine professionals consider this novel tool for lipolysis enhancement.

Consent

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

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Letter to the Editor

Radiological improvement of psoriatic arthritis by biologic therapy

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Sir,

Since the introduction of biologics, the treatment efficacy of psoriatic arthritis (PsA) has much improved. Biologics are usually considered to prevent the progression of bone and joint deformity, but not to recover existing deformities. Herein, a case of PsA in which a radiological improvement in the peripheral joint was achieved by biologics is reported.

A 40-year-old female visited our department complaining of skin lesions on the trunk and extremities seen for more than 8 years. Joint pain appeared one year before. Upon physical examination, scaly erythematous plaques were found coalesced, involving large areas of the trunk and extremities, with a Psoriasis Area and Severity Index (PASI) score of 24.6. Furthermore, some of the fingers were deformed and did not yield to bending (Fig. 1a). A biopsy specimen from the trunk revealed hyperkeratosis with parakeratosis, a regular elongation of the epidermis, and mononuclear cell infiltration around the dilated blood vessels in the papillary layer, which are the characteristic features of psoriasis. A roentgenogram revealed a narrowing of the proximal interphalangeal (PIP) joint space of the fourth and fifth right fingers (Fig. 1b) and the fifth left finger. She was initially treated with infliximab (5 mg/kg intravenously at weeks 0, 2, and 4, followed by every 8th week), which dramatically improved the skin lesions. She no longer complained of joint pain, as the joint pain was also reduced. However, because secondary failure for the skin lesions appeared 1 year and 2 months after the initiation of infliximab, treatment was switched to secukinumab (300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, and every 4 weeks thereafter). The cutaneous psoriasis was successfully treated with secukinumab and resulted in a clear PASI score 3 months later. Arthralgia did not relapse and remained well controlled. The crooked fingers straightened almost completely (Fig. 1c). An X-ray 1 year and 2 months after the initiation of secukinumab showed improvement in the joint space narrowing (Fig. 1d).

Our case showed a radiographic improvement of PsA after treatment with biologics, which are often thought to inhibit, but not reverse, the progression of joint deformity. In this case, however, not only clinical but also radiographic remission was achieved by biologics. To date, few cases of radiological improvement of rheumatoid arthritis and juvenile idiopathic arthritis by biologics have been reported [1-4], where tocilizumab, an interleukin-6 receptor (IL-6R) antibody, restored damaged cartilages. However, as far as we know, there have been no reports showing the radiological improvement of PsA by biologics. In our case, bone erosions were repaired by anti-tumor necrosis factor (TNF) antibody and anti-IL-17A antibody, both over a 14-month treatment period. Unfortunately, no radiological evaluation was performed at the time of switching from infliximab to secukinumab. Matrix metalloproteinase (MMP) is a tissue-destroying enzyme regulated by IL-1 and TNF. In addition, Th17 plays an important role in upregulating MMP expression [5]. In our case, the joint pain was in remission, and an X-ray was done 3 years after the initiation of biologics. Hence, the limitation of our analysis is that we do not know whether the radiographic improvement was effected by infliximab or secukinumab, because at the time of the switching of the biologic, an X-ray examination was not performed. However, modulating the TNF- and Th17-pathways may have altered MMP activity, reduced tissue destruction, and, therefore, improved the outcome.

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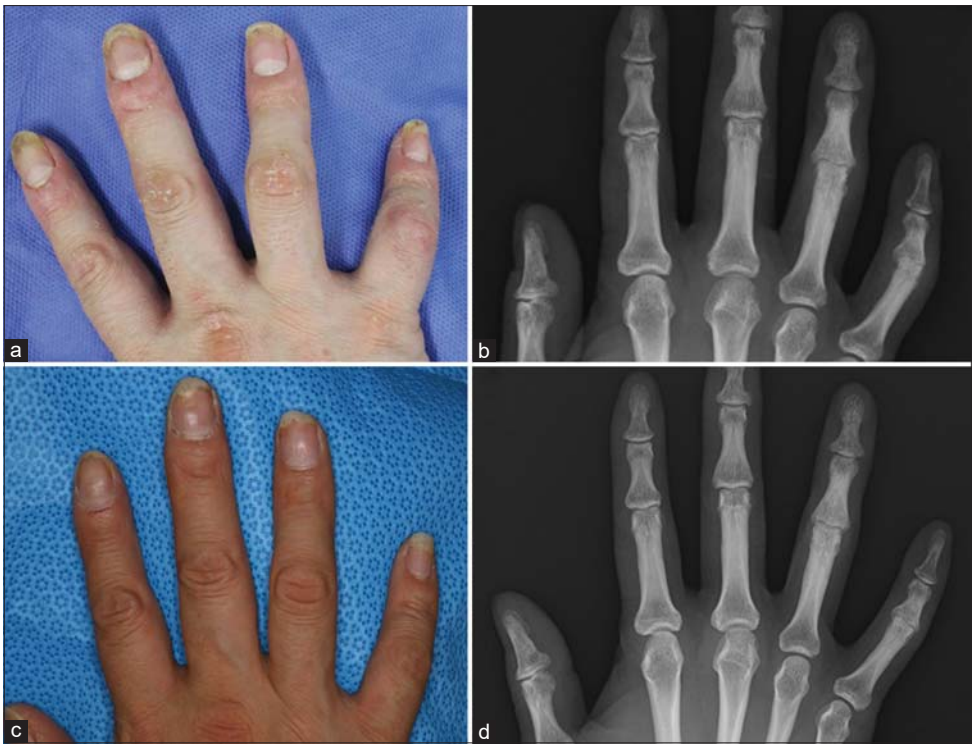

Figure 1: (a) Deformed fourth and fifth right fingers before biologic therapy. (b) Radiographic findings showing a narrowing of the PIP joint spaces of the fourth and fifth fingers. (c) Finger deformity much improved 28 months later. (d) Radiographic findings showing partial recovery of joint spaces.

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 have given 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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Letter to the Editor

The Koebner phenomenon in seborrheic pemphigus

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Sir,

The Koebner phenomenon (KP) manifests itself as lesions typical of a certain dermatosis in areas of healthy skin that were previously stimulated by various types of trauma [1,2]. Herein, we present the case of a patient with seborrheic pemphigus initially developed on a surgical scar.

A 25-year-old female, who underwent Cesarean section six months earlier for fetal distress, was hospitalized for a rash initially localized on the Cesarean section, which then gradually spread. A clinical examination revealed good general condition but erythematous squamous and crusty lesions on the surgical scar (Fig. 1a), trunk (Fig. 1b), and back. Oily dander was also noted with erythema on the scalp (Fig. 1c). The mucous membranes and nails were without abnormality, and the Nikolsky sign was absent.

A skin biopsy (Fig. 2) and direct immunofluorescence were in favor of superficial pemphigus. Anti-intercellular substance antibodies were at 1280. Both anti-nuclear antibodies and native anti-DNA antibodies were negative. In light of these results, the diagnosis of seborrheic pemphigus was reached and prednisone treatment was initiated at a rate of 1.5 mg/kg/day with good progress.

The Koebner phenomenon (KP) is one of the most well-known entities in dermatology, first described in 1876 by Heinrich Koebner in only psoriatic patients. This isomorphous phenomenon is now well known in psoriasis, vitiligo, lichen planus, and Darier's disease [1,2]. Some rare cases have been described in pemphigus vulgaris but, to the best of our knowledge, our patient is the first case of the KP in seborrheic pemphigus.

The pathogenesis of the KP is still poorly understood but may involve cytokines, stress proteins, adhesion molecules, and auto-antigens [2]. In our patient, the KP might be explained by the fact that scar tissue tends to develop koebnerization more easily, which in turn is explained by changes in vascularization and chronic mast cell infiltrate that affects the regional endothelium.

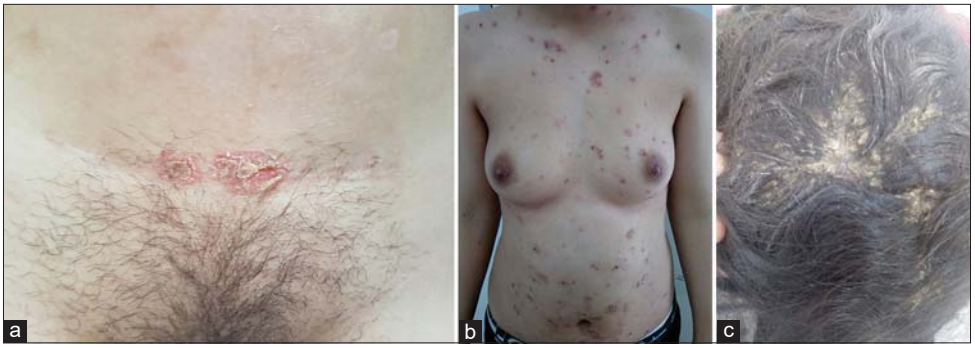

Figure 1: (a) Superficial pemphigus lesions on the surgical scar, illustrating the Koebner phenomenon, (b) Superficial pemphigus lesions on the trunk (c) Oily dander with erythema on the scalp.

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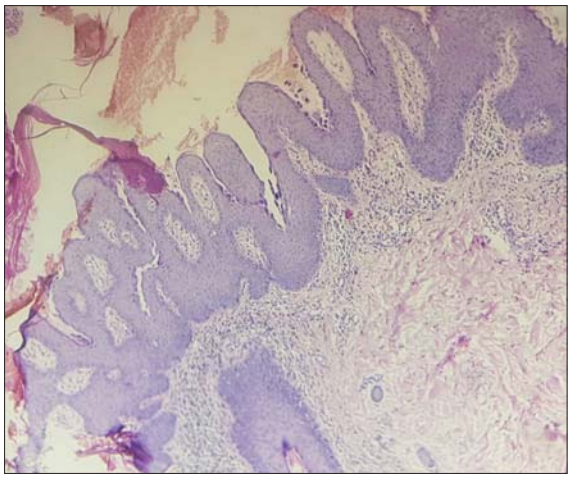

Figure 2: Histological image showing superficial acantholysis and a papillomatous epidermis.

Unlike pemphigus vulgaris, seborrheic pemphigus is clinically characterized by erythematous squamous lesions rather than bullous lesions. Thus, lesions of seborrheic pemphigus may more closely mimic postoperative wound infections and contact eczema. This can lead to delayed diagnosis, especially in patients with no history of pemphigus [3].

Therefore, exercising clinical suspicion of the various dermatoses with koebnerization that can follow skin surgery may allow for a more rapid diagnosis and immediate management.

Consent

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Letter to the Editor

Clinical, histopathological, and dermoscopic features of melanotic macules of the glans penis

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Sir,

Melanotic macules of the glans penis are benign pigmented lesions that may clinically mimic melanomas [1-3]. Herein, we report a case of this condition with clinicopathological and dermoscopic findings.

A 37-year-old Japanese male presented himself with a five-year history of pigmented lesions on the glans penis. The patient underwent circumcision for the treatment of phimosis seven years ago but had no family history of melanoma.

A physical examination revealed serpiginous black and brown macules on the glans penis (Fig. 1a). Our differential diagnoses included melanotic macules, melanocytic nevus, pigmented lichen planus, and melanoma. A dermoscopic examination revealed multiple patterns, including a light brown structureless zone in the center with dark brown circles and dots and lines at the periphery (Fig. 1b). The lesion was generally globular and arranged asymmetrically. Sharp whitish lines were seen along the skin grooves, which excluded melanoma. A histopathological examination of a punch biopsy from the dark brown macule showed abundant melanin in basal keratinocytes without increase in melanocytes (Fig. 1c). There was no evidence of malignancy. Based on these features, the diagnosis of melanotic macules of the glans penis was reached.

Dermoscopy is a useful method for the accurate diagnosis of pigmented skin lesions, particularly melanomas [1]. The number-needed-to-excise (NNE) value is calculated by dividing the total number of lesions excised by the number of malignant melanomas. A study of over 300,000 cases of melanomas and melanocytic nevi demonstrated that NNEs were significantly lower in "specialized clinical settings" than in "non-specialized settings," and improved over time only in "specialized clinical settings"—which might have been contributed to by more frequent use of dermoscopy [2].

Pigmented lesions of the genital region are relatively uncommon [1-3]. Particularly, there have been only a few dermoscopic studies of pigmented genital lesions in males [4], whereas vulvar melanotic macules have been more frequently studied with dermoscopy [5]. Cengiz et al. reported that melanosis was the most common pigmented lesion in the genital region, and that the glans penis was the most frequent location for pigmented lesions in males [4]. Half of the cases of melanosis of the genital region had multifocal lesions, of which approximately 70% showed two to three colors and half showed a globular pattern [4].

Our patient had a multifocal two-colored pigmented lesion with a globular pattern, which is considered a common dermoscopic feature of melanotic macules of the glans penis.

In conclusion, dermoscopy is a useful technique for the differentiation of melanotic macules of the glans penis from other pigmented lesions in the genital region.

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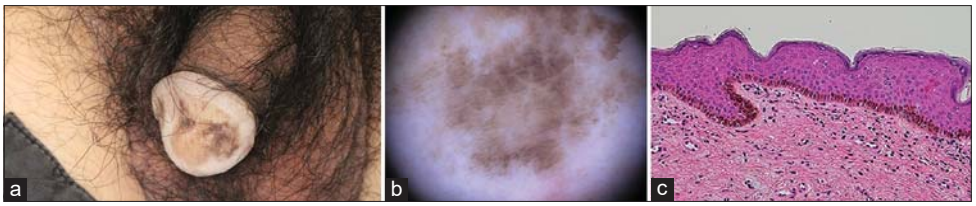

Figure 1: Clinical, dermoscopic, and histopathological features in our case. (a) Clinical features on the glans penis. (b) Dermoscopic findings. (c) Histopathological features (H&E, 400×).

Consent

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Letter to the Editor

Neglected mycosis fungoides transformed into cutaneous CD30⁻ T-cell lymphoma

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Sir,

Mycosis fungoides accounts for around half of primary cutaneous T-cell lymphomas. Prognosis is relatively favorable, but the possibility of several clinical presentations (large simulator) and the nonspecific nature of early eczema-like lesions delay the diagnosis and raise the possibility of transformation into other entities, whose prognosis might be more reserved and whose treatment might be intensified, as the following clinical case demonstrates [1-3].

A 45-year-old man with a history of chronic smoking, occasional alcoholism, and thin scaly arciform erythematous lesions evolving for more than 5 years and sitting at the roots of the limbs, buttocks, and sacral region (Fig. 1a and 1b). Consulted for an ulcerous, necrotic, and hemorrhagic tumor on the right elbow atop an arciform lesion, as much as 12 cm in diameter and evolving for 6 months in a context of conservation of the general condition (Fig. 2a). Clinical examinations revealed an axillary adenopathy 16 mm in diameter. Histology was in favor of mycosis fungoides with net epidermotropism without follicular mucinosis in the arcuate lesions. Mycosis fungoides transformed into CD30⁻ large T-cell lymphoma as an elbow tumor with lymph node involvement. The tumor was staged as T3N2M0, and the patient received polychemotherapy (8CHOP) with a favorable evolution over five years of recoil (Fig. 2b and 2c). Our case highlights the particular advantage of keeping such diagnosis before any chronic dermatosis in adults and of knowing how to perform and repeat skin biopsies before any suspicion of dermatosis.

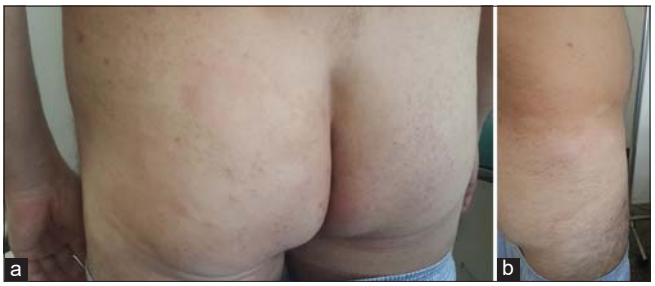

Figure 1: (a-b) Arcuate lesions with an infiltrated erythematous periphery and a hypopigmented center at the roots of the limbs, buttocks, and sacral region.

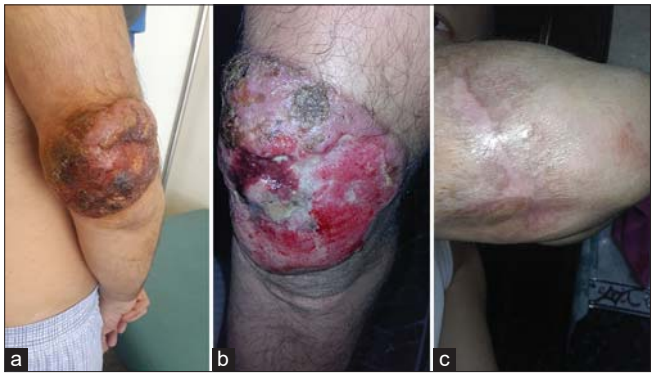

Figure 2: (a) An ulcero-budding tumor of the right elbow on a preexisting arciform lesion. (b-c) The tumor after the first and the last session of chemotherapy.

Consent

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Letter to the Editor

A case of pagetoid squamous cell carcinoma *in situ*: Bowen's disease of the glans penis requiring differentiation from extramammary Paget's disease

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Sir,

An 84-year-old Japanese male visited us with a six-month history of an erosive lesion involving almost the entire glans penis (Fig. 1a), unresponsive to topical diflucortolone valerate. The past history included only surgery for a left hip dislocation. The family history revealed no skin cancer.

All routine laboratory test results were within normal limits. MRI revealed neither subcutaneous invasion of the skin lesions (Fig. 1b) nor pelvic lymphadenopathy.

A skin biopsy revealed a thickened epidermis composed of tumor cells with disordered cell arrangement and inflammatory cell infiltration in the upper and middle dermis (Fig. 1c). There was no evidence of invasion of the tumor cells into the dermis. The entire epidermis was replaced by large pagetoid cells with clear, slightly basophilic cytoplasm, and intercellular bridges were present between the clear cells (Fig. 1d).

As the differential diagnoses of the intraepithelial neoplasia on the glans penis with a cellular morphology resembling Paget's disease, which was found in our patient, we considered four diseases: primary extramammary Paget's disease (EPD) [1], secondary EPD as epidermotropism of coexisting dermal or internal malignancies in the pelvis [2], malignant melanoma *in situ* [3], and squamous cell carcinoma (SCC) *in situ* (Bowen's disease) [4]. SCC *in situ* (Bowen's disease) confined to non-hair bearing genital areas is also referred to as erythroplasia of Queyrat.

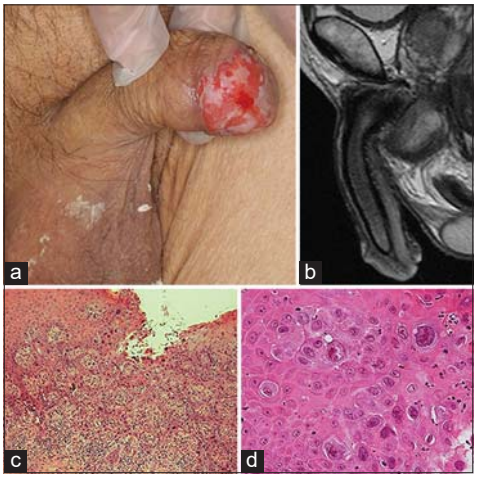

Figure 1: Clinical, MRI, and histopathological features in our case. (a) Clinical features of the lesion on the glans penis. (b) The results of MRI of the penile region. (c-d) Histopathological features under magnification: (c) 100× and (d) 400× (H&E).

We first excluded the possibility of malignant melanoma by epithelial morphology with intercellular bridges.

For the differentiation of the other three conditions, we performed immunohistochemical studies for cytokeratin-7 (CK-7) [1], CAM5.2 [2,3], and carcinoembryonic antigen (CEA) [4] as the markers for primary EPD, CK-20 [1] as the marker for secondary EPD, CK-5/6 [2] and p40 [5] as the markers for Bowen's disease. The tumor cells in our patient were positive for CK-5/6 and p40 (Fig. 2) and negative for CK-7, CK-20, CAM5.2, and CEA (data not shown).

The negative staining for CK-7, CAM5.2, and CEA excluded primary EPD. Although the negative staining

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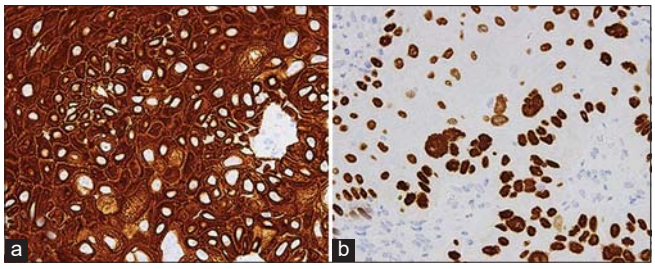

Figure 2: The results of immunohistochemical studies. (a) Staining for CK-5/6 (magnification: 400×). (b) Staining for p40 (magnification: 400×).

for CK-20 cannot completely exclude secondary EPD [1], the clearly positive staining for CK-5/6 and p40 of the tumor cells led us to the final diagnosis of pagetoid SCC *in situ* (Bowen's disease).

Because the lesions extended to the urethral meatus, to exclude invasion into the urethra, a urologist performed cystoscopy, which revealed no obvious neoplastic lesions in the urethra, bladder, or ureters. The corpus spongiosum and a portion of the urethra were resected according to the penile carcinoma protocol, although invasions into the dermis were not apparent. No recurrence was observed during a follow-up period of three years.

A literature survey revealed that our patient had been the seventh case of pagetoid Bowen's disease found in a genital area.

The patient had provided written informed consent 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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Letter to the Editor

Multiple vegetating tumors on the upper left limb

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Sir,

We report the case of a 54-year-old male without a significant medical history presenting to our department for multiple vegetating tumors located on the upper left limb seen for the past two months. A dermatological examination revealed multiple vegetating tumors confluent on the left arm with other well-circumscribed tumors on the left forearm (Fig. 1). There was no axillary lymphadenopathy. Laboratory values, including the level of lactate dehydrogenase (LDH) and the complete blood cell count, were within normal limits. Computed tomography of the thoracoabdominal region was normal, and there was no evidence of a systemic involvement. A skin biopsy of the vegetating tumor was performed, revealing an infiltration of the dermis extending to the deep dermis with large lymphoid cells (Fig. 2a). The tumor cells were large, pleomorphic, and anaplastic with round, irregularly shaped nuclei and abundant pale cytoplasm (Fig. 2b). The tumor cells expressed CD2, CD4 and, weakly, CD3. More than 75% of the tumor cells expressed CD30 (Fig. 2c). The tumor cells were also negative for EMA (epithelial membrane antigen) and ALK (anaplastic lymphoma kinase). Combined clinical and histopathological findings allowed us to confirm the diagnosis of primary cutaneous anaplastic large-cell lymphoma (PCALCL). The patient received radiotherapy treatment with a favorable outcome. A 4-year follow-up revealed no recurrence.

Herein, we report a case of primary cutaneous anaplastic large-cell lymphoma (PCALCL), which is characterized by large T cells with prominent nuclear polymorphism and expression of CD30 by more than 75% of the tumor cells [1]. In this particular type of T-cell lymphoma, there is, as in our case, a male predominance, also usually affecting elderly patients in the sixth decade of their life. Clinically, it can manifest itself as a solitary tumor or grouped nodules in an anatomical location with a rapid tumor growth. The lesions are often vegetating, as in our patient, but can also be ulcerated [2]. A location on the extremities, as in our case, represents the preferred site of PCALCL. The differential diagnosis includes mainly lymphomatoid papulosis type C, the tumor stage of mycosis fungoides, cutaneous metastases from an internal malignancy, systemic large-cell lymphoma, and cutaneous B-cell lymphoma. The main differential diagnosis is lymphomatoid papulosis, with which PCALCL shares clinical and histological features. The differences arise upon close clinical examination and medical history taking. In fact, the lesions of lymphomatoid papulosis are smaller and more diffuse, and do not progress with time [2].

Besides, histopathology and an immunohistochemical study are the key to the diagnosis of PCALCL.

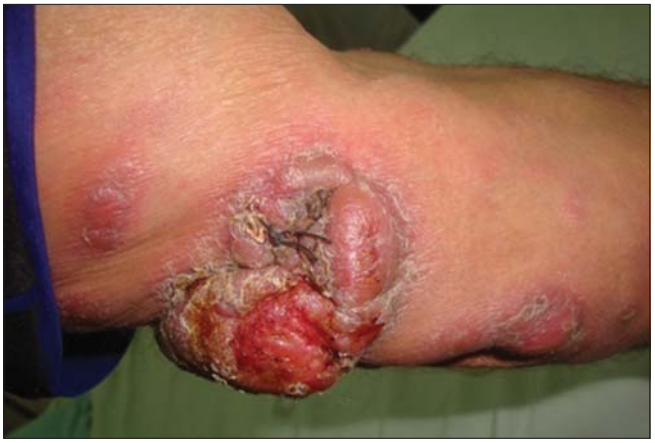

Figure 1: Multiple vegetating tumors on the left arm.

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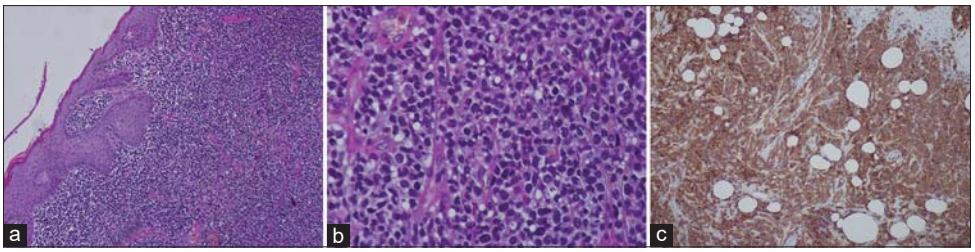

Figure 2: (a) Dense lymphocytic infiltration of the dermis (H&E, ×40). (b) Large pleomorphic and anaplastic lymphoid cells (H&E, ×100). (c) CD30 stain highlights the large and anaplastic tumor cells.

Typically, the tumor manifests itself as circumscribed nodular infiltrate of an arrangement of large lymphoid cells extending to the deep dermis, with tumor cells often pleomorphic, anaplastic, with round, irregularly shaped nuclei and abundant pale cytoplasm [3]. Epidermotropism is usually absent. The characteristic feature of PCALCL is expression of CD30 by at least 75% of its tumor cells, as defined by the WHO classification [4]. Treatment relies mainly on surgical excision of the tumors and radiotherapy for solitary and grouped lesions at a dose of 20 Gy. Chemotherapy is advised for extracutaneous tumors spread beyond locoregional lymph nodes. This type of lymphoma typically gives a good prognosis with a 5-year survival rate of 90% [4].

In summary, primary cutaneous anaplastic large-cell lymphoma (PCALCL) is both a diagnostic and a therapeutic challenge. Our case highlights the importance of clinicopathological correlation and the importance of early diagnosis and treatment to avoid disease progression and unnecessary aggressive treatment modalities. However, even in the presence of a good prognosis, long-term follow-ups are necessary.

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 have given 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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Letter to the Editor

Apocrine hidrocystoma of the scalp: Additional case report

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Sir,

We have read with interest a recent report by Dahhouki et al. on a case of apocrine hidrocystoma in a rare location [1]. Herein, we describe an additional case of apocrine hidrocystoma that appeared on the scalp. The patient had a history of lung cancer, and a skin biopsy was performed to rule out skin metastasis.

An 80-year-old female, diagnosed with lung adenocarcinoma (pT1bN0M0, stage IA) two years before, was referred to our department complaining of an asymptomatic scalp nodule that appeared a few months prior to the referral. The lung cancer was surgically resected and the subsequent metastasis to the brain was treated with radiation. A physical examination revealed a smooth, dome-shaped, light blue nodule 1 cm in size on the scalp (Fig. 1). The patient had not received any treatment for the lesion. A skin biopsy was conducted to rule out skin metastasis. Histological features involved a cyst wall consisting of one to several layers of epithelial cells, some of which showing decapitation secretion indicative of apocrine secretion (Figs. 2a and 2b). The parietal cells did not show atypia and no inflammatory cell infiltration was observed. Immunohistochemistry demonstrated that the tumor cells were strongly positive for CEA and partially positive for 34βE12 (Figs. 3a and 3b), but negative for EMA, GCDFP-15, S-100, CK20, CAM5-2, and α-SMA. Therefore, a diagnosis of apocrine hidrocystoma was established.

Apocrine hidrocystomas are benign cystic tumors that arise from the secretory portion of apocrine sweat glands in middle-aged and elderly people. They most frequently occur on the face—with a frequency of over 60%—followed by the trunk, extremities, and scalp [2]. According to an analysis of 167 Japanese cases conducted between 1968 and 2003 by Anzai et al. [3], tumors were most commonly found on the face (n = 102; 61.1%), followed by the trunk (23; 13.7%), the scalp (21; 12.6%), and the extremities (20; 12.0%). As far as we know, there have, since 2003, been three cases of apocrine hidrocystoma on the scalp [4-6]. One developed apocrine cystadenoma in a lesion associated with sebaceous nevus syndrome [4]. The other cases

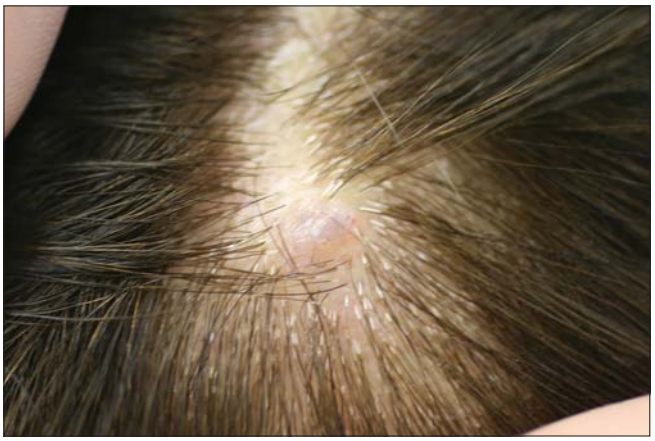

Figure 1: Smooth, dome-shaped, light blue nodule 5 mm in diameter on the scalp.

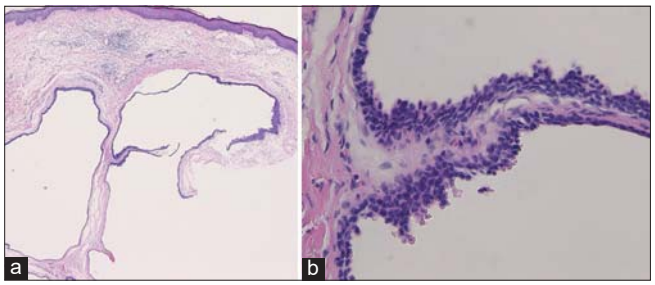

Figure 2: (a) Cystic structure in the dermis (H&E; 40×). (b) The epithelial cells with decapitation secretion further magnified (H&E; 200×).

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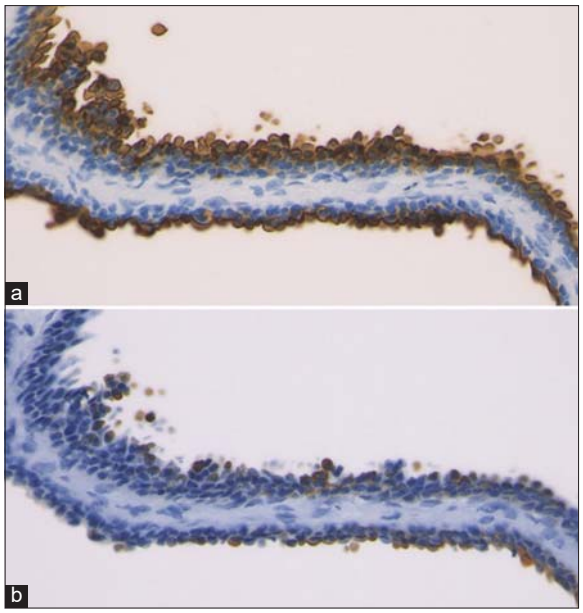

Figure 3: The tumor cells (a) strongly positive for CEA and (b) partially positive for 34βE12 (H&E; (a-b): 200×).

showed clinical features mimicking subcutaneous dermoid cysts [5] and a giant cell tumor [6]. We suggest that apocrine hidrocystoma ought to be considered as a differential diagnosis of cystic tumors on the scalp.

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

Letter to the Editor

"Bouquet of white roses": A dermoscopic marker for hypertrophic lichen planus

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Sir,

Lichen planus hypertrophicus manifests itself clinically as itchy hyperkeratotic plaques and nodules and is a condition easily confused with prurigo nodularis, lichen simplex chronicus, and many others. There are certain dermoscopic features more specific to lichen planus hypertrophicus, such as corn pearls and blue-grey globules [1]. Herein, we propose a new dermoscopic metaphor, "bouquet of white roses," specific to lichen planus hypertrophicus, as well as explain its evolution.

A 48-year-old patient presented itchy, hyperkeratotic, violaceous-to-grey lesions on the lower extremities persistent for the past two years (Fig. 1a). Dermoscopy was performed with a DermLite III dermatoscope with 10× magnification and polarized light. The dermoscopic examination revealed comedo-like openings filled with keratinous plugs and corn pearls along with Wickham's striae. A diagnosis of hypertrophic lichen planus was considered (Fig. 1b). Dermoscopic evaluations were subsequently performed every few months. At first, the corn pearls increased in number to, later, begin to increase in both number and size: hyperplasia and hypertrophy setting in (Figs. 2a–2c). Seven months previously, the same patient developed a nodule on the preexisting plaque. Dermoscopy revealed that the hypertrophied corn pearls had begun to aggregate (Fig. 2d). A few months later, the nodule further increased in size to form a verrucous mass. The dermoscopic picture now showed a conglomeration of corn pearls in a curvilinear manner, each spiraling toward the apex. This structure was akin to the arrangement of the petals of a white rose and the conglomeration of these structures together resembled a "bouquet of white roses" when viewed aerially. This phenomenon corresponds histologically to the hyperkeratosis atop wedge-shaped hypergranulosis enclosed in hyperplastic appendages [2]. A biopsy of the nodule confirmed the diagnosis of hypertrophic lichen planus and ruled out malignancy (Fig. 2e – 2g). This sign is not seen in other forms of lichen planus as the degree of hyperkeratosis essential to produce a conglomeration of such structures is absent in other forms. The hyperkeratosis in hypertrophic lichen planus lies atop follicular or acrosyringeal openings and this is not the scenario in prurigo nodularis and lichen simplex chronicus. Hence, the hyperkeratosis with underlying wedge-shaped hypergranulosis centered atop hyperplastic appendages in hypertrophic lichen planus produces the "bouquet of white roses" on dermoscopy and this sign is absent in other hypertrophic conditions [3,4].

Thus, we propose that the presence of the dermoscopic sign of "bouquet of white roses" not only delineates hypertrophic lichen planus from other forms of lichen planus but also helps to establish a clinical diagnosis of hypertrophic lichen planus ruling out other hypertrophic clinical mimics.

Consent

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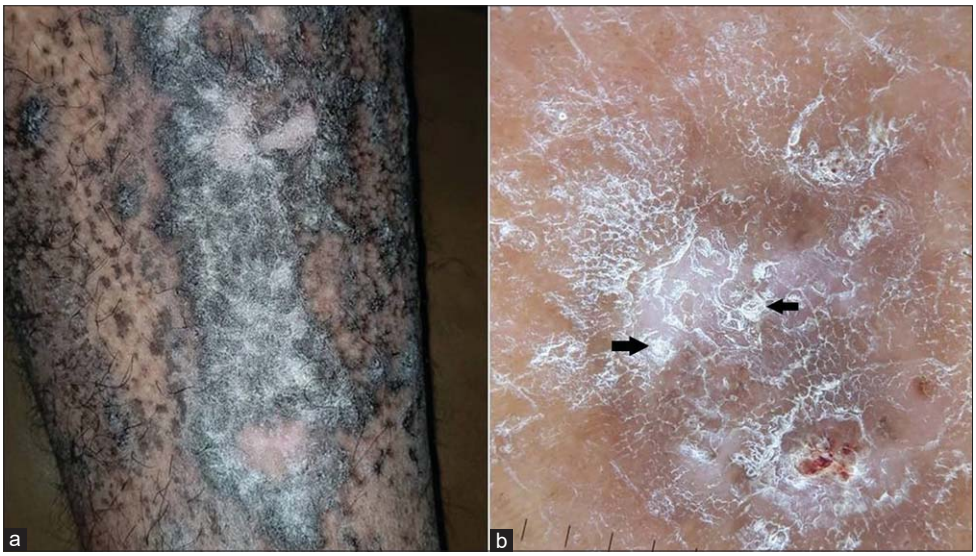

Figure 1: a. Multiple hyperkeratotic and hypertrophic violaceous-to-grey plaques on the shin persistent for two years. b. Dermoscopy of these plaques showed the presence of several corn pearls (at the arrows): comedo-like openings filled with keratinous material. Note the presence of Wickham's striae between the corn pearls. Wickham's striae are seen as pearly white structures. Dermoscopy demonstrated classical signs of hypertrophic lichen planus.

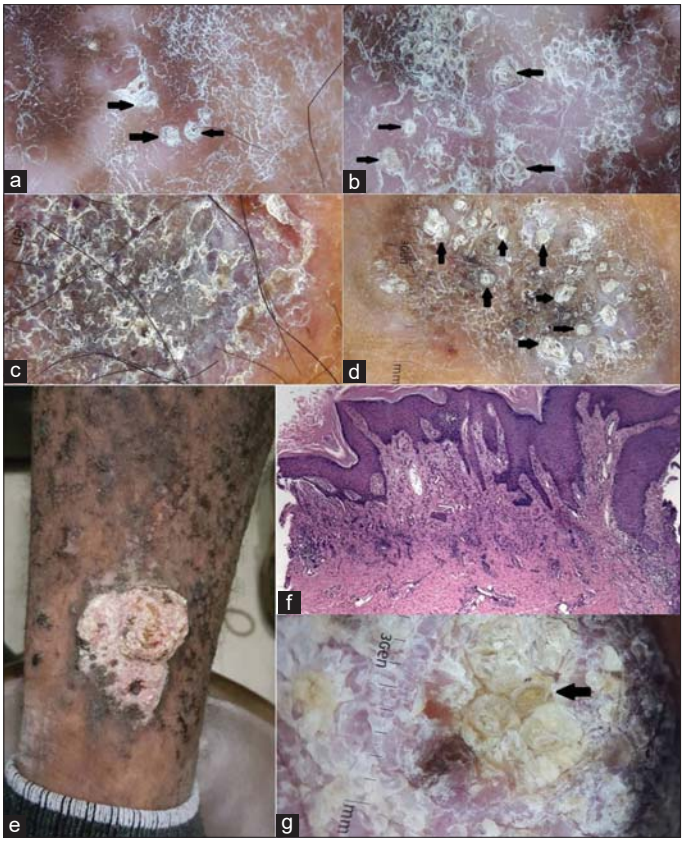

Figure 2: a.Repeated dermoscopic evaluation showed an increase in the number of corn pearls. b. Over a period of time, the corn pearls increased in size as well and showed some degree of hypertrophy. c. A subsequent dermoscopic evaluation demonstrated a simultaneous increase in the number and size of the corn pearls. d. As the patient developed a small nodule on a preexisting plaque of lichen planus, the hypertrophied corn pearls began to aggregate. e. The nodule increased in size to form a white-to-pink verrucous mass. f. Dermoscopy of the nodule showed that the corn pearls had conglomerated to form a "bouquet of white roses." g. A biopsy showed irregular epidermal hyperplasia. Wedge-shaped hypergranulosis was seen within hyperplastic appendages. The conglomerated corn pearls on dermoscopy, which formed the "bouquet of white roses" sign, histologically corresponded to the hyperkeratosis atop wedge-shaped hypergranulosis enclosed in hyperplastic appendages. (H&E, 10×).

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Letter to the Editor

A case of generalized morphea complicated by autoimmune hepatitis

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Sir,

Morphea, also known as localized scleroderma, is a fibrosing disorder of the skin and underlying tissues. Morphea is differentiated from systemic sclerosis based on the absence of sclerodactyly, Raynaud's phenomenon, and nail fold capillary changes [1]. It is mainly classified into five groups: plaque, generalized, bullous, linear, and deep [2]. With certain exceptions, it produces no serious systemic complications but is sometimes associated with autoimmune disorders, such as Hashimoto thyroiditis, rheumatoid arthritis, and alopecia areata [3]. Herein, we report a case of generalized morphea (GM) complicated by autoimmune hepatitis (AIH).

In 2002, a 27-year-old male presented himself with generalized sclerotic skin lesions, which he noticed two months earlier. There were no other systemic symptoms, and the patient denied exposure to organic solvents. A clinical examination revealed multiple well-defined, indurated, ivory-colored plaques on the trunk and extremities (Fig. 1a and 1b). Neither sclerodactyly (Fig. 1b) nor Raynaud's phenomenon was present. A histopathologic examination of the upper arm revealed swollen collagen bundles (Fig.1c) and inflammatory cell infiltrate composed of lymphocytes and plasma cells around blood vessels and sweat glands (Fig. 1d). A diagnosis of GM was reached and oral prednisolone 40 mg/day was initiated. Following the improvement of the skin lesions, prednisolone was gradually tapered to 5 mg/day. However, the patient failed to attend the scheduled clinical appointment and discontinued the prescribed medication in 2007. In 2013, the patient presented himself with an aggravation of the preexisting skin lesions. Laboratory tests revealed increased liver values (AST at 300 IU/L, ALT at 835 IU/L, GGT at 157 IU/L, and total bilirubin at 2.9 mg/dL). There was an increase in the serum level of IgG at 3,485 mg/dL and IgA at 816 mg/dL. An immunological investigation revealed positive anti-nuclear antibodies (ANA) (1:160, homogeneous), with negative antibodies to smooth muscle, mitochondrial, liver-kidney microsome type 1 (LKM-1), centromere, Scl-70, RNA polymerase III, U1 RNP, dsDNA, and histone. Viral serologies, including the anti-hepatitis A IgM antibody, hepatitis B surface antigen, and anti-hepatitis C virus antibody, were negative. A liver biopsy revealed lymphocellular and plasmocellular infiltrate in portal areas and rosetting of hepatocytes (Fig. 1e and 1f). He denied a history of hepatotoxic medication or alcohol abuse. A diagnosis of AIH was reached and the patient was administered intravenous methylprednisolone 500 mg/day for three days followed by oral prednisolone 40 mg/day. The patient has been in a remission of AIH with no progression of the skin lesions over five years on a maintenance dose of prednisolone 5 mg/day.

AIH is a chronic inflammatory liver disease characterized by elevated serum aminotransferases, elevated IgG, the presence of autoantibodies, and interface hepatitis with plasma cell infiltration in liver biopsies. AIH is often associated with autoimmune disorders such as autoimmune thyroiditis, and ulcerative colitis [4],

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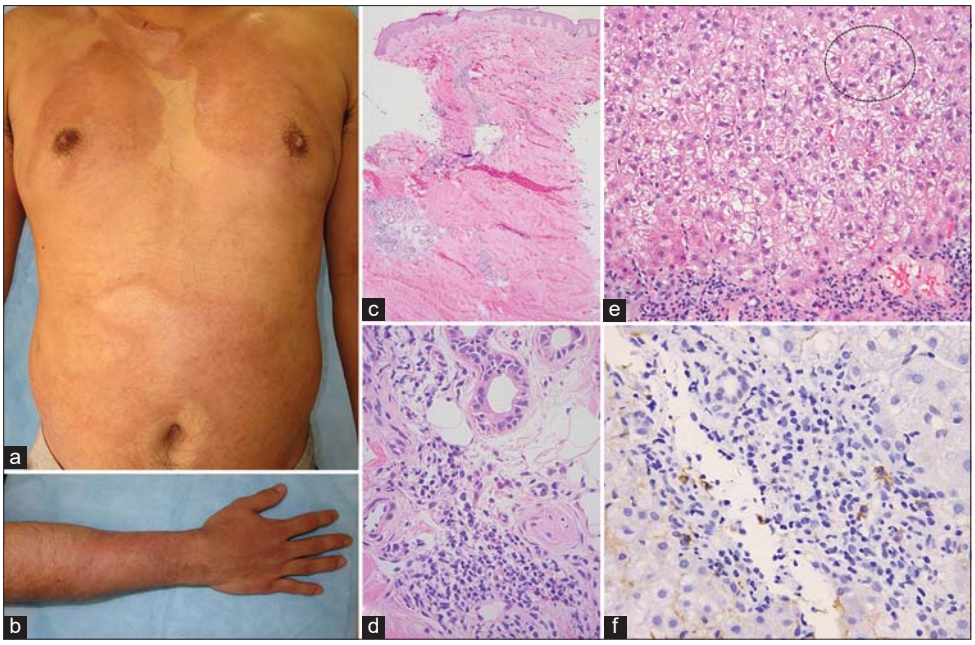

Figure 1: (a) Multiple well-defined, indurated, ivory-colored plaques on the trunk. (b) Sclerosis of the right forearm with the right hand and fingers intact. Histopathologic examination of a skin biopsy from the upper arm showing (c) swollen collagen bundles, replacing the fat around the sweat glands and extending into the subcutis (H&E, 50×) and (d) inflammatory cell infiltrate composed mainly of lymphocytes and plasma cells around blood vessels and sweat glands (H&E, 400×). Histopathologic examination of a liver biopsy showing (e) rosetting of hepatocytes (at the dotted circle) and lymphocellular and plasmocellular infiltrate in portal areas (H&E, 200×) and (f) immunohistochemical staining of the specimen with CD138 (marked brown) showing infiltration of plasma cells (H&E, 400×).

whereas there have been only two cases of AIH associated with morphea: One case involved GM affecting the extremities and the trunk [5]; the other was located on the buttock and on the right thigh [6]. In both, steroid-based immunosuppressive therapies were initiated [5,6]. A recent review of 245 cases of morphea revealed that GM produces a higher prevalence of concomitant autoimmune disorders and ANA positivity than the other types of morphea, such as plaque or linear [7]. In our case, the development of AIH after discontinuation of prednisolone reinforces the opinion that GM is a systemic disorder and ought to be monitored against the presence of autoimmune disorders and treated with immunosuppressant drugs if indicated.

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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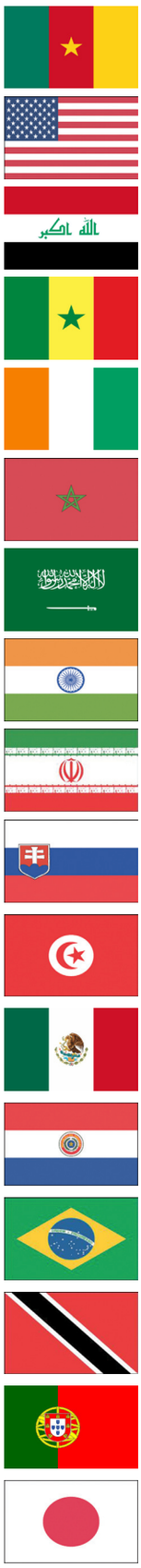

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