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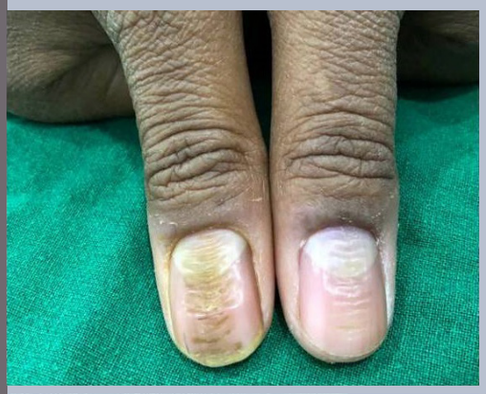

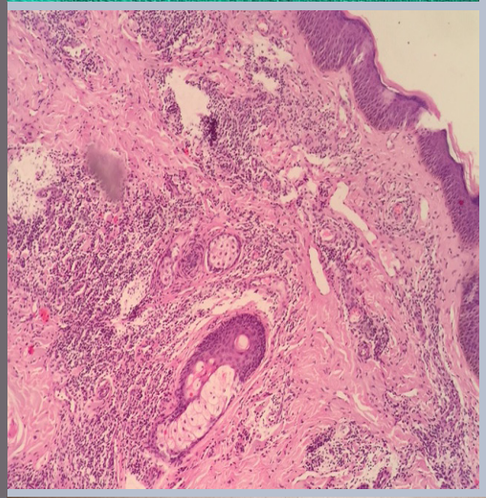

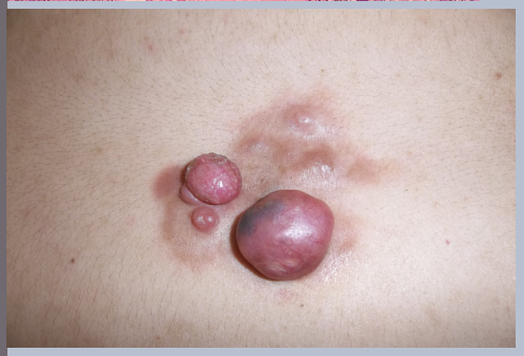

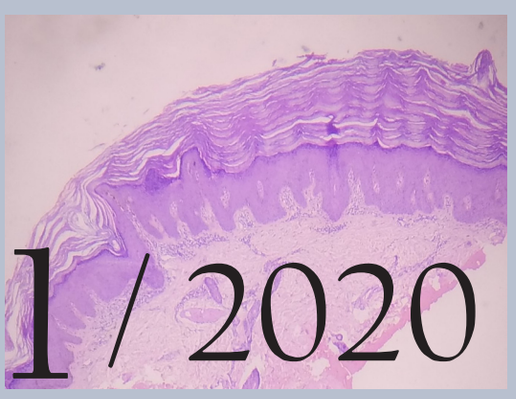

Editorial Pages

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Original Article

Candida balanitis. Clinical and mycological study about the efficacy of a single-day oral treatment with itraconazole (400 mg)

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ABSTRACT

Objective: To assess the efficacy of a single dose of itraconazole (400mg/day), divided into two doses in the treatment of Candida balanitis. **Material and Methods:** We carried out a prospective, non-compared study in patients with clinically verified *Candida* balanitis and through direct examinations, stains and cultures. Each of the patients was given a treatment scheme of itraconazole 400mg/day, divided into two doses. Revisions were carried out at baseline and subsequently on days 3, 7, and 15. **Results:** We included 26 cases, with an average age of 43.5 years. A predominance of *Candida albicans* was obtained in 69.2% and the remaining were *Candida* non-*albicans* species. At the end of the treatment and follow-up for 7 days, clinical and mycological cure was obtained in 22/26 patients (84.6%). Side effects were presented in two patients (7.7%), one with moderate dyspepsia and the other with moderate headache. **Conclusion:** The treatment of *Candida* balanitis with a single dose of 400mg of oral itraconazole is effective, well tolerated and represents a new therapeutic alternative of short duration.

Key words: Balanitis; *Candida albicans*; *Candida* no-albicans; Itraconazole; Treatment

INTRODUCTION

Balanitis caused by several species of *Candida* or *Candida* balanitis (CB), is an opportunistic mycosis that is observed with relative frequency, representing 11% of sexually transmitted diseases (STD) [1-3], and 30-35% of the infectious balanitis [4,5]. It is commonly observed in acute or subacute form (5-7 days) and usually affects young adults. CB clinically manifests in the form of a balanitis or balanopostitis, affecting the mucosa of the penis, particularly glans, body of the penis (balanitis) and balanoprepucial zone (balanopostitis), as erythematous plaques often with micropustules and whitish plaques, which over time evolvedto erythematous plaques with erosions and fissures. Patients initially refer moderate to severe itching and subsequently burning [2,6].

CB is a classic opportunistic infection caused mainly by *Candida albicans*, but also by other *Candida* spp. Its presence is closely related to vulvovaginitis and most cases are influenced by sexual activity in women who have the disease or simply, have an increased microbiota of *Candida* sp. Other risk factors include: diabetes mellitus; chronic use of topical and systemic corticosteroids, as well as immunosuppression [2,6,7].

Diagnosis of CB is eminently clinical and should be corroborated with mycological tests [4,6,8].The treatment of CB include one of the following options: Topical treatments include nystatin or imidazolic derivatives such as clotrimazole, ketoconazole, or fenticonazole. However, though the mentioned treatment is particularly useful, the time of therapy is longer and thus, the decrease in symptoms and

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signs is slower and some authors have reported significant local irritation [1]. Fluconazole is a triazole derivative and the most effective and fast-response oral antifungal, and it is considered to be the treatment of choice according to the treatment guidelines [6,7].

This study aims to assess the efficacy of a single dose of itraconazole (400mg/day), divided into two doses in the treatment of CB.

MATERIAL AND METHODS

In this prospective and non-controlled study, we included uncircumcised patients with balanitis and balanopostitis caused by *Candida* species. All patients gave their informed consent before they were admitted to the study. CB was diagnosed clinically and by the following mycological studies: Direct examinations with KOH (10%) and blue cotton, observing pseudohyphae and blastoconidia or only abundant blastoconidia. Isolation in two culture media: Sabouraud dextrose agar, Biggy-Nickerson (Difco Co®) and CHROMagar-Candida®. The identification of *Candida* species was made by the reading of the second culture medium and confirmed by the degradation of carbohydrates by the commercial biochemical method of API-yeast-20® and confirmed by the proteomic method of MALDI-TOF MS (VITEK2®) [4,8,9].

The treatment scheme was a single dose of 400mg of oral itraconazole, distributed into two doses: 200mg after breakfast and 200mg after dinner. Clinical reviews and mycological studies were carried out: at baseline and on days 3, 7, and 15 after medication. During the follow-up time, the patients receive any topical or oral antifungal and those patients who presented signs and symptoms of balanitis at visit 3 (7 days after medication), and positive mycological study (yeasts and pseudohyphae), were considered therapeutic failures and continued with another therapy.

Statistical Analysis

Clinical and mycological data were analyzed by using chi-square test to compare the results of treatment during control visits. Fisher exact test was used when expected values were less than 5. Statistical significance was set at P= <0.001. SPSS version 23 for Windows was used for analysis.

RESULTS

Twenty-six cases of balanitis and balanoposthitis caused by several *Candida* species were included. The main demographic and mycological data of the study is presented in Table 1.

In all cases, the response to treatment was evaluated at baseline and subsequent visits (3, 7, and 15 days). The results were the following: At visit 2 (3 days after treatment), three patients showed signs or symptoms of CB and tested positive for mycological studies. At visit 3 (7 days of follow-up), one more patient presented clinical and mycological activity. At visit 4 (15 days of follow-up), only 19 patients attended to the evaluation, of which none had signs or symptoms of CB, and direct examinations and cultures were negative (Table 2).

The clinical cure of balanitis was observed from 3 days of use of itraconazole, at 15 days of management with itraconazole efficacy was in 100% of cases (Table 2). In Table 3, it is mentioned that the mycological cure

Table 1: Main demographic and mycological data of the study

Male patients	26 cases
Age (years), range.	43.5 (18-72)
Disease evolution (days), range.	5.6 (2-18)
Predisposing factors, (%)	
After sexual contact.	15 (57.7)
Topical corticosteroid use	4 (15.38)
Type 2 diabetes mellitus	3 (11.53)
After sexual contact + typo 2 DM	1 (3.84)
None identified	3 (11.53)
Direct examination (%)	
Pseudohyphae and blastoconidia	22 (85)
Only blastoconidia	4 (15)
Etiologic agents (%)	
Candida albicans	18 (69.23)
Candida glabrata	4 (15.38)*
Candida tropicalis	2 (7.69)
Candida krusei	1 (3.84)
C. albicans + C. glabrata	1 (3.84)

Table 2: Clinical efficacy of itraconazole in patients with *Candida* balanitis

Clinical examination	3 days (%)*	7 days (%)*	15 days (%)*
Cure	23 (88.5)	22 (85)	19 (100)
Failure	3 (11.5)	4 (15)	0
Total	26 (100)	26 (100)	19 (100)

* x^2, P= ≤0.01

Table 3: Mycological efficacy of itraconazole in patients with *Candida* balanitis.

Mycological examination	3 days (%)	7 days (%)	15 days (%)
Candida albicans	16 (89)	16 (89)	13 (68.4)
Candida non-albicans	6	6	5 (31.6)
Total	22 (100)	22 (100)	18 (100)

Mixed case was excluded for analysis. * Fisher, P= ≤0.01.

of balanitis in *Candida albicans* species was observed from 3 days of use of itraconazole in 73% of the cases, maintaining this efficacy at 15 days of management. In *Candida* non-albicans species was 27% in 3 weeks, not modified at 15 days of treatment.

The four patients who failed treatment had the following predisposing factors: 2 had previous treatments with topical steroids and the other two had type 2 diabetes mellitus. Three of the therapeutic failure cases were caused by *C. albicans* and one case by *C. tropicalis*. The rest of the etiological agents, included the mixed case, presented therapeutic success (Table 3). Side effects were present in two patients (7.7%). One patient showed moderate dyspepsia and one had a moderate headache. None of the patients required additional treatment.

DISCUSSION

Clinically, balanitis and balanoposthitis can present in a similar way. Most of them are caused by yeasts, especially *Candida* spp. Some reports indicate that in a third of the cases, these are caused by bacteria, especially b-hemolytic *Streptococcus*, *Staphylococcus aureus*, *Pseudomonas* sp., and *Gardnerella vaginalis*, among others [1,5,10-13].

Mycotic balanitis is frequently caused by *C. albicans* and, to a lesser extent, by other *Candida* species, and exceptionally by other yeasts such as: *Rhodotorula mucilaginosa* and *Saccharomyces cerevisiae* [6,7,12,13]. *Malassezia spp.* have also been reported. Its role is like normal microbiota of the preputial space and probably influences the condition [6,13,14]. CB is an infection that is directly related to *Candida* vulvovaginitis (VVC) due to sexual relations (vaginal, anogenital, and urogenital) and other predisposing factors [1-3,15,16]. In general, CB is a superficial infection, of a rapid course and with few complications, but occasionally, it can cause urethritis [16].

In CB, systemic antifungals are the main choice of treatment. The advantage of oral therapy over topical therapy is that it is simpler and faster than the second, leading to a faster decrease in signs (erythema and fissures) and symptoms (itching and burning) [2,12,17,18].

The first oral antifungal that showed great impact on genital candidiasis was ketoconazole. Its use is currently limited due to side effects and drug interactions [6,19]. Subsequently, triazole derivatives emerged with a higher spectrum indicated for mycosis and exhibiting lower MICs against the different species, allowing the shortening of the treatment schemes [18,19].

The first short-treatment scheme for genital candidosis (VVC and CB) was fluconazole, often used in adults at a single 150mg dose. It obtained a high rate of therapeutic response. In some studies, the cure percentage was 92% [18]. Moreover, the European guidelines for the management of CB considered that fluconazole is the first-line treatment for CB [7]. However, one of the drawbacks of the indiscriminate use of fluconazole is related to the high resistance acquired by various strains of *C. albicans*, and non-albicans species, especially *Candida krusei*, which has developed an intrinsic resistance, and *C. glabrata*, which has developed an acquired resistance [6,7,19]. Despite the fact that fluconazole and itraconazole are two triazolic derivatives, they have not been shown to share the resistance to the triazole ring [20].

Our study aims to determine the efficacy of a single 400mg dose of itraconazole for the management of CB. This scheme has been tested with good results in cases of VVC and in CB isolated cases [10,21]. According to our study, the cure rate after three days of follow-up was 88.5 and it was 85% after 7 days.

In our study, we observed that at three days of treatment, 23/26 patients (88.5%) showed decreased signs and symptoms of the disease. On the other hand, when a patient developed relapse, this was caused by the same etiologic agent. According to the statistical analysis, it is concluded that both groups of species (*C. albicans* and *C.* non-*albicans*) are cured within 3 days and do not present recurrence 15 days later. The results that we obtained can be compared with those obtained in VVC. Although they are clinically different entities, some reports indicate that results of efficacy can be achieved by more than 95% [21,22]. Spacek et al [23], obtained better results with a single 400mg dose compared to the dose of 200mg for three days, with the clinical and mycological cure in 97.1% and 76.9% respectively, indicating that the first one is effective in VVC and, according to our study, also in CB.

Sixty-nine percent of our cases were caused by *C. albicans* and the remaining by non-*albicans* species. This is similar to the observed results in other studies [1,2,4,10]. We observed that the therapeutic failures were presented in three strains of

C. albicans and one of *C. tropicalis*, while in the four cases produced by *C. glabrata* and one by *C. krusei*, therapeutic successes were obtained in all patients. This is relevant for clinical practice, since the last two species are resistant to fluconazole, and itraconazole is an effective option [6,19].

A possible explanation for the therapeutic failure of the four cases (15.38%) is not related to the etiological agent, because itraconazole has a spectrum and MICs are suitable for most species, but to the predisposing factors [20]. Therapeutic failure was observed in two patients who previously used topical steroids, while among the other two cases of failure occurred in diabetic patients, so we recommend that the use of a short 400mg dose is not enough in cases with a predisposing factor, and it probably requires a prolonged treatment.

There are no comparative studies between itraconazole and fluconazole in CB. However, in the literature, there are reports in VVC [24] pointing to a greater efficacy of itraconazole when compared with fluconazole (93.8% vs 79.03% respectively, $P=.008$). However, Pitsouni et al [25] reported a meta-analysis of controlled and randomized studies, indicating that both drugs are effective without statistically significant differences. A recent study of Hu et al [26] reported a case of penile infection by *C. albicans*, with proven resistance to fluconazole and terbinafine, and it was successfully treated with itraconazole.

In our trial, we did not perform laboratory studies to evaluate possible drug adverse events, due to the fact that the hematological and hepatic abnormalities are not detected at the dose used [20]. It is usual for other types of mycosis such as onychomycosis or deep mycosis to be managed at higher doses and longer times without presenting alterations. It is important to emphasize that both triazolics (fluconazole and itraconazole) have drug interactions due to the metabolism of cytochrome p-450 (CYP 3A4) [27] however, when administered in a short duration schedule in particular at a single dose, it is difficult to present. The absorption of itraconazole is limited with the use of antacids, and thus its concomitant administration should be avoided [20].

Only two patients presented collateral symptoms (7.7%). One patient presented with dyspepsia and the other with moderate headache, both effects have been previously reported [20] and did not require additional treatment.

It is necessary to perform future comparative studies between itraconazole (400mg) and fluconazole (150mg) in a short scheme, which would give us a better picture of both drugs in the management of CB.

CONCLUSIONS

According to the results, we conclude that the use of itraconazole at a dose of 400 mg/day divided into two doses is effective and safe for CB with high cure rates. The treatment of CB should begin with mycological diagnosis and confirmation, identification of the etiological agent, and evaluation and control of possible predisposing factors, as well as include clinical follow-up after treatment.

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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Original Article

Clinical patterns and associated comorbidities of vitiligo in Kandahar, Afghanistan. A case-control study

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ABSTRACT

Background: Vitiligo is an idiopathic acquired depigmentary skin/mucous membrane disorder. Main objective of this study was to find out demographic data, clinical patterns, and comorbidities associated with vitiligo in Kandahar, Afghanistan. **Material and Methods:** This was a case-control study conducted in Kandahar University Teaching Hospital between July 2017–June 2018. Descriptive statistics, Chi-square test, and logistic regression were used for data analysis. **Results:** A total of 400 patients (200 cases and 200 controls) were recruited. Mean age ± standard deviation (SD) of cases were 21.7±13.8 with most of the patients (77/200 [38.5%]) in age group 11–20 years. Female cases were more (107/200 [53.5%]) than males. Family history of vitiligo, accompanying altered immunity and autoimmunity disorders, psychological stress, premature graying of hair, halo nevus, vitamin D deficiency, vitamin B_{12} deficiency, and folate deficiency were present in 60/200 (30%), 26/195 (13.3%), 95/200 (47.5%), 31/200 (15.5%), 24/200 (12%), 22/200 (11%), 16/200 (8%), and 14/200 (7%) of the cases, respectively. Most of the patients (148/200 [74%]) had vulgaris, followed by focal (30/200 [15%]) and segmental (11/200 [5.5%]) types of vitiligo. Logistic regression analysis showed that family history, accompanying altered immunity and autoimmunity disorders, premature graying of hair, halo nevus, and atopic diathesis were the possible risk factors of vitiligo with odds ratios of 37.1, 9.0, 6.0, 13.9, and 3.9 respectively. **Conclusions:** Vitiligo affects women more than men, observed mostly in second decade of life. Vitiligo vulgaris is the most prevalent type.

Key words: Vitiligo; Kandahar; Afghanistan; Clinical patterns; Comorbidities; Skin

INTRODUCTION

Vitiligo is an acquired, idiopathic depigmentation disorder of skin and hair with characteristic white macules and patches. Vitiligo affects 0.1–2% of global population [1]. Highest incidence of this disorder is observed in India and Mexico [2]. In India, its prevalence is nearly 3–4% of patients visiting skin clinics of different hospitals [3]. Its prevalence is nearly equal between males and females [4]. Vitiligo causes decreased self-esteem, poor body images, problems in sexual relations, as well as cosmetically and psychologically devastating. Most of its impact on quality of life is observed in individuals with darker skin phototype [5].

Vitiligo is a refractory skin disorder for which the risk factors and treatment modalities have not yet been established [6]. Vitiligo has three clinical types, i.e., generalized vitiligo (spreads widely over the body), segmental vitiligo (dermatomal spread along the course of a nerve), and localized vitiligo (it is unclassifiable and can develop into either generalized or segmental type in the future) [7]. Pathogenesis of vitiligo has not yet been explained fully. Some of the proposed theories are autoimmune [8],

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neurogenic [9], self-destruct [10], genetic factors [11], biochemical defects [12], and recently transepidermal malanocytorrhagy [13]. Its onset is gradual and asymptomatic. The initial lesion usually has depigmented macules different in size, shape, number, and location with unpredictable course. However, it is progressive in >80% of patients [14]. Patients with a positive family history, mucosal involvement, isomorphic Koebner's phenomenon, and nonsegmental vitiligo are usually associated with progressive vitiligo. Presence of positive family history can be observed in 20–30% of cases [2] with polygenic or autosomal dominant gene inheritance. Vitiligo seems to be related with autoimmune disorders like thyroid disorders (especially hypothyroidism) [15], alopecia areata, type 1 diabetes mellitus [16,17], SLE (systemic lupus erythematosus), psoriasis, rheumatoid arthritis, Addison's diseases, and pernicious anemia [18,19]. The most commonly occurring autoimmune disorder is hypothyroidism.

Afghans are suffering from vitiligo too. This disorder is creating problems for all age groups, especially causing cosmetic problems and stigma in female and male adolescents before their marriages. Currently there is no published data showing the situation of vitiligo in Afghanistan. Null-hypothesis of our study was there is no difference in demographic data and associated factors between cases and controls. Main objectives of this study were to find out the epidemiology of vitiligo by observing the demographic data, clinical patterns of vitiligo, as well as common possible risk factors associated with vitiligo in Kandahar, Afghanistan.

MATERIALS AND METHODS

Study Design and Period

This was a case-control study. Data was collected from the patients who fulfilled the eligible criteria of the study during 1-year-period (July 2017–June 2018).

Study Population

The study population was comprised of cases (patients having clinically diagnosed vitiligo) and controls (patients not having vitiligo) attending skin OPD clinic of Kandahar University Teaching Hospital, Kandahar, Afghanistan. Controls were sex- and age-matched randomly selected patients.

Research Question

What are the demographic data, clinical patterns, and possible risk factors of vitiligo in Kandahar, Afghanistan?

Primary Objective

To find out the epidemiology of vitiligo by observing the demographic data and clinical patterns of vitiligo.

Secondary Objective

To assess the common possible risk factors associated with vitiligo in Kandahar, Afghanistan.

Inclusion Criteria

- Patients having clinically diagnosed vitiligo
- All age and sex groups
- Patient consenting to the study
- Permanent residents of Kandahar.

Exclusion Criteria

- Patients who do not want to take part in the study
- Patients with depigmentation of skin due to causes other than vitiligo
- Control group patient with autoimmune or altered immune disorders.
- Control group patient with family member in case group.

Sample Size Calculations

Sample size was determined using the formula: $n = Z2pq/d^2$. Our sample size was 200 patients. As it was a case-control study, 200 more subjects were added as controls.

Ethical Considerations

Written informed consents were taken from all the patients prior to the study. Names and other identification information of all the patients will not be disclosed. Ethical approval was taken from Kandahar University Ethics Committee.

Data Analysis

Data was analyzed using SPSS statistical software (version 22). For the analysis of data; descriptive statistics, Chi-square test, and logistic regression were

used. *P*-value of <0.05 was assumed as statistically significant.

Operational Definitions

1. Clinical patterns of vitiligo [20]
   - Focal vitiligo: lesions confined to one or a few patches localized in a particular area.
   - Segmental vitiligo: lesions distributed in a segmental/dermatomal pattern.
   - Acrofacial vitiligo: lesions noted over both face and acral regions.
   - Vitiligo vulgaris: lesions affecting many parts of the body.
   - Mucosal vitiligo: lesions confined only to mucous membranes.
   - Universal vitiligo: when more than 80% of the skin is depigmented.
2. Signs and symptoms of vitamin D deficiency [21]
   - Getting sick or infected often, fatigue and tiredness, bone and back pain, depression, impaired wound healing, bone loss, hair loss, muscle pain.
3. Signs and symptoms of B12 deficiency [22]
   - Pale or jaundiced skin, weakness and fatigue, sensation of pins and needles, changes to mobility, glossitis and mouth ulcers, breathlessness and dizziness, blurred vision, mood changes, high temperature.
4. Signs and symptoms of folate deficiency [23]
   - Persistent fatigue, Weakness, Lethargy, Pale skin, Shortness of breath, Irritability.

RESULTS

A total of 400 patients were recruited for this study, with 200 patients as cases and 200 as controls. The age and gender distribution were same in cases and controls with no statistically significant difference. Mean age ± standard deviation (SD) of the patients were 21.7±13.8 years and 21.1±12.7 years in cases and controls, respectively. Demographic characteristics of patients enrolled in this study are summarized in Table 1. More than half (107/200 [53.5%] and 108/200 [54%]) of the patients were females in both cases and controls, respectively. Family history of vitiligo was present in 60/200 (30%) and 3/200 (1.5%) patients in cases and controls, respectively (*p*-value <0.001). Among these patients, 37/66 (56.1%) were unemployed while 29/66 (43.9%) employed. More than half of the patients (35/66 [53%]) were students. Most of the patients (77/200 [38.5%] and 71/200 [35.5%]) were of age group 11–20 years in both cases and controls, respectively.

Table 1: Age distribution of the patients

Age group (years)	Cases		Controls	
	Frequency	Percent (%)	Frequency	Percent (%)
1–10	40	20	45	22.5
11–20	77	38.5	71	35.5
21–30	37	18.5	39	19.5
31–40	29	14.5	30	15
41–50	8	4	7	3.5
51–60	5	2.5	5	2.5
61–70	4	2	3	1.5
>70	0	0	0	0
Total	200	100	200	100

Among cases, most of the patients (148/200 [74%]) had vulgaris, followed by focal (30/200 [15%]) and segmental (11/200 [5.5%]) types of vitiligo. Different patterns of lesions are shown in Table 2.

Accompanying disorders with altered immunity and autoimmunity were present in 26/195 (13.3%) cases and 2/200 (1%) controls as compared to 169/195 (86.7%) cases and 198/200 (99%) controls not having any accompanying immune diseases. Among 26 cases having accompanying altered immunity and autoimmunity disorders, 6/26 (23.1%) were having alopecia areata while 6/26 (23.1%) were having atopic dermatitis. Only 2 control group patients were having accompanying altered immunity and autoimmunity disorders, with one patient having atopic dermatitis while one patient having psoriasis (Table 3).

Accompanying disorders with no altered or autoimmunity present among cases and controls are summarized in Table 4. Isomorphic phenomenon, premature graying of hair, and halo nevus were present in 63 (31.5%), 31 (15.5%), and 24 (12%) cases while in 0 (0%), 5 (2.5%), and 2 (1%) controls; respectively. Vitamin D, vitamin B_{12}, and folate deficiencies were present in 22 (11%), 16 (8%), and 14 (7%) cases while in 59 (29.5%), 3 (1.5%), and 2 (1%) controls; respectively. In all the above diseases, *p*-value was <0.05.

Logistic regression was conducted for all the variables with *p*-value <0.05. Highest odds ratio was seen in family history (37.12 with 95% CI 9.87–139.63) followed by halo nevus (13.89 with 95%CI 2.5–77.06) and accompanying altered immunity and autoimmunity disorders (9.04 with 95%CI 1.55–52.82). Lowest odds ratio was seen in vitamin D deficiency (0.09 with 95%CI 0.03–0.29) followed by folate deficiency (1.32

Table 2: Demographic characteristics of patients in both cases and controls

Variable	Cases		Controls		*p*-value
	Frequency	Percent (%)	Frequency	Percent (%)	
Gender					0.92
Male	93	46.5	92	46	
Female	107	53.5	108	54	
Total	200	100	200	100	
Occupation					0.16
Self-employed	24	36.4	25	39.1	
Government employee	5	7.6	3	4.7	
House wife	2	3	0	0	
Student	35	53	36	56.3	
Total	66	100	64	100	
Place of living					1.0
Urban	126	63	126	63	
Rural	74	37	74	37	
Total	200	100	200	100	
Place of living					
Kandahar City	121	60.5	126	63	
Arghandab District	5	2.5	3	1.5	
Spin Boldak District	13	6.5	13	6.5	
Shah Wali Kot District	6	3	12	6.0	
Arghistan District	3	1.5	1	0.5	
Maiwand District	7	3.5	3	1.5	
Zharai District	8	4	3	1.5	
Panjwai District	8	4	10	5	
Takhta Pul District	2	1	7	3.5	
Daman District	8	4	9	4.5	
Dand District	15	7.5	9	4.5	
Ghorak District	1	0.5	2	1	
Khak Rez District	2	1	1	0.5	
Nesh District	1	0.5	1	0.5	
Total	200	100	200	100	

Table 3: Different patterns of lesions

Pattern of lesion	Cases	
	Frequency	Percent (%)
Vulgaris	148	74
Focal	30	15
Segmental	11	5.5
Acrofacial	7	3.5
Mucosal	4	2
Universal	0	0
Total	200	100

with 95%CI 0.05–31.93) and psychological stress (1.57 with 95% CI 0.84–2.94) (Table 5). Logistic regression of our data showed that family history, accompanying altered immune or autoimmune disorders, premature graying of hair, halo nevus, and atopic diathesis were the possible risk factors of vitiligo with odds ratios of 37.1, 9.0, 6.0, 13.9, and 3.9 respectively (Table 6).

Blood groups of all the patients (both cases and controls) were checked. In cases; 56 (28%), 54 (27%), 53 (26.5%), 36 (18%), and 1 (0.5%) patients were having A (Rh+), B (Rh+), O (Rh+), AB (Rh+), and O (Rh–) blood groups, respectively. Meanwhile in controls; 46 (23%), 63 (31.5%), 48 (24%), and 43 (21.5%) patients were having A (Rh+), B (Rh+), O (Rh+), and AB (Rh+) blood groups, respectively (Table 7).

DISCUSSION

In this case-control study 400 patients were recruited with 200 cases and 200 controls. In our study, more than half of the patients were females (107/200 [53.5%]). Similar results have been reported from studies in Turkey (62.5%) [24] and Saudi Arabia (53.5% [19] 56% [25]). Increased number of females among vitiligo patients is may be due to the fact that females are usually more concerned about pigmentation changes of their skin. So social stigma and marital concerns prompt females to seek early medical consultation.

Vitiligo can occur in all age groups with highest prevalence among young adults [26]. In our study, mean age of the patients was 21.7 years, with majority (38.5%) of patients in 11–20 years' age group. A study in Tunisia showed that most (66%) of the patients

developed vitiligo in their adulthood [27], mean age of occurrence of vitiligo was 18.8 years among Chinese patients [28], while a Turkish study reported that vitiligo occurred early in life with mean age of 10 years [(24)]. Some studies have reported mean age ranging from 24.5–34 years [29-34].

Table 4: Accompanying disorders with altered immunity and autoimmunity

Disorder	Cases		Controls	
	Frequency	Percent (%)	Frequency	Percent (%)
Alopecia areata†	6	23.1	0	0
Atopic dermatitis*	6	23.1	1	50
Diabetes mellitus (type 1)†	3	11.5	0	0
Lichen planus*	5	19.2	0	0
Psoriasis*	4	15.4	1	50
Total	26	100	2	100

* Disorder with altered immunity. †Disorder with autoimmunity.

In our study family history was present in 30% of cases as compared to 1.5% controls (p-value <0.001). Similarly, family history of vitiligo (42.8% [19], 25% [31], 24% [32], and 18% [29]) has also been observed in other studies.

Most of the patient (63%) in our study were living in urban areas, where there are many environmental pollutants. A study in India also reported that majority of the patients (78%) were living in urban areas [35]. Contrary, a study in China showed that there is no significant difference between rural and urban residents [36]. In the etiology of vitiligo, Slominki et al. pointed out several environmental factors; including sunlight, stress, and extreme exposure to pesticides [37].

Most of the patients (74%) in our study had vulgaris type of vitiligo. Similarly, other studies showed higher numbers with 64.9% [35], 49.6 [38], 57.4% [39],

Table 5: Accompanying disorders with no altered or auto-immunity

Disorder	Cases		Controls		*p*-value
	Frequency	Percent (%)	Frequency	Percent (%)	
Psychological Stress					<0.001
Present	95	47.5	46	23	
Absent	105	52.5	154	77	
Total	200	100	200	100	
Isomorphic phenomenon					<0.001
Present	63	31.5	0	0	
Absent	137	68.5	200	100	
Total	200	100	200	100	
Premature graying of hair					<0.001
Present	31	15.5	5	2.5	
Absent	169	84.5	195	97.5	
Total	200	100	200	100.0	
Halo nevus					<0.001
Present	24	12	2	1	
Absent	176	88	198	99	
Total	200	100	200	100	
Atopic diathesis					0.001
Present	19	9.5	3	1.5	
Absent	180	90.5	197	98.5	
Total	199	100	200	100	
Vitamin D deficiency					<0.001
Present	22	11	59	29.5	
Absent	178	89	141	70.5	
Total	200	100	200	100	
Vitamin B_{12} deficiency					0.002
Present	16	8	3	1.5	
Absent	184	92	197	98.5	
Total	200	100	200	100	
Folate deficiency					0.002
Present	14	7	2	1	
Absent	186	93	198	99	
Total	200	100	200	100	

Table 6: Logistic regression for possible risk factors of vitiligo

Variable	OR (Odds Ratio)	95% CI	*p*-value
Family history	37.12	9.87–139.63	<0.001
Accompanying altered immunity and autoimmunity disorders	9.04	1.55–52.82	0.014
Premature graying of hair	6.01	1.74–20.68	0.004
Halo nevus	13.89	2.5–77.06	0.003
Atopic diathesis	3.86	0.86–17.42	0.079
Psychological stress	1.57	0.84–2.94	0.16
Vitamin D deficiency	0.09	0.03–0.29	<0.001
Vitamin B_{12} deficiency	3.28	0.16–65.8	0.44
Folate deficiency	1.32	0.05–31.93	0.86

Table 7: Blood groups of cases and controls

	Cases		Controls	
	Frequency	Percent (%)	Frequency	Percent (%)
A (Rh +)	56	28	46	23
B (Rh +)	54	27	63	31.5
O (Rh +)	53	26.5	48	24
AB (Rh +)	36	18	43	21.5
O (Rh –)	1	0.5	0	0
Total	200	100	200	100

59.8% [26], and 42.3% [40] of patients having vulgaris pattern. Contrary, other studies reported localized type in most of the cases (77% [41], 60% [31], 48.5% [42], and 32.4% [33]).

There is association of vitiligo with autoimmune disorders [25]. In our study 13.3% of the cases while 1% of the controls were having accompanying altered immunity and autoimmunity disorders which was statistically significant (*p*-value <0.001). Our main observed accompanying altered immunity and autoimmunity disorders were alopecia areata and atopic dermatitis. Other studies have also reported association of autoimmune disorders in Canada (19%) [43], North America and UK (23%) [44], and China (8%) [44].

For finding the possible risk factors of vitiligo, we conducted logistic regression of our data. It showed that family history, accompanying altered immune or autoimmune disorders, premature graying of hair, halo nevus, and atopic diathesis were the risk factors of vitiligo with odds ratios of 37.1, 9.0, 6.0, 13.9, and 3.9 respectively. In a large retrospective Japanese study with 713 vitiligo patients, younger age of onset and higher antinuclear antibodies (ANA) were the main risk factors [6]. A retrospective Chinese study on 101 vitiligo-associate halo nevus patients showed that personal history of thyroid diseases, Koebner phenomenon, multiple halo nevus, and familial history of vitiligo were risk factors associated with halo nevus vitiligo [45].

There were limitations in our study. Data was collected among patients attending one hospital. It would be better if data was collected randomly from different hospitals and clinics of the city and surrounding districts. Deficiencies of vitamin D, vitamin B12, and folate were detected using clinical signs and symptoms, not by laboratory examinations. Also, we could not work on all the possible risk factors of vitiligo (especially thyroid disorders). All these were due to limited funds, facilities, and personnel. Further more detailed studies are needed (in Kandahar and other regions of Afghanistan) to describe the demographic features, clinical patterns, and possible risk factors of vitiligo in details.

In conclusion, vitiligo affects women slightly more than men. Mean age of vitiligo patients is 21.7 years, observed mostly in second decade of life. Vitiligo vulgaris is the most prevalent type, affecting 74% of the patients. Common risk factors of vitiligo are family history, accompanying altered immunity/autoimmunity disorders, premature graying of hair, halo nevus, and atopic diathesis.

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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

Infectious complications during connective tissue diseases: A prospective study on 234 cases

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ABSTRACT

Background: The infectious complications during connective tissue diseases are favored by immunosuppression linked on the one hand to systemic disease and on the other hand to their treatment. The aim of this study was to identify the different infectious complications associated with these systemic diseases. **Materials and Methods:** It was a multicenter descriptive study over a period of 8 months in two Dermatology departments in Dakar. All patients followed for connective tissue disease who had evidence of infection during the study period were included. **Results:** We identified 231 cases of connective tissue disease. We had noted the occurrence of an infection in 56 cases. Infections were noted during: systemic scleroderma in 19 cases, systemic lupus in 15 cases, mixed connective tissue disease in 12 cases and dermatomyositis in 10 cases. The different types of infection that were observed during these systemic diseases were fungal (41cas), bacterial (34cas), viral (12cas) and parasitic (6cas). Patients developed an infection before taking corticosteroids in 34 cases (36.6%) and after taking corticosteroids in 59 cases (63.4%). **Conclusion:** Connectivites are a group of autoimmune diseases that are exposed to an infectious risk during their evolution. The search for these infections at the beginning and during the treatment of these system diseases improves their prognosis.

Key words: Systemic diseases; Infection; Corticosteroids

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Our Dermatology Online

Original Article

Les complications infectieuses au cours des connectivites: Une étude prospective sur 234 cas

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RESUME

Introduction: Les complications infectieuses au cours des connectivites sont favorisées par l'immunodépression liée d'une part à la maladie de système et d'autre part à leur traitement. Notre objectif était d'identifier les différentes complications infectieuses associées à ces connectivites. **Matériels et méthodes:** Il s'agissait d'une étude multicentrique descriptive sur une période de 8mois dans deux services de Dermatologie à Dakar. Tous les malades suivis pour une connectivite et qui présentaient des signes d'infection durant la période de l'étude ont été inclus. **Résultats:** Nous avons recensé 231 cas de connectivite. Nous avions noté la survenue d'une infection dans 56cas soit une prévalence hospitalière des infections de 24,2%. Les infections étaient notées au cours: de la sclérodermie systémique dans 19cas, du lupus systémique dans 15cas, de la connectivite mixte dans 12cas et de la dermatomyosite dans 10cas. Les différents types d'infection qui ont été observés au cours de ces connectivites étaient d'origine fongique (41cas), bactérienne (34cas), virale (12cas) et parasitaire (6cas). Les malades ont développé une infection avant la prise des corticoïdes dans 34cas (36,6%) et après la prise des corticoïdes dans 59cas (63,4%). **Conclusion:** Les connectivites constituent un groupe de maladies auto-immunes qui sont exposés à un risque infectieux au cours de leur évolution. La recherche de ces infections au début et au cours du traitement de ces maladies de système permet d'améliorer leurs pronostics.

Mots clés: Connectivite; Infection; Corticothérapie

INTRODUCTION

Les connectivites regroupent avec les vascularites les « maladies systémiques » qui sont des affections auto-immunes et/ou inflammatoires non spécifiques d'organe. Les manifestations dermatologiques constituent souvent une circonstance de découverte et facilitent le diagnostic précoce [1,2]. La gravité est liée au diagnostic tardif, aux atteintes viscérales notamment la néphropathie glomérulaire, la fibrose pulmonaire, les troubles du rythme et de la conduction cardiaque et le risque de sepsis lié aux complications infectieuses [3,4]. Ces complications infectieuses sont secondaires à l'immunodépression causée par la connectivite ainsi qu'aux effets iatrogènes du traitement par les corticoïdes et les immunosuppresseurs utilisés dans ces pathologies auto-immunes [5-8]. L'objectif de cette étude était d'identifier d'une part les différentes complications infectieuses observées dans ces connectivites, d'autre part les facteurs de risque associés à ces infections ainsi que leurs modalités de prise en charge.

MATÉRIELS ET MÉTHODES

Il s'agissait d'une étude multicentrique descriptive avec un recrutement prospectif réalisée de janvier 2018 en Aout 2018 (8 mois) dans les deux services de Dermatologie à Dakar. Nous avons inclus tous les malades suivis en hospitalisation ou en externe pour une connectivite et qui présentaient des signes d'infection durant la période de l'étude. Le diagnostic de connectivites était retenu selon

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les manifestations dermatologiques de la connectivite et les critères de l'American College of Rheumatology ACR (1997) pour le lupus systémique, de l'EULAR (2013) pour la sclérodermie systémique et de Bohan et Peter pour la dermatomyosite.

Le diagnostic d'infection était retenu devant:

I. des signes cliniques
- généraux: température < 36°C ou > 38°C; fréquence cardiaque > 90/min; fréquence respiratoire > 20/min
- dermatologiques: squames du cuir chevelu, lésions érythémato-squameuses prurigineuses, lésions vésiculo-bulleuses douloureuses, muguet buccal, croutes mélicèriques, ulcérations douloureuses
- Des signes extra-dermatologiques: brulures mictionnelles, toux, râles à l'auscultation pulmonaire, douleurs auriculaires, diarrhée.

II. des explorations paracliniques
- Biologiques à la recherche d'une: CRP élevée, hyperleucocytose ou leucopénie.
- Bactériologiques: hémocultures, examen cytobactériologique des urines ou des crachats
- Parasitaires: prélèvement vaginal, selles KAOP
- Mycologique: prélèvement mycologique, scotch test
- Radiologiques: radiographie de thorax, scanner thoracique, échographie abdominale et pelvienne, échographie des parties molles, radiographie panoramique dentaire.

Le traitement anti-infectieux était instauré selon le type d'infection.

L'évaluation était faite à J14 et J30 sur la base des données cliniques et paracliniques de contrôle.

La saisie et l'analyse des données étaient effectuées sur le logiciel SPSS IBM Statistics version 22. L'étude descriptive était réalisée par le calcul de fréquences pour les variables qualitatives. Pour les données quantitatives, l'étude était réalisée par le calcul des moyennes.

L'étude analytique était faite avec des croisements de variables à l'aide de tableaux de contingence à double entrée. Pour comparer les fréquences, le test du KHI 2 et celui de Fischer étaient utilisés, avec un seuil de significativité alpha inférieur à 0,05.

RÉSULTATS

Nous avons recensé 231 cas de connectivite parmi 7685 malades suivis durant la période de l'étude soit une fréquence hospitalière de 3%.

Parmi ces 231 cas de connectivite, nous avions noté la survenue d'une infection dans 56cas. La prévalence hospitalière des infections au cours des connectivites était de 24,2%. Les connectivites dont survenaient ces infections étaient par ordre de fréquence la sclérodermie systémique (88cas), le lupus systémique (70cas), la connectivite mixte (42cas) et la dermatomyosite (31cas). Les connectivites mixtes associaient plusieurs maladies systémiques notamment (la sclérodermie systémique et la dermatomyosite) dans 5cas, (le lupus systémique et la dermatomyosite) dans 3cas, (le lupus systémique et la sclérodermie systémique) dans 2cas, (le lupus systémique, la sclérodermie systémique et la dermatomyosite) dans 2cas. Les malades étaient de sexe féminin dans 46cas et de sexe masculin dans 10cas soit un sexe ratio de 0.21.

L'âge moyen était de 40,5 ± 13,9 ans avec des extrêmes de 16 et 80 ans.

Les circonstances de découverte des infections étaient fortuites lors du suivi de la connectivite dans 22 cas (39,3%), soit au décours d'une poussée de la connectivite dans 19 cas (33,9%) ou avec des signes fonctionnels de l'infection dans 15 cas (26,8%). La durée d'évolution des connectivites était inférieure à une année dans 22 cas (39,3%), entre 1an et 3ans dans 21cas (37,5%), entre 3ans et 5ans dans 8cas (14,3%) et supérieur à 5ans dans 5 cas (8,9%).

Les infections étaient notées au cours: de la sclérodermie systémique dans 19cas, du lupus systémique dans 15cas, de la connectivite mixte dans 12cas et de la dermatomyosite dans 10cas. Les différents types d'infection qui ont été observés au cours de ces connectivites étaient d'origine fongique (41cas), bactérienne (34cas), virale (12cas) et parasitaire (6cas). Les malades ont développé une infection avant la prise des corticoïdes dans 34cas (36,6%).Ces infections étaient d'origine fongique (15cas), bactérienne (12cas), virale (4cas) et parasitaire (3cas). La fig. 1 illustre la répartition des différents types d'infections survenues avant la prise des corticoïdes en fonction des connectivites. Les malades ont présenté une infection après la prise des corticoïdes dans 59cas (63,4%).Ces infections étaient d'origine mycosique (27cas), bactérienne (21cas), virale (8cas) et parasitaire (3cas). La fig. 2 illustre la répartition des différents types d'infections survenues après la prise des corticoïdes en fonction des connectivites. Les malades qui présentaient une infection étaient à des doses de corticoïdes variables. La répartition des malades en fonction de la dose de

prise orale des corticoïdes est illustrée sur la fig. 3. Les corticoïdes étaient associés aux immunosuppresseurs dans 9cas parmi lesquels le méthotrexate (4cas), l'azathioprine (2cas) et le cyclophosphamide en bolus (3cas). Les infections avaient une durée d'évolution variable en fonction des connectivites. Cette durée était inférieure à une semaine dans 21 cas, entre 1 et 4 semaines dans 25 cas, supérieure à 4 semaines dans 10 cas. Les localisations des différentes infections sont illustrées dans le tableau 1. Les types d'infection étaient variables en fonction des différentes connectivites. Le tableau 2 illustre la répartition des malades selon le type d'infection. Les agents pathogènes ont été isolés dans 26cas (46,4%). Il s'agissait d'agent pathogène bactérien: *Bacille de Koch*, *Salmonella enterica*, *Escherichia coli*, *Proteus mirabilis*, *Staphylocoque aureus*, *Acinetobacter*, *Klebsiella pneumoniae*; fongiques: *Microsporum canis*, *Trichophyton rubrum*, *Candida albicans*, *Trichophyton mentagraphytes*, *Trichophyton schoenleinii* et parasitaires: Trichomonas *vaginalis*. Les différents types de traitement local et général utilisés pour la prise en charge des infections sont répertoriés sur le tableau 3. L'évolution des infections était marquée par une guérison dans 7 cas au cours du lupus systémique, dans 17 cas dans la sclérodermie systémique, 5 cas dans la dermatomyosite et 9cas au cours des connectivites mixtes. A l'étude analytique les connectivites mixtes étaient plus associées aux épisodes infectieux itératives (p=0.009). La dermatomyosite était statistiquement plus liée à la survenue d'une infection virale (p=0.018) et la sclérodermie plus aux infections bactériennes (p = 0.048).La prise de corticoïdes était associée aux risque de survenue des infections (p < 0.001).

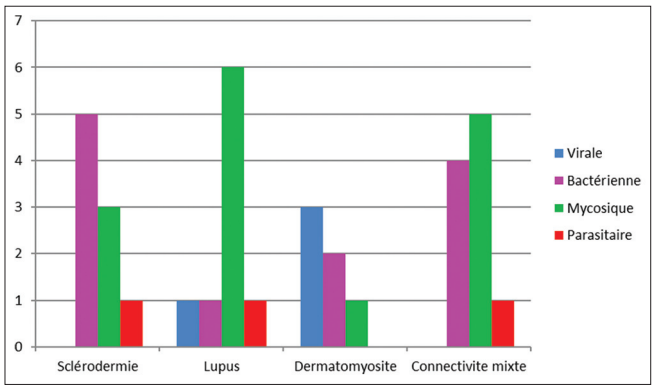

Figure 1: Répartition des types d'infection avant la prise de corticoïde.

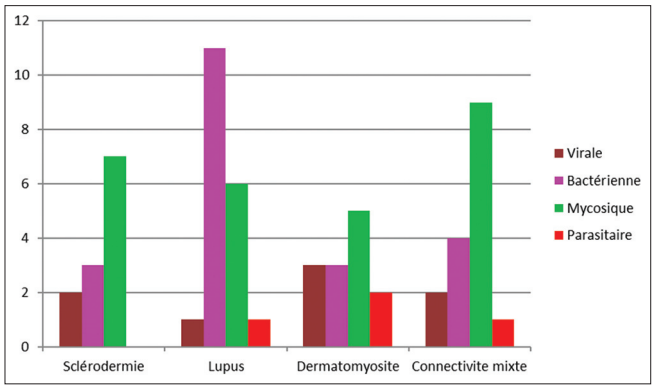

Figure 2: Répartition des types d'infection après la prise de corticoïde.

DISCUSSION

Notre rapportons une fréquence élevée de 24,2% des infections au cours des connectivites. Les circonstances de découverte étaient le plus souvent fortuites dans 39,3%. Ces infections survenaient le plus souvent après l'administration des corticoïdes dans 63,4% et parfois existaient avant la corticothérapie dans 36,6%. Elles étaient à prédominance mycosiques et bactériennes avec une fréquence particulière des infections virales au cours de la dermatomyosite et des infections bactériennes au cours de la sclérodermie. La fréquence des infections (21,4%) au cours du lupus systémique dans notre étude est comparable aux autres études rapportées en Inde (26,5%) et au Canada (25%) [9,10]. Cependant la fréquence de ces infections était plus élevée en France (40%) [3]. Concernant la fréquence des infections au cours de la sclérodermie systémique, très peu d'études s'y sont intéressés et elles portaient seulement sur les infections opportunistes, ces dernières représentent 2 à 9% des causes de décès au cours de cette maladie [11].

Table 1: Répartition des malades selon la localisation de l'infection

Localisations	Lupus	Sclérodermie	Dermatomyosite	Connectivites mixtes	Total
Peau	14	19	16	19	68
Poumon	3	3	1	0	7
Urogénitale	0	2	1	4	7
Digestive	0	4	0	1	5
ORL	2	1	0	1	4
Ganglionnaire	1	0	0	0	1
Musculaire	0	0	1	0	1
Total	20	29	19	25	93

Dans notre étude, 32,1% de cas de lupus avaient développé des infections avant la prise des corticoïdes ce qui rejoint l'étude de Zonana qui ont rapporté une fréquence de 40% au cours du lupus systémique [12]. Cette immunodépression semble être liée d'une part à une hyperactivation spontanée des lymphocytes B à l'origine d'une augmentation de la production d'immunoglobulines et d'autre part à des anomalies quantitatives et qualitatives des lymphocytes T. La résultante est une baisse de la synthèse de divers facteurs (interleukines 1 et 2, interférons, facteurs de croissance hématopoïétiques) qui joue un rôle majeur anti-infectieux [13-15].

Cependant dans notre étude, la majorité de nos patients (67,9%) avaient développé des infections au cours du traitement par les corticoïdes avec un lien statistiquement significatif entre la survenue des infections et la prise de corticoïdes ($p<0.001$). Ceci rejoint les résultats d'une méta-analyse comparant les corticoïdes versus placebo qui montrait que la prise de corticoïdes était un facteur de risque d'infection avec un risque relatif de 1,6 [8]. Une étude en France rapportait que la dose cumulée était un facteur de risque principal des infections. Le taux d'infection serait deux fois plus élevé chez des patients recevant 1 à 20 mg de prednisone et quatre fois plus élevé chez les patients recevant 50 mg par jour [3]. Dans notre étude, le lien n'était pas statistiquement significatif entre la dose de corticoïdes et le nombre d'épisodes infectieux. Le faible risque infectieux retrouvé chez nos patients sous forte dose de corticoïdes (29,8%) pourrait être expliqué par le suivi rapproché et le bilan infectieux pré-thérapeutique exhaustif réalisé avant de les traiter par des corticoïdes. La majorité des patients (70.2%) avaient développé des infections aux doses de corticoïdes inférieures à 20 mg par jour. La durée prolongée de la corticothérapie semble être un facteur inductif. Les infections fongiques étaient plus fréquentes au cours du lupus systémique (55%) et au cours des connectivites mixtes (56%). Il s'agissait de mycoses superficielles à type de dermatophyties

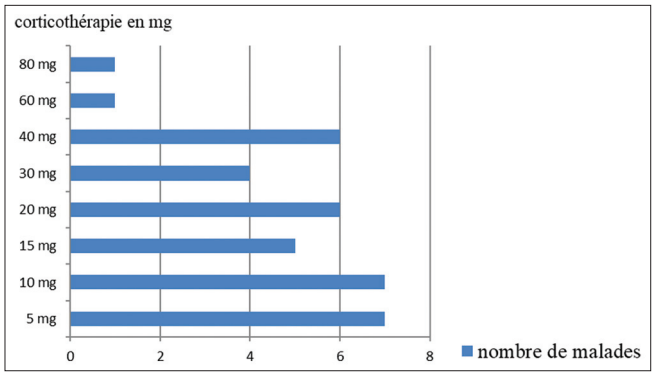

Figure 3: Répartition des malades selon la dose de prise des corticoïdes.

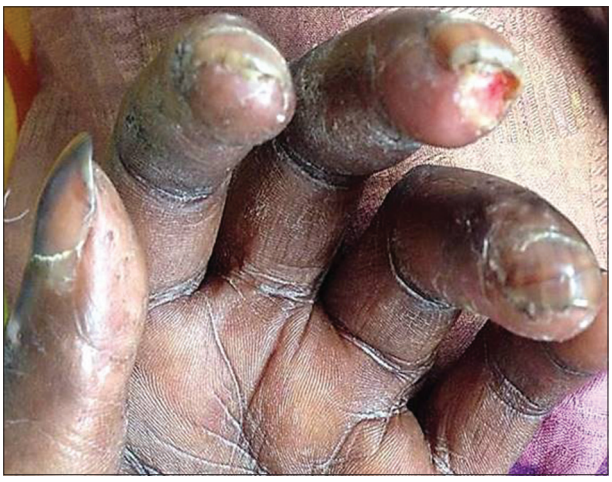

Figure 5: Dactylite au cours du syndrome de Raynaud dans la sclérodermie systémique.

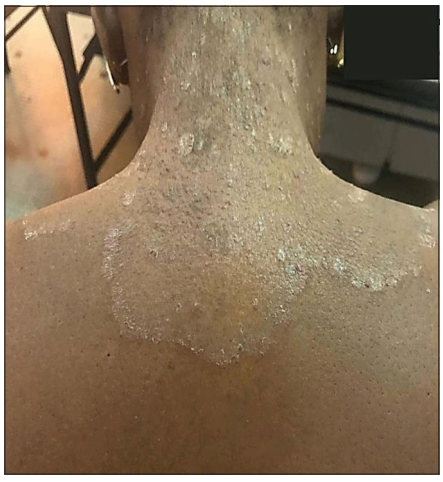

Figure 4: Dermatophytie du cou au cours du lupus systémique.

Figure 6: Zona intercostal et brachial au cours d'une connectivite mixte (lupus et dermatomyosite).

Table 2: Répartition des malades selon le type d'infection

Type infection	sclérodermie	Lupus	Dermatomyosite	Connectivite mixte
Virale	Herpès cutané	Herpes cutané	Herpès cutané	Zona intercostal
		Zona intercostal	Zona brachial	Herpès génital
Bactérienne	Dactylite	Otite moyenne	Erysipèle de jambe	Cystite
	Pneumopathie	Pneumopathie	Pneumopathie	Carie dentaire
	Gastroentérite	Tuberculose	Abcès parties molles	Impétigo
	Cystite		Impétigo	Gastroentérite
	Carie dentaire			Dactylite
	Impétigo			
Mycosique	Candidose buccale	Dermatophytie cutanée	Candidose cutanée	Dermatophytie cutanée
	Dermatophytie cutanée	Teigne cuir chevelu	Dermatophytie cutanée	Teigne cuir chevelu
	Pytiriasis versicolor	Candidose		Candidose buccale
	Teigne cuir chevelu			Pytiriasis versicolor
Parasitaire	Gale	Gale	Gale	Vaginose à *Trichomonas vaginalis*
		Vaginose à *Trichomonas vaginalis*		

Table 3: Les traitements locaux et généraux des infections

Classe thérapeutique	Molécule	Traitement général (nombre)	Traitement local (nombre)
Antifongiques	Fluconazole	7	
	Terbinafine	2	3
	Griséofulvine	14	4
	Kétoconazole		4
	Cyclopiroxolamine		17
Antibiotiques	Amoxicilline	17	
	Ceftriaxone	5	
	Doxycycline	5	
	Métronidazole	2	
	Ciprofloxacine	5	
	Spiramycine	2	
	Acide fucidique		2
	RZHE*	1	
Antiviraux	Acyclovir	8	
Antiparasitaires	Benzoate de benzyle 10%		2

RHZE * : R (rifampicine), H (isoniazide), Z (pyrazinamide), E (ethambutol)

cutanées (fig. 4) et les candidoses buccales et génitales, ceci étaient concordant avec l'étude de Diallo et al [16] qui a montré qu'elles étaient les plus fréquentes et parfois une des circonstances de découverte du lupus systémique dans 33%.

Pour les infections bactériennes, elles étaient majoritaires dans plus de la moitié des cas (55,2%) au cours de la sclérodermie systémique, il existait un lien statistiquement significatif (p=0,048). Les dactylites (fig. 5) étaient favorisées par le phénomène de Raynaud présent chez les 5 malades ayant développés cette complication ainsi que les ulcères digitaux qui pouvaient être d'origine vasculaire.

La gastroentérite infectieuse était secondaire au syndrome de malabsorption et à la pullulation microbienne intestinale observée chez 10 à 25% des malades atteints de sclérodermie [17-19]. Nous avons noté un seul cas de tuberculose multifocale au cours du lupus systémique avant le traitement par les corticoïdes. Elle constituait la circonstance de découverte du lupus.

Les infections virales étaient fréquentes au cours de la dermatomyosite avec un lien statistiquement significatif (p=0,018). Il s'agissait d'infections cutanées à *Herpès simplex* (fig. 6) et à *Virus Varicelle-zona* concordant avec les études antérieures qui ont observé une haute prévalence de ces deux virus [20-22]. Les infections parasitaires étaient les moins fréquentes elles étaient représentées par la vaginose à *Trichomonas vaginalis* et la gale.

L'évolution était favorable dans 87,5% avec un traitement anti infectieux spécifique. Nous n'avons noté aucun cas de décès secondaire aux infections. Les facteurs de mauvais pronostic rapportées dans la littérature étaient les infections opportunistes telles

que les pneumopathies à *Pneumocystis carinii*, les candidoses profondes, les aspergilloses pulmonaires et les pneumopathies à cytomégalovirus [23].

CONCLUSION

Les connectivites constituent un groupe de maladies auto-immunes dont la prise en charge repose essentiellement sur la corticothérapie et ou les immunosuppresseurs. L'immunodépression secondaire à ces maladies de système et la corticothérapie constituent un risque infectieux majeur au cours de leur prise en charge. La recherche de ces infections au début et au cours du traitement de ces maladies de système permet d'améliorer le pronostic des malades et leurs suivis au long court.

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Our Dermatology Online

Original Article

Profile of adult erythroderma in hospitals in Lomé (Togo): study of 147 cases

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ABSTRACT

Objective: The aim of this study was to describe the epidemiological and clinical profile of erythroderma in hospital setting in Lomé (Togo). **Methods:** We reviewed the epidemiological and clinical data of adults patients diagnosed with erythroderma in dermatology departments over a 20-year period (1997 through 2016). **Results:** In total, one hundred and forty seven patients were diagnosed with erythroderma during the study period (0.4% of all consulted patients). The average age at the onset of the disease was 41.1 years with a male: female ratio of 1.5:1. The most frequent cause of erythroderma was exacerbation of preexisting dermatoses (80.8%), including eczema (84.3%) and psoriasis (11.7%). No cause could be identified in forty one cases (27.9%). Apart from erythema and scaling, that were present in all patients, clinical findings were dominated by pruritus (62.33%), fever (8.2%), and altered general condition (8.8%). Treatment was symptomatic and etiologic in all patients. The evolution was favorable in 47.62% of the cases, and one death occurred in a patient with cutaneous lymphoma. **Conclusion:** This study outlines that erythroderma is rare in Lomé (Togo). Our series had a high percentage of erythroderma secondary to preexisting dermatoses and idiopathic cases.

Key words: Erythroderma; Adult; Lomé (Togo)

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Our Dermatology Online

Original Article

Profil des érythrodermies de l'adulte en milieux hospitalier à Lomé: étude de 147 cas

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RÉSUMÉ

Objectif: Le but de cette étude était de décrire le profil épidémiologique, clinique, et évolutif des érythrodermies en milieu hospitalier à Lomé. **Méthode:** Il s'est agi d'une étude rétrospective descriptive portant sur les dossiers des patients âgés de plus de 15 ans ayant été suivi pour une érythrodermie dans les services publics de dermatologie à Lomé de janvier 1997 à décembre 2016. **Résultats:** Au total, 147 patients ont été inclus dans l'étude soit une fréquence de 0,4% des motifs de consultation. L'âge moyen des patients était de 41,1ans et le sex-ratio (H/F) de 1,5. Le prurit était présent chez 62,33% des patients, une fièvre et une altération de l'état général chez respectivement 8,2% et 8,8% des patients. La majorité (80,8%) des patients présentaient une érythrodermie sèche. Sur le plan étiologique, les dermatoses érythrodermiques (69,4%) étaient au premier plan, suivi des causes idiopathiques (27, 9%). Les principales dermatoses érythrodermiques étaient l'eczéma (84,3%) et le psoriasis (11,76%). Le traitement était symptomatique et étiologique dans certains cas. L'évolution était favorable dans 47,62% des cas, et un décès était survenu chez un patient ayant un lymphome cutané. **Conclusion:** Les érythrodermies constituent une affection rare en consultation dermatologique à Lomé. Les étiologies les plus fréquentes restent les dermatoses érythrodermiques.

Mots-clés: Érythrodermies; Adulte; Lomé

INTRODUCTION

L'érythrodermie ou dermatose exfoliatrice est un syndrome associant un érythème confluant touchant plus de 90 % de la surface corporelle, une desquamation et une évolution prolongée [1]. C'est une urgence dermatologique pouvant mettre en jeu le pronostic vital des patients. Il s'agit d'un syndrome d'installation aigue ou subaiguë et qui implique une recherche étiologique. Les causes des érythrodermies varient en fonction de l'âge. Chez l'adulte, plusieurs circonstances peuvent être à l'origine de la survenue d'une érythrodermie notamment les dermatoses érythrodermiques ou les toxidermies. En Afrique du Nord, les érythrodermies représentaient 0,3% des motifs de consultations en dermatologie [2]. Peu d'études ont porté sur les érythrodermies en Afrique sub-Sahara [3].

Le but de notre étude était de documenter le profil épidémiologique, clinique et évolutif des érythrodermies de l'adulte en consultation dermatologique à Lomé.

MATERIALS AND METHODS

Il s'agit d'une étude rétrospective descriptive ayant concerné les services de dermatologie des Centre Hospitalier Universitaire (CHU) Sylvanus Olympio et Campus, et du service de dermatologie du Centre de

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Gbossimé à Lomé. Les dossiers des patients vus dans les différents services du 1er Janvier 1997 au 31 décembre 2016 ont été revus. Les patients âgés de plus de 15 ans chez qui le diagnostic d'érythrodermie était retenu ont été inclus. Etait considéré comme érythrodermie, les patients ayant un érythème diffus, touchant plus de 90% de la surface corporelle avec squames et d'évolution prolongée. Les toxidermies à type de nécrolyse épidermique toxique (ou syndrome de Lyell) étaient exclues de cette étude. Une fiche d'enquête à été pré établie précisant les données sociodémographiques (âge, sexe, profession, antécédents pathologiques et/ou antécédents d'érythrodermie des patients); cliniques (signes fonctionnels, signes généraux, aspects cliniques, étiologies) et paracliniques. L'analyse des données est réalisée avec le logiciel Epi info7. La signification statistique a été définie comme $p < 0,05$. Nous avons utilisé le test exact de Fisher et le test non paramétrique de Kruskal-Wallis pour comparer les moyennes.

Ethics Statement

Le protocole d'étude a été soumis et a été approuvé par le comité de bioéthique du ministre de la Santé et des centres hospitaliers concernés par l'étude. Les chefs des différents services concernés par l'étude ont donnés leurs accords pour l'exploitation des dossiers.

RESULTS

Durant la période d'étude, 147 (0,4%) des 37567 patients âgés de plus de 15 ans ont consultés pour une érythrodermie, ce qui correspond à 8 cas en moyenne par an. L'âge moyen des patients était de 41,1±15 (extrêmes: 17 et 80 ans) et le sex-ratio (H/F) de 1,5. Les patients ayant une érythrodermies étaient en général des adultes jeunes avec une prédominance de la tranche de 26 ans à 35 ans 49 patients (33,33%). L'érythrodermie était de survenue tardive chez les hommes (âge moyen = 45,1 ans; extrêmes: 19 et 80 ans) que chez les femmes (âge moyen = 34,9 ans; extrêmes 17 et 80 ans), p = 0,0001

La majorité des patients (80,9%) présentaient une érythrodermie sèche. Le prurit était le signe fonctionnel le plus fréquent chez nos patients (71,4%). Une fièvre (supérieure à 38°C) et une altération de l'état général était retrouvées chez respectivement 12 (8,16%) et 13 (8,84%) des patients. Un œdème des extrémités était noté chez 23 (15,64%) des patients. L'hyperkératose palmo-plantaire et les dystrophies unguéales à type d'hyperkératose sous unguéale, mélanonychie ou onycholyse étaient retrouvées chez respectivement chez 11 (7,5%) et 12 (8,2%) des patients et des adénopathies périphériques étaient observées chez 19 (12,9%) des patients.

Sur le plan paraclinique, la vitesse de sédimentation était accélérée chez 47 des 61 patients l'ayant réalisée. Une anémie et une hyperleucocytose étaient notées chez respectivement 29 et 38 des 61 patients ayant réalisé une numération formule sanguine. Seul 11 (7,5%) patients avaient bénéficié d'une biopsie cutanée. Tous les cas de lymphomes cutanés étaient confirmés par histologie.

Sur le plan étiologique, les dermatoses érythrodermiques étaient les étiologies les plus fréquentes avec 102 (69,4%) suivies des causes idiopathiques (27,9%). Parmi les dermatoses érythrodermiques, l'eczéma érythrodermique 86 (84,3%) (Fig. 1) et le psoriasis érythrodermique 12 (11,8%) (Fig. 2) étaient les plus

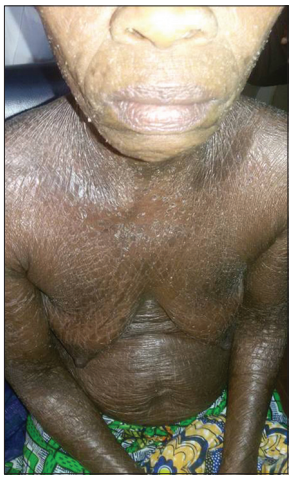

Figure 1: Erythroderma due to eczema.

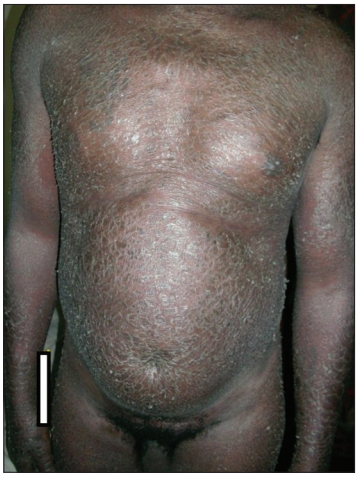

Figure 2: Erythroderma due to psoriasis in an adult.

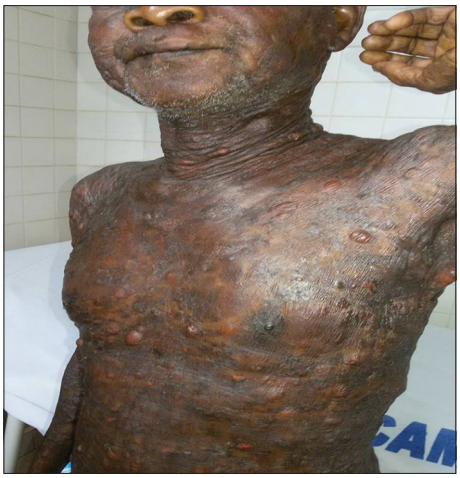

Figure 3: Erythroderma during fungus mycosis in a 62-year-old patient.

fréquentes (Tabl. I). Sur les 86 patients atteints d'un eczéma érythrodermique, 8 (9,3%) avaient un antécédent personnel d'atopie dont 7 cas d'asthme et 1 cas de rhinite allergique. Les patients ayant un eczéma érythrodermique étaient relativement plus jeune que les patients ayant une autre étiologie d'érythrodermie (âge moyen =39,03 ans) (p= 0,002). Aucune association significative n'est notée entre le sexe et les étiologies des érythrodermies, p=0,93

Les lymphomes cutanés comme cause d'érythrodermie dans notre étude étaient le mycosis fongoïde (1,37%) (Fig. 3) et le Syndrome de Sézary (0,68%). Un cas de DRESS syndrome était retrouvé chez une fille de 21 ans infectée par le VIH sous traitement antirétroviral. La molécule incriminée était l'Abacavir.

La prise en charge de l'érythrodermie avait nécessité une hospitalisation chez 18 (12,2%) des patients. La durée moyenne d'hospitalisation était de 8 jours avec des extrêmes de 5 et 32 jours. L'évolution était favorable chez 69 (47,6%) patients et 76 (51,7%) étaient perdus de vue au cours du suivi. Un décès était survenu chez un patient ayant un lymphome cutané. L'évolution était favorable dans 44% des cas d'érythrodermies idiopathiques.

DISCUSSION

Nous avons enregistré environ 8 cas d'érythrodermie par an, ce qui est compris entre les 6,3 cas et 9,4 cas par an rapportés respectivement en Tunisie et au Portugal [4,5]. Les érythrodermies constituent donc une affection rare en milieu hospitalier à Lomé puisqu'elles ne représentent que 0,4% des motifs de consultation. L'âge moyen des patients était de 41,1ans et la tranche d'âge de 26 ans à 35 ans était prédominante. Ceci signe une prédominance de l'affection chez les sujets jeunes dans notre étude contrairement à l'étude de César et al. et de Hulmani et al. ou l'affection était plus fréquente dans la 6ème décade [5,6]. Nous avons noté une prédominance masculine des érythrodermies avec une sex-ratio de 1,53. Cette prédominance masculine des érythrodermies à été également rapportée dans plusieurs études avec une sex-ratio variant entre 1,8 et 2,2 [2,7].

D'une façon générale, les dermatoses érythrodermiques (69,4%) étaient les étiologies les plus fréquentes chez l'adulte. Les dermatoses érythrodermiques ont été rapportées comme cause fréquente des érythrodermies par plusieurs auteurs [5,8-10] avec une fréquence allant de 33,3% à 74,4%. Cependant, les eczémas érythrodermiques sont au premier plan des dermatoses érythrodermiques dans notre étude (84,32%) suivi du psoriasis (11,76%) contrairement en Afrique du Nord [4], en Inde et en Chine où le psoriasis érythrodermique était la dermatose érythrodermique la plus fréquentes (30,5% à 55,0%) [5,6,8-11]. La rareté des psoriasis érythrodermiques dans notre étude peut s'expliquer par sa faible prévalence hospitalière faible (0,62%) de l'affection en Afrique subsaharienne [12].

Les érythrodermies due à une toxidermie médicamenteuse étaient peut fréquente dans notre étude (0,7%). Les érythrodermies secondaires à une toxidermie représentaient respectivement 16,6% et 18,4% des étiologies des érythrodermies en Inde et au Brésil [5,6]. Ceci est due au fait que nous avons exclut de notre étude les nécroses épidermiques toxique qui ne répondent plus à la définition actuelle des érythrodermies [13].

Aucune cause n'était identifiée chez environ un quart (27,9%) de nos patients. Cette valeur est proche de celle de Vasconcellos et al. (29,2%) au Portugal [11]. Par contre elle est nettement supérieure à celle de l'étude de Yuan et al. (6,1%) en Chine [10]. Le taux élevé des érythrodermies idiopathiques dans cette étude pourrait aussi s'expliquer par le faible taux de réalisation des examens anatomopathologiques dans notre étude (10 biopsies réalisées sur les 147 cas).

L'évolution était favorable dans 47,6% des cas et 1 (0,7%) patient était décédé. Li et al avaient également noté un faible taux de décès (5 sur 260 patients) [8]. Ces données montrent que dans la majorité des

cas les dermatoses érythrodermiques (majorité des étiologiques) n'engagent pas le pronostic vital à court terme.

CONCLUSION

Les érythrodermies constituent une affection rare en consultation dermatologique à Lomé. Il s'agit d'affections retrouvées plus fréquemment chez les adultes jeunes de sexe masculin. Les principales causes de ces érythrodermies chez les adultes étaient les dermatoses érythrodermiques dont principalement l'eczéma érythrodermique suivi du psoriasis érythrodermique.

ACKNOWLEDGEMENTS

- L'érythrodermie est un syndrome cutané peu fréquent en Afrique subsaharienne.
- Peu d'étude ont rapportées les aspects épidémiologiques et cliniques des érythrodermies.

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

Dermatofibrosarcoma protuberans (Report of 49 cases)

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SUMMARY

Background: retrospective study to elucidate the epidemio-clinical and pathological characteristics, management and evolutional aspects of DFS with comparison with the data of the literature. **Procedure:** a thirty seven-year study of all cases of DFS. **Results:** Forty-nine cases of DFS (22 males and 27 females) were diagnosed. Mean age at diagnosis was 48.2 years. The tumor appeared before the age of 15 years in five patients (10%). This was a recurrence in 12% of cases. Five patients reported a history of trauma. The average delay before consultation was 5.6 years. A solitary nodule was the predominant clinical aspect of DFS (59.2%). Mean size was 4.7 cm. The tumor was mainly located on the trunk. The diagnosis of dermatofibrosarcoma protuberans was histologically confirmed in all cases. Immunohistochemical study was achieved in 34 cases and showed positive staining for CD34. The treatment consisted of large surgical excision in all patients. Four patients had revision surgery because of tumor margins. Eight cases (17.4%) presented a local recurrence after a mean delay of 12.5 months. **Conclusion:** DFS is a low-malignancy potential skin tumor. Treatment of choice is surgery. The main risk is tumor relapse. A long follow-up is then very important to detect it.

Key words: Darier-Ferrand; Dermatofibrosarcoma protuberans; Treatment; Surgery; Recurrence

How to cite this article: Frikha F, Mseddi M, Bahloul E, Chaabouni R, Masmoudi A, Boudaya S, Chami I, Amouri M, Turki H. Dermatofibrosarcoma protuberans (Report of 49 cases). Our Dermatol Online. 2020;11(1):25-31.

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Our Dermatology Online

Original Article

Le dermatofibrosarcome de Darier Ferrand (Etude de 49 cas)

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RÉSUMÉ

Problématique: étude rétrospective afin de décrire les aspects épidémiologiques, cliniques, anatomopathologiques, thérapeutiques et évolutifs avec comparaison aux données de la littérature. **Matériel et Méthodes:** Etude de tous les dossiers des patients ayant présenté un DFS sur une période de 37 ans. **Résultats:** Quarante-neuf cas de DFS (22 hommes et 27femmes) avaient un âge moyen de 48,2 ans. La tumeur était apparue avant l'âge de 15 ans chez cinq patients (10%). Il s'agissait d'une récidive dans 12% des cas. La notion d'un traumatisme local était rapportée dans 5 cas. Le délai moyen de consultation était de 5,6 ans. L'aspect clinique prédominant était un nodule unique (59,2%). La taille moyenne était de 4,7 cm. Le tronc était la localisation préférentielle (55,1%). Le diagnostic positif était dans tous les cas confirmé par l'examen anatomopathologique. L'étude immunohistochimique était réalisée dans 34 cas et montrait un marquage des cellules tumorales vis-à-vis du CD34. Le traitement reposait sur l'exérèse chirurgicale. La reprise chirurgicale était indiquée chez quatre malades devant des limites atteintes. Une récidive locale était notée dans huit cas (17,4%) avec un délai moyen de 12,5 mois. **Conclusion:** Le DFS est un sarcome de faible degré de malignité. Le traitement chirurgical reste le seul traitement adapté de nos jours. L'évolution du DFS est surtout émaillée de récidives locales. Une surveillance clinique prolongée est nécessaire pour les détecter.

Mots clés: Darier-Ferrand; Dermatofibrosarcome protubérant; Traitement; Chirurgie; Récidive

INTRODUCTION

Le DFS est une tumeur mésenchymateuse rare, à malignité intermédiaire, caractérisée par son évolution lente, sa forte agressivité locale et des métastases exceptionnelles avec une forte tendance à la récidive. Cette tumeur, dont la fréquence est non négligeable dans les pays africains, pose encore plusieurs problèmes en rapport avec son aspect clinique trompeur évoquant surtout une cicatrice chéloïde (fréquente chez la population africaine) et responsable souvent d'un retard diagnostic. Sa gravité est liée à son agressivité locale et son très haut risque de récidive locale [1-4]. Nous présentons une étude rétrospective de 49 cas de DFS dans le but de décrire ses aspects épidémiologiques, cliniques, anatomopathologiques, thérapeutiques et évolutifs. Nos résultats seront comparés aux données de la littérature.

MATERIELS ET METHODES

Nous avons réalisé une étude rétrospective portant sur 49 cas de DFS histologiquement prouvés (sur biopsie cutanée et/ou sur pièce opératoire), répertoriés au service de dermatologie vénéréologie du centre hospitalier universitaire Hédi Chaker Sfax Tunisie, durant une période de 37 ans (1981-2017). Nous avons étudié les caractéristiques épidémiologiques, cliniques, paracliniques, l'aspect anatomopathologique, la prise en charge thérapeutique et le suivi des patients. Le recueil de données a été réalisé à partir des dossiers cliniques des patients.

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RESULTATS

Nos 49 patients étaient répartis en 22 hommes (44,9%) et 27 femmes (55,1%). La moyenne d'âge des patients au moment du diagnostic était de 48,2 ans avec des extrêmes de 17 et 84 ans. L'âge de début de la tumeur variait entre un an et 81 ans avec une moyenne de 39,5 ans. Cinq patients (10%) ont rapporté un début avant l'âge de 15 ans (huit mois, un an, sept ans, 11 ans et 14 ans) et 12 patients un début après l'âge de 50 ans. La notion de traumatisme antérieur était retrouvée dans cinq cas (10,2%). Le délai moyen de consultation était de 5,6 ans avec des extrêmes de trois mois et 30 ans. Six patients (12%) se sont présentés pour une récidive d'une tumeur opérée auparavant, une première récidive dans quatre cas et une deuxième récidive dans deux cas.

La tumeur était nodulaire dans 29 cas (59,2%) (Figs. 1 - 4), multinodulaire dans 16 cas (32,6%) (Figs. 5 et 6), et sous forme d'une plaque infiltrée dans quatre cas (8,2%) (Fig. 7). Elle était ulcérée dans six cas et hémorragique dans trois cas. La taille de la tumeur variait de un cm à 20 cm (moyenne de 4,7 cm). Elle

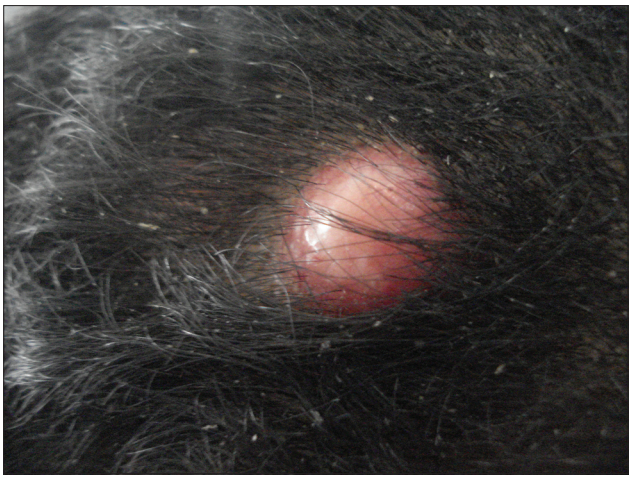

Figure 3: Lésion nodulaire érythémateuse du cuir chevelu.

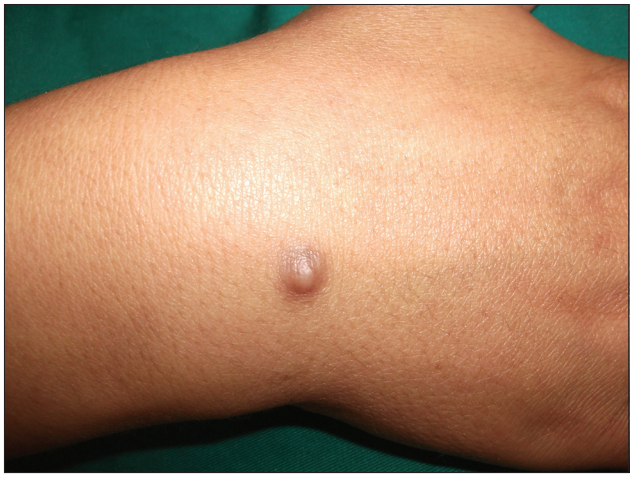

Figure 1: Un petit nodule légèrement pigmenté du dos du poignet.

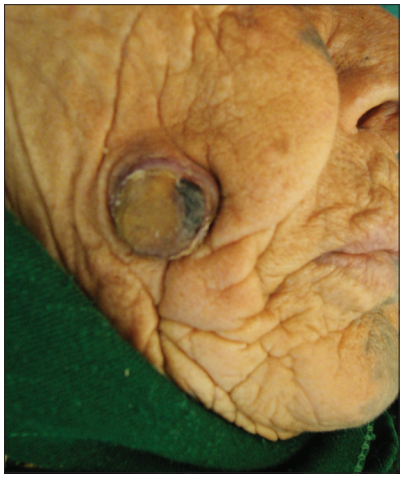

Figure 4: Lésion nodulaire de la joue.

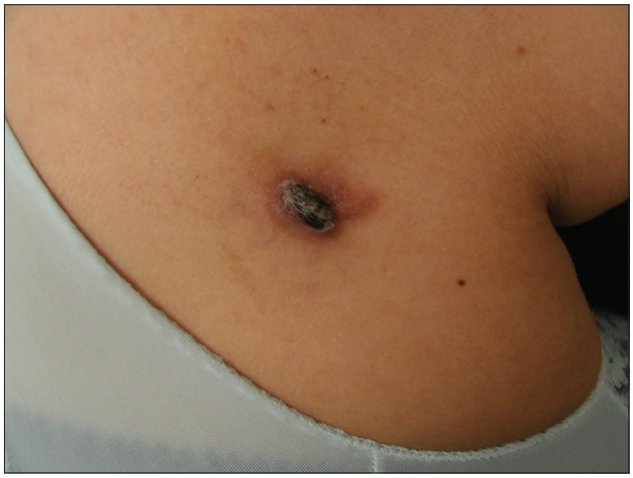

Figure 2: Une lésion nodulaire noirâtre infiltrée de la région scapulaire.

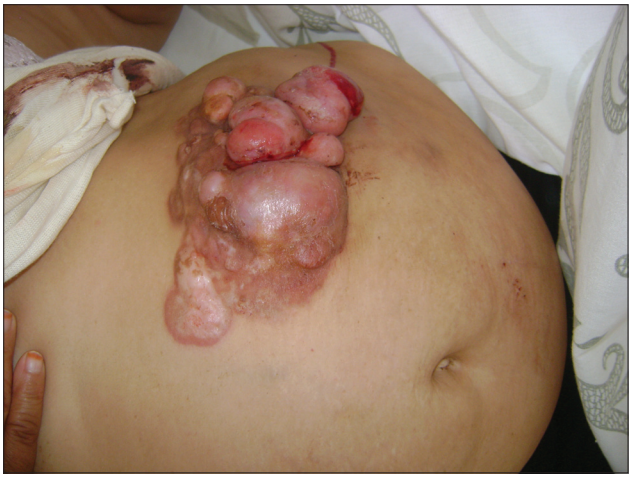

Figure 5: Une plaque multi-nodulaire géante du flanc.

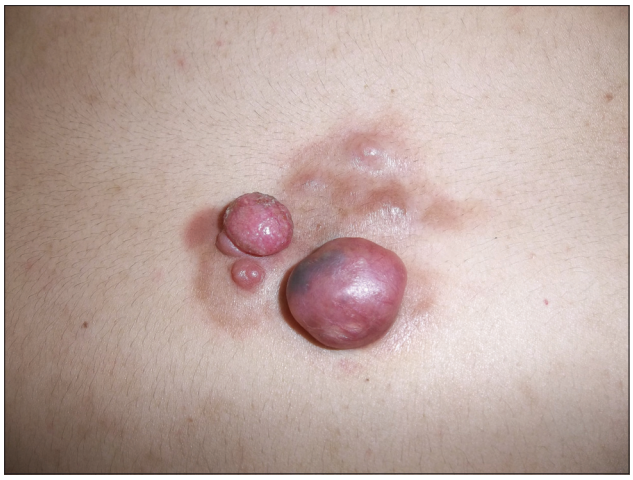

Figure 6: Une plaque mutinodulaire de la région lombaire.

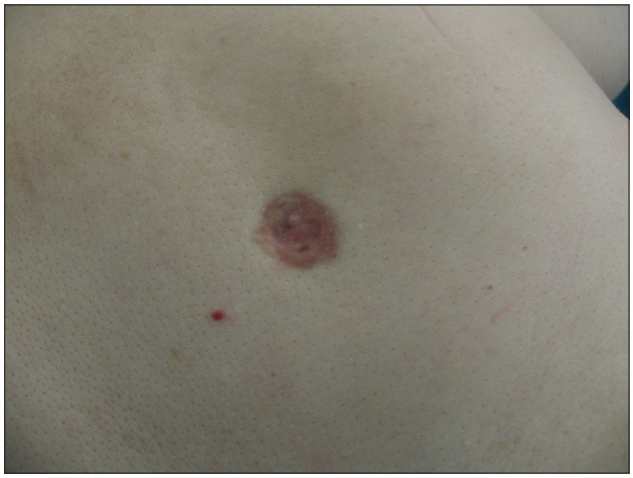

Figure 7: Une plaque infiltrée du dos.

était supérieure à dix cm chez cinq patients (Fig. 5). Le tableau I résume les principales localisations du DFS.

L'examen anatomopathologique a confirmé le diagnostic de DFS dans tous les cas montrant une prolifération dermo-hypodermique de faisceaux courts entrecroisés d'architecture storiforme, composés de cellules fusiformes uniformes peu ou modérément atypiques. L'hypoderme était envahi dans 44 cas (91% des cas) et un envahissement du muscle strié était retrouvé dans deux cas. Deux variantes histologiques particulières étaient retrouvées: DFS myxoïde caractérisé par un stroma myxoïde (deux cas) et DFS pigmenté (tumeur de Bednar) caractérisé par la présence de pigment mélanique dans le cytoplasme des cellules (un cas).

L'étude immunohistochimique, faite pour 34 patients (69%), montrait un marquage diffus (cytoplasmique et membranaire) et intense pour le

Tableau I : Localisation du DFS

Localisation du DFS	Nombre de cas (%)
Tronc	27 (55,1)
Membres	13 (26,5)
Tête	5 (10,2)
Cou	4 (8,2)

CD34 dans tous les cas. L'étude cytogénétique n'a pas été réalisée.

Quarante-six patients ont été opérés, l'exérèse chirurgicale était large avec des marges latérales de sécurité de cinq à dix cm chez 12 patients (26%) et de deux à quatre cm chez 34 patients (74%). En profondeur, l'exérèse emportait systématiquement une barrière anatomique saine (l'aponévrose dans 26 cas (56,5%), le périoste dans cinq cas (11%), une parotidectomie exo-faciale était réalisée dans un cas et une excision musculaire dans deux cas). La reprise chirurgicale était indiquée chez quatre malades devant des limites atteintes. La réparation de la perte de substance engendrée par l'exérèse chirurgicale faisait appel aux différents procédés de la chirurgie plastique: une suture directe chez 19 patients (41%), une greffe de peau chez 14 patients (31%) et un lambeau dans 11 cas (24%) et la cicatrisation dirigée chez deux patients (4%). Aucun patient n'a eu une radiothérapie ou une thérapie ciblée. Les récidives locales étaient notées dans huit cas (17,4%) après un délai moyen de 12,5 mois (deux mois à quatre ans). Le délai de récidive était de moins de trois ans dans 87,5% des cas. Ces récidives étaient multiples dans deux cas (un cas avait deux récidives et un cas avait huit récidives).

DISCUSSION

Le DFS, une tumeur à développement intradermique, a été décrite pour la première fois en 1890 par Taylor [5] comme une tumeur sarcomateuse ressemblant à une cicatrice chéloïde. Le DFS fut rapporté ensuite par *Darier* et *Ferrand* en 1924, et *Hoffman* en 1925 [5] qui l'intitule «dermatofibrosarcoma protuberans». En 1951, *Pack* et *Tabah* ont publié la première série importante [6] et en 1962, *Taylor* et *Helwig* ont établis les caractéristiques histologiques de cette entité [4,5].

L'âge de survenue du DFS se situe généralement entre 20 et 50 ans avec des moyennes oscillant entre 28 et 47 ans selon les auteurs [7-9]. L'âge médian de nos patients était de 39,5 ans (un an à 81 ans). L'affection n'épargne pas les sujets des âges extrêmes. C'est ainsi que sont décrits des cas chez l'enfant, des cas congénitaux et

même après 80 ans [9,10]. Les cas pédiatriques (enfant de moins de 15 ans) de DFS sont rares [11-13]. Dans notre série, on avait cinq cas de DFS de l'enfant et 12 cas étaient apparus après l'âge de 50 ans. Aucune relation de cause à effet n'a été démontrée [14,15]. Différents auteurs ont évoqué des facteurs exogènes dans la survenue de l'affection tels que des cicatrices de brûlure, de vaccination, de radiothérapie, des nævi traumatisés, des lésions syphilitiques, des microtraumatismes sur peau saine [9,16]. Dans notre série, aucun de ces facteurs n'a été retrouvé mais 10,2% des patients ont rapporté la notion de traumatisme antérieur. Cette notion est retrouvée dans 10 à 20% des cas selon les différentes séries [8,14,15]. Le retard diagnostique est comparable à celui observé dans les autres études pouvant atteindre 82 ans [2,7,9]. Le délai moyen séparant l'apparition de la lésion et la première demande de soins dans notre série est de 5,6 ans (un mois et 30 ans). Ce retard est expliqué par l'évolution lente et progressive de la lésion et l'absence de signes fonctionnels et de troubles généraux [9]. Dans notre série, six cas étaient des récidives (12%). Cette tendance à la récidive locale en l'absence d'une chirurgie adaptée est une donnée classique [7,17-19]. Cliniquement, le stade de début correspond à une plaque indurée, recouverte d'une peau d'aspect et de coloration normale, parfois brun rouge ou violacée. A un stade plus avancé (stade nodulaire), la plaque s'étale, sa surface devient irrégulière et bosselée, réalisant au bout de quelques mois à quelques années, une masse multinodulaire, souvent polychrome et dure. Cette évolution en deux stades n'est pas constante car certaines formes sont d'emblée uni-nodulaires ou multi-nodulaires [20]. Dans notre série, le DFS était le plus souvent nodulaire (59,2%). Non traitées, ces lésions peuvent devenir très volumineuses, ou bien s'ulcérer pour devenir douloureuses et hémorragiques [2,5,6,8]. L'ulcération était notée chez six patients et l'hémorragie dans trois cas. La lésion était douloureuse dans 24,5%. Ce taux est superposable aux données de la littérature où la douleur est notée dans 10 à 25% des cas [8].

Selon les publications, la tumeur mesure en moyenne un à cinq cm [8,9]. Dans notre série, la taille moyenne était de 4,7 cm. La taille maximale était de 20 cm, inférieure à celle de la série de *Hammas* (30 cm) [5]. Le DFS peut toucher n'importe quelle partie du corps avec une prédominance au niveau du tronc (surtout sa face antérieure) et des membres [9,13]. Selon les données de la littérature, l'atteinte du tronc est estimée entre 50 et 67% des cas [5,13]. Dans notre série, la topographie correspond aux données de la littérature avec une atteinte préférentielle du tronc dans 55,1% et des membres dans 26,5% des cas.

Comme dans notre série, l'état général des patients reste longtemps conservé [9]. Les métastases ganglionnaires et les métastases viscérales sont rares voire exceptionnelles et ne peuvent être retrouvées qu'après de longues évolutions ou une transformation sarcomateuse [9,16,17]. Elles n'ont été retrouvées chez aucun patient de notre série.

L'examen histologique est indispensable pour le diagnostic. La tumeur est faite d'une prolifération cellulaire dense, mal limitée, non encapsulée, occupant le derme, le plus souvent dans sa totalité. Elle envoie de fins prolongements parfois très profonds dans l'hypoderme, ce qui expliquerait la survenue de récidives même avec des marges de résection larges [5,9]. L'épiderme est respecté. Les cellules sont allongées, fusiformes, à cytoplasme plus ou moins abondant, à noyau ovalaire, régulier. Les mitoses sont variables avec de rares atypies. Le stroma est variable d'une zone à l'autre [5,9,16]. Les fibres collagènes et réticuliniques sont plus ou moins abondantes, tandis que les fibres élastiques sont refoulées à la périphérie de la tumeur. Au sein des amas de cellules néoplasiques, on distingue un nombre variable d'espaces vasculaires et des coulées cellulaires péri-nerveuses. Dans le temps survient une diminution progressive de la composante fibreuse conjonctive et une augmentation de la densité cellulaire. Sur le plan architectural, les cellules sont disposées en faisceaux rayonnants (aspect en "rayon de roue") ou tourbillonnants. Quelques sous types histologiques particuliers et rares [14,15], méritent d'être mentionnés: la forme myxoide et la forme pigmentée ou tumeur de Bednar, retrouvées chacune dans un cas. Le DFS infiltre sans détruire et les annexes sont longtemps conservées. Il n'existe pas de réaction inflammatoire. Il s'agit d'une tumeur de faible grade de malignité [20]. En général, l'aspect histologique permet de guider le diagnostic. Dans les cas douteux, l'immunohistochimie permet de distinguer le DFS des autres tumeurs à cellules fusiformes. Elle montre une positivité intense et diffuse du CD34 et une négativité constante de la desmine et de la PS100 [4,9,21]. Les zones en transformation sarcomateuse n'expriment qu'exceptionnellement et de façon très faible le CD34 [9]. Les techniques de cytogénétique mettent en évidence deux types d'anomalies du caryotype à type de chromosome en anneau surnuméraire [17,22] ou une translocation [17,22]. Le bilan d'extension n'est recommandé que pour les patients dont l'examen

clinique fait suspecter des métastases, en cas de DFS récurrent, ou en cas de transformation sarcomateuse. Ce bilan inclut une radiographie thoracique, une échographie abdominale et du trajet lymphatique [14].

Le traitement est difficile en raison de l'extension infra-clinique de la tumeur, pouvant être à l'origine d'une récidive. L'exérèse chirurgicale large est donc le traitement de référence [20]. Elle consiste à effectuer nécessairement des excisions larges et profondes en emportant une marge périphérique en peau saine de trois à cinq cm et en profondeur une barrière anatomique saine (13,20,22-26]. Il est évident que pour certaines localisations, telle que la face, cette marge de sécurité ne peut être respectée et devient même impossible. Dans ces localisations, la technique de Mohs mérite d'être discutée. Cette technique, faite avec de coupes horizontales, permet de réduire les marges à deux cm en moyenne, les marges étant réalisées sur mesure [27]. Elle a montré des taux de récurrence réduits avec une exérèse complète du DFS [21]. La reconstruction se fait par suture directe, cicatrisation dirigée ou par greffe cutanée ou lambeaux cutanés ou musculo-cutanés en fonction de la taille des lésions et leurs localisation. Le curage ganglionnaire systématique n'a aucun intérêt [8,13,16,28].

En raison de sa faible activité mitotique, le DFS n'est pas radiosensible [9,16]. La radiothérapie est préconisée dans les récidives multiples, les marges d'exérèse insuffisantes ou envahies, les tumeurs de très grande taille, les tumeurs primaires inopérables et les localisations empêchant une chirurgie large [13,14,26]. La chimiothérapie n'est pas une méthode efficace, toutefois, un certain espoir avec l'Imatinib (Glivec*) existe, et actuellement, plusieurs études cliniques sur le rôle néo adjuvent de cette molécule sont en cours [20,29].

Une surveillance clinique rigoureuse doit être maintenue, du fait de l'évolution lente et du haut pouvoir récidivant de cette tumeur [20]. Un suivi de trois à six mois est recommandé pour les trois à cinq premières années et un suivi annuel après [14,30]. Les récurrences après 5 ans peuvent se produire. Le suivi clinique peut être complété par une IRM dans quelques cas sélectionnés [14]. Le DFS est particulier par son agressivité locale et sa tendance aux récidives en l'absence de chirurgie adaptée. Ces dernières sont fortement corrélées avec des marges de résection incomplètes et sont estimées à 20% avec des extrêmes allant de 0 à 60% [20,21]. Les métastases sont beaucoup plus rares (5%) et sont pour la plupart pulmonaires [17,20]. La survenue de plusieurs récurrences est un facteur favorisant de cette dissémination [20] ainsi que la transformation sarcomateuse franchement maligne qui est exceptionnelle et qui se voit à un stade très tardif [5].

Les facteurs qui conditionnent le pronostic sont: la taille, la localisation au niveau de l'extrémité céphalique, une poussée évolutive rapide, des récidives rapides et surtout la qualité de l'exérèse initiale [2,5,13,20]. Celle-ci doit être radicale car elle constitue le facteur pronostique essentiel, conditionnant le risque de rechute locale [5,13].

CONCLUSION

Intermédiaire entre l'inoffensif fibrome et le redoutable sarcome, le DFS de DARIER FERRAND réalise une tumeur fibreuse de la peau d'un type particulier, rare, apparaissant à tout âge mais surtout à l'âge adulte. La localisation à la face antérieure du tronc est prédominante. Son évolution est locale sans troubles fonctionnels ni signes généraux. Le diagnostic, souvent tardif, est évoqué cliniquement et confirmé histologiquement, le recours à l'immunohistochimie se fait en cas de doute diagnostic. L'exérèse chirurgicale d'emblée large et profonde est le traitement de choix. Les thérapeutiques adjuvantes ne semblent avoir aucune place. Le pronostic vital étant rarement engagé par la prolifération, le pronostic est évalué sur le risque de récidive. Ainsi, le DFS est de bon pronostic lorsque le traitement est bien mené mais exige néanmoins une surveillance clinique longue.

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

Brief Report

A comparative trial of ice application versus EMLA cream in alleviation of pain during molluscum contagiosum removal by needle extirpation

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ABSTRACT

Background: Molluscum contagiosum is a common viral disease seen among the pediatric age group. A wide variety of treatment modalities are available for their management but no therapy is universally effective. Destructive modalities like cryotherapy, extirpation and radiofrequency removal are commonly used but are painful. **Aims and Objectives:** To evaluate the efficacy of Eutectic Mixture of Local Anesthetics (EMLA) cream versus ice application in alleviation of pain during molluscum contagiosum removal by extirpation. **Materials and Methods:** In this prospective study, 30 patients underwent molluscum contagiosum removal by needle extirpation. In 15 patients, EMLA cream was applied prior to the procedure and in the other half, ice was applied directly before the removal. Pain was evaluated using a Visual Analog Scale and the differences were compared. **Results:** Statistically, there was a significant difference in pain control between EMLA cream group and ice application group ($p<0.05$). The average pain score among patients where EMLA cream was applied was 7.6 (SD=0.81), whereas it was 5.1 (±0.9) in the ice group. **Conclusion:** In this study, use of ice application is helpful in reducing pain in comparison to EMLA cream during molluscum contagiosum needle extirpation.

Key words: Molluscum contagiosum; Extirpation; EMLA; Local anesthetics

INTRODUCTION

Molluscum contagiosum (MC) is a common viral infection caused by DNA Poxvirus. It has no other reservoir than humans and is transmitted directly by skin-to-skin contact or indirectly through fomites. It's a widely prevalent infection commonly affecting children, sexually active adults, and immunodeficient individuals [1]. A large number of treatments exist for treatment of MC which includes destructive therapies like curettage, cryotherapy, pricking with a sterile needle, electrodessication, photodynamic therapy and lasers. Other topical medications include salicylic acid, tretinoin, potassium hydroxide, trichloroacetic acid and imiquimod. However, no therapy is universally effective and most of these treatment modalities are not well tolerated as they are painful [2-4].

We carried out this study to evaluate the efficacy of Eutectic Mixture of Local Anesthetics (EMLA) cream versus ice application in alleviation of pain during molluscum contagiosum removal by extirpation.

MATERIALS AND METHODS

It was a prospective study carried out over a period of six months in which 30 patients (M:F 18:12), aged between 18-65 years were included. The patients were divided randomly in two groups. There were no statistical differences between the 2 groups in terms of baseline preoperative and operative characteristics. In 15 patients, EMLA cream was applied prior to the procedure and in the other half, ice was applied directly before the removal.For each patient, EMLA cream was

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applied for 1 hour before the procedure. An ice cube was applied for few seconds (3–5 seconds) immediately before the procedure. Pain was assessed by a numeric pain rating scale, where 0 indicated no pain and 10 the worst possible pain. Each patient was asked to self-report the pain intensity during the procedure. The molluscum were extirpated by using a 20g needle.

RESULTS

The pain score was assessed immediately after the procedure. The mean pain score among all patients at the end of procedure was 6.2 (±0.9). The mean pain score was slightly higher among females (6.4±0.4) as compared to males (5.8±0.3). There was not much difference in pain score among patients aged >50 years (5.8±0.6) and patients aged <50 years (5.6±0.4). The mean pain score was also higher among patients with more than 5 molluscum lesions (6.7±0.5) than among those with less than 5 lesions (5.2±06). The average pain score among patients where EMLA cream was applied was 7.6 (±0.81), whereas it was 5.1 (±0.9) in the ice group ($p<0.05$). During the study, no side effects were reported other than discomfort and pain from ice application noticed in 2 patients.

DISCUSSION

A large variety of treatment modalities have been used for molluscum but most of these involve destructive modalities which are painful so use of topical anesthesia becomes imperative for molluscum removal. Cooling of the skin is simple and cheap form of anesthesia. The exact mechanism of action of anesthesia by cooling is unknown, but several mechanisms, such as decreased nerve conduction, reduction in muscle spasms, prevention of edema after injury, a decrease in the release of pain-production substances locally, release of endorphins, and pain inhibition through inhibitory interneurons (pain gate), have been suggested [5-8]. These neural effects increase the patient's pain threshold and can diminish the need for pharmacologic interventions, such as narcotics or local anesthetics. Cold-induced analgesia has been shown to begin after the skin surface temperature lowers to ~13.6°C and stops when temperature rises to more than 15.6°C [8].

The present study shows that the application of ice cube for few seconds prior to extirpation result in a significant pain reduction. Mahshidfar et al reported a significant reduction in pain with ice application before injection for wound site injections [9]. In our study, a change in the pain score was evident after the procedure with cooling. Although the absolute numbers were small, the changes were perceptible to the patients. Certainly, it is an inexpensive intervention and particularly ideal in resource-constrained facilities, such as those in developing communities.

Limitations

Our study had certain limitations. The small sample size of the study group was one of the limitations. Due to the nature of the procedure (i.e., the application of an ice pack over the procedure site), blinding of the patients and staff was not possible, therefore the subjects were only blindly randomized. The positive compression effect may also contribute to pain relief.

CONCLUSION

In the present study, the analgesic effect of cooling was assessed and found to be associated with less pain during removal of molluscum contagiosum. It can be used as a safe, cheap and effective modality of analgesia in dermatological procedures.

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

Brief Report

Pattern of cutaneous infections in pediatric age group – A clinico-observational study

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ABSTRACT

Background: Among the various pediatric health problems, skin conditions constitute a significant proportion. Cutaneous problems can cause significant morbidity in the pediatric population. The pattern of skin problems in pediatric population differs from adults with infections and infestations being the most common problems followed by conditions like eczema and psoriasis. **Aims and Objectives:** We carried out this study to assess the clinical pattern of infections and infestation in pediatric age group. **Materials and Methods:** It was a prospective, observational study carried out over a period of two years in which two hundred children aged between 0-18 years, presenting with cutaneous infections in our centre were included. A detailed history, complete dermatological examination, along with routine investigations wherever required were recorded in a predesigned proforma. **Results:** The study group comprised of 200 children (M: F 114:86), with 44 children aged <5 years, 80 between 5-10 years and 76>10 years of age. Infections were seen in 164 children while infestations like scabies and lice were seen in 36 children. Bacterial infections were the most common infection seen in 64 children, followed by fungal infections in 56 and viral infections in 44 children. Scabies was the most common infestation seen in 28 children while lice infestation was seen in 8 children. **Conclusions:** The dermatoses such as infections and infestations are very common in the pediatric age group.

Key words: Pediatric dermatoses; Infections; Infestations; Impetigo

INTRODUCTION

Pediatric dermatology is a highly specialized subentity of dermatology practice. Skin diseases are a major health problem in the pediatric age group with children constituting around 30% of all outpatient visits to the dermatologist [1]. Cutaneous problems can cause significant morbidity in the pediatric population. The pattern of skin problems in pediatric population differs from adults with infections and infestations being the most common problems followed by conditions like eczema and psoriasis.

We carried out this study to assess the clinical pattern of infections and infestation in pediatric age group.

MATERIALS AND METHODS

It was a prospective, observational study carried out over a period of two years in which two hundred children aged between 0-18 years, presenting with cutaneous infections in our centre were included. A complete history including age, sex, duration of the disease, family history complete dermatological examination, along with appropriate investigations such as KOH examination, Tzanck test, Gram's staining, hematological investigation, biochemical investigations and skin biopsy etc., wherever required were recorded in predesigned proforma.

RESULTS

The study group comprised of 200 children (M:F 114:86), with 44 children aged <5 years, 80 between 5-10 years and 76 children>10 years of age. Majority of children (n=124) belonged to urban background while 76 were from a rural areas and most of the children were school-going (n=172). Bacterial infections were the most common infection seen in 32%(n=64)

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children, followed by fungal infections in 28% (n=56) and viral infections in 22% (n=44) children. Scabies was the most common infestation seen in 28 children while lice infestation was seen in 8 children. Bacterial infections were the most common infection in patients aged <5 years whereas fungal infections were more common in children aged >10 years. The pattern of various infections and infestations in our study group is presented in Table 1. Family history of similar infections and infestations was present in 22% cases.

DISCUSSION

The pattern of skin lesions in children is different from adults and is greatly influenced by climatic factors, dietary patterns, and socioeconomic status. Infections and infestations are the most common dermatoses encountered in the pediatric population. Different studies have reported the prevalence rates of infections and infestations ranging between 32-85% in the pediatric population with cutaneous dermatoses [2-5]. They are a cause of significant morbidity in the pediatric population. Skin diseases are the most frequent diseases of school children in many developing countries. The school environment makes children vulnerable to the cross transmission of communicable skin diseases among themselves and their family [6] The prevalence of pediatric dermatoses is higher in rural areas as compared to urban areas in relation to poor socioeconomic status, poor personal hygiene, overcrowded, families lack of general awareness, lack of education, sanitation and specialized health facilities [7].

Table 1: Pattern of infections and infestations in the study population

	Age <5 yrs	5-10 yrs	>10 yrs	Total
Bacterial 64				
Folliculitis	6	16	10	(32)
Impetigo	12	10	2	(24)
Secondary infections	2	2	2	(6)
Acute paronychia	0	0	2	(2)
Fungal 56				
Dermatophytosis	4	10	12	(32)
Candidiasis	14	0	2	(16)
Pityriasis versicolor	2	0	6	(8)
Viral 44				
Molluscum	6	8	2	(16)
Warts	4	4	6	(14)
Varicella	2	5	3	(10)
Hand foot mouth disease	3	1	0	(4)
Pityriasis rosea	0	3	1	(4)
Infestations 36				
Scabies	9	5	14	(28)
Pediculosis	0	3	5	(8)

In our study, bacterial infections were the most common, seen in 32% children with folliculitis being the most common infection, seen in 16% followed by impetigo in 12%. It was similar to the studies by various researchers, who also observed bacterial infections to be the most common pediatric skin infection [4,5] (Fig. 1). Fungal infections of the skin were the second most common infection in our study, seen in 28% children. The incidence of fungal infections has been reported to vary from 3.3% to 8.5% in various other studies [8,9].Dermatophytic infections like tinea corporis, tinea cruris and tinea faciei were more common in older children while candidal infections like intertrigo were more common in infants and younger children (Fig. 2). Pityriasis versicolor was also more common in the older age group owing to increased sweating tendency.

Viral infections were seen in 22% of our study group. Reddy et al reported an incidence of 40% of viral

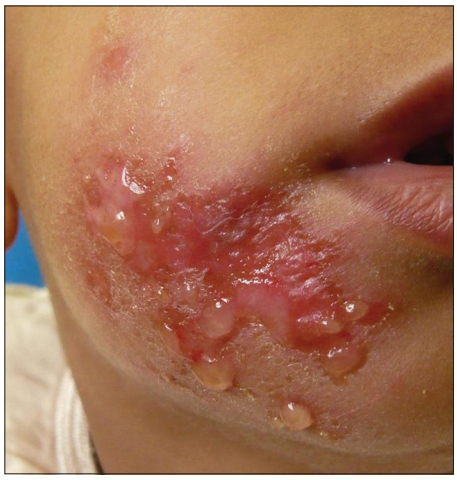

Figure 1: Bullous impetigo in a 3-year old child.

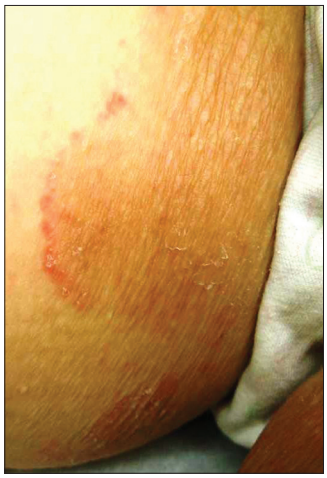

Figure 2: Tinea cruris in a 8-year old child.

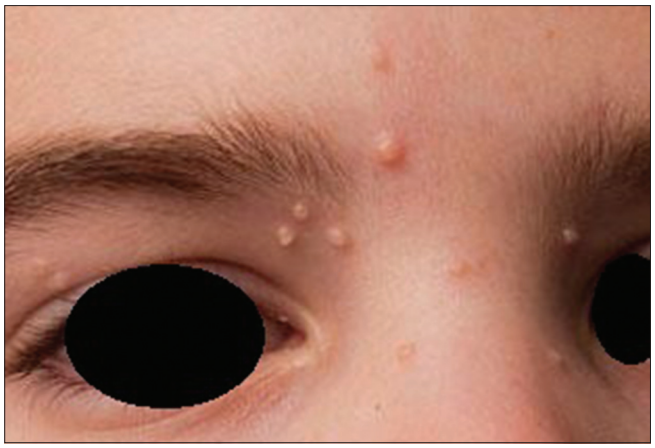

Figure 3: Molluscum contagiosum in a 5-year old child.

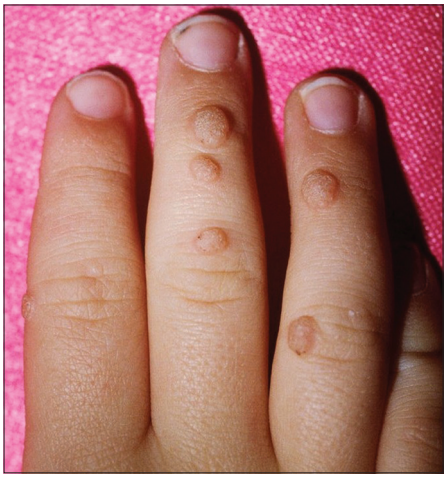

Figure 4: Multiple warts in a 7-year old child.

infections [9]. Molluscum contagiosum was the most common viral disease in our study seen in 8% cases, followed by warts in 7%, varicella in 5%, hand foot mouth disease and pityriasis rosea in 1% each. Reddy et al also observed molluscum to be the most common viral infection (38%) followed by warts in 20% [9] (Figs. 3 and 4). Scabies was the most common infestation in our study, seen in 14%. The incidence of scabies has been reported to vary from 5% to 22% in different studies. A family history of scabies was seen in 22 out of 28 patients which can be attributed to its mode of transmission by close contact.

Our study had few limitations. It was conducted in a single center and sample size was small. A large, prospective multicentric study needs to be conducted to know more about pediatric infective dermatoses.

CONCLUSIONS

The dermatoses such as infections and infestations are very common in the pediatric age group with bacterial infections being the most common infections followed by fungal infections. A detailed knowledge about the pattern of pediatric dermatoses is useful in implementing essential changes in health education and disease control.

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

Case Report

A newly diagnosed South African case of congenital erythropoietic porphyria

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ABSTRACT

Congenital Erythropoietic Porphyria (CEP) is a rare disease due to the marked deficiency of uroporphyrinogen III synthase (UROS) enzyme, which leads to the accumulation of uroporphyrin 1 and coproporphyrin 1 isomers. We report a 3-year-old girl presenting with a one-year history of sun induced blistering skin lesions born to a HIV-positive mother in South Africa. She had systemic disease as evidenced by a severe hemolytic anemia and splenomegaly. The biochemical fraction analysis of porphyrines in urine and stool samples confirmed our clinical diagnosis. The UROS enzyme defect in red blood cells and fibroblast can be cured via stem cell transplantation. Our patient is on the waiting list for bone marrow transplant. CEP has a multisystemic involvement including cutaneous, ocular, skeletal and hematological complications, requiring a multidisciplinary management approach.

Key words: Congenital erythropoietic porphyria; Stem cell transplantation; Children; Skin

INTRODUCTION

Congenital Erythropoietic Porphyria (CEP), also named as Günther's disease, is an extremely rare condition. There have been approximately 300 cases reported in the English literature. CEP has no racial predilection and occurs equally in both genders. It has a broad range in age (median 1.75 years, from 30 weeks' gestation to 40 years), manifestations and varying severity at the onset of the disease [1]. A marked deficiency of uroporphyrinogen III synthase (UROS) enzyme leads to the accumulation of uroporphyrin 1 and coproporphyrin 1 isomers in all tissues of the body [2]. The genetic defect is most commonly in the gene encoding UROS enzyme in an autosomal recessive manner, and rarely in the GATA1 gene as an X-linked manner. *CF3R* mutation of the UROS gene is accounting for 20% of the reported mutations in CEP [3].

CASE REPORT

A 3-year-old girl was brought to the Dermatology Outpatient Clinic with a one year history of blistering skin lesions on the sun exposed areas of her face ear lobes and dorsum of her both hands mostly following sun exposure. She was the only child and there was no one in her family with a similar skin condition. She was HIV exposed but was tested negative at birth, 6 weeks, 10 weeks and lastly 6 weeks after stopping 6 months of breastfeeding, therefore received prophylactic nevirapine treatment.

Her clinical features included hypertrichosis of her cheeks, erosions and scarring on her face, ear lobes and dorsum of her both hands, and a few intact vesicles located on her hands (Fig. 1). Her teeth showed a reddish brown discoloration (Fig. 2). Abdominal examination revealed significant splenomegaly. Her urine was red in color, and microscopic examination excluded hematuria. The clinical presentation suggested the diagnosis of CEP which was additionally supported by orange red fluorescence of her teeth and urine under Wood's lamp examination (Fig. 3). Histopathological examination of an intact blister revealed a large cell-poor subepidermal blister, festooning of dermal papillae into the blister cavity base, and superficial, thick walled sized vessels with PAS positive material within the

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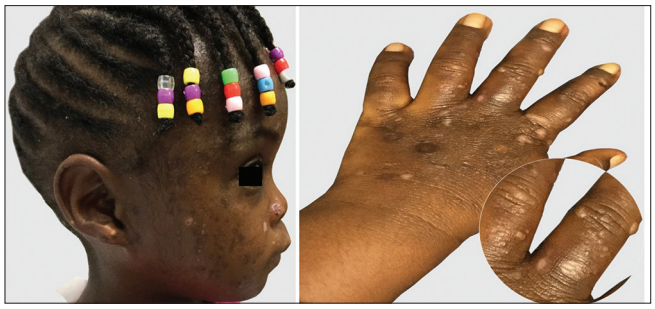

Figure 1: Hypertrichosis, erosions and scarring on the face. Scarring and an intact vesicle located on her hand.

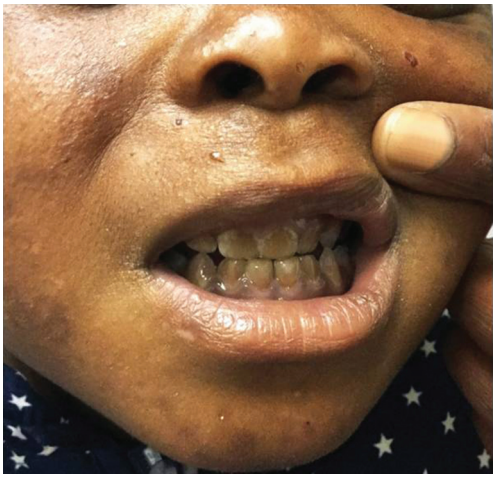

Figure 2: Erythrodontia.

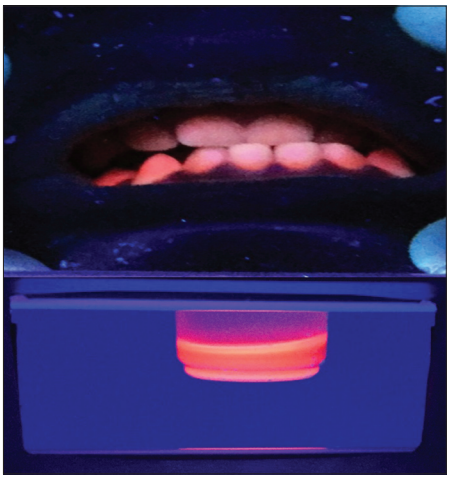

Figure 3: Wood's lamp examination showing orange red florescence of her teeth and urine.

vessel wall. Immunofluorescence revealed a positive C3 and lgG staining at the dermoepidermal junction and in the blood vessel walls.

Urine analysis showed markedly raised porphyrin level (100617.4 nmol/L). Fraction analysis revealed raised uroporphrin (+++) and coproporphyrin (+). Stool analysis showed raised porphyrin level (7096 nmol/gm). Fraction analysis revealed raised protoporphyrin (+), uroporphrin (+) and coproporphyrin (+++). Isocoproporphrin in stool which is diagnostic for porphyria cutanea tarda was undetected. During acute intermittent porphyria attacks urinary porphobilinogen and δ-aminolevulinic acid excretion is high with normal faecal porphyrin levels, which were normal in our case. The biochemical fraction analysis supported our clinical diagnosis of CEP. She had no polycythemia, but she had a significant hemolytic anaemia (Hb:12.0 gr/dL, Direct Coomb's Test +, LDH:742 U/L). Serological investigations for liver and renal function tests, vitamin D and calcium levels were unremarkable. Hepatitis markers (HptA Ag, HptB Ag, HptC Ag) and HIV were negative. The history, clinical presentation, urine and stool investigations and biochemistry confirmed the diagnosis of CEP.

The mother was informed about the photoprotective measures, the limited management options and the prognosis of the disease. The patient was HLA typed for a bone marrow transplantation, and she is currently on the waiting list.

DISCUSSION

Cutaneous photosensitivity, blistering eruptions and increased fragility of the sun exposed skin are early cutaneous manifestation of CEP. The appearance of reddish colored urine on diapers is the first manifestation at birth. Secondary infections could cause scarring and may lead to severe deformity and disfigurement. Hypertrichosis may be seen in some patients [4]. Haemolytic anemia and splenomegaly are manifestations of systemic involvement, whereas the onset of haematological manifestations by the age of 5 is reported to be a poor prognostic indicator [1]. Deposition of porphyrin in the eye may lead to corneal ulcers, scarring and eventually to blindness [5]. Porphyrin deposits in bone lead to osteopenia, osteoporosis and increased risk in the tendency of spontaneous fractures. Additionally, vitamin D deficiency from prolonged periods of sun avoidance needs to be monitored [6].

Patient education and sun avoidance is crucial in the management of the disease. Blood transfusion and splenectomy can be considered in patients with severe hemolytic anaemia [2].

The UROS enzyme defect can be cured via stem cell transplantation (SCT) (including bone marrow and umbilical cord transplants) by replacing the defective

enzyme in bone marrow erythroblasts, which makes the SCT the only known cure available for this disease. SCT was used first time in 1991, and since then there has been approximately 24 patients successfully treated with SCT due to CEP. SCT spectacularly improves cutaneous and systematic manifestations of CEP; however the treatment is associated with mortality due to severe complications (i.e. infections) and requires long term outcome studies [7].

CEP is a rare disease with multisystemic involvement requiring a multidisciplinary management approach.

Consent

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

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Our Dermatology Online

Case Report

Onychomadesis in children: think about a late complication of hand-foot-mouth disease

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ABSTRACT

Hand foot mouth disease (HFMD) is considered to be the most common infectious disease in association with onychomadesis. Coxsackie A6 may be the major subtype associated with onychomadesis after HFMD. A 2-year-old female child was referred to our department for an acute vesiculobullous eruption since two days with fever. Dermatological examination revealed a vesiculobullous eruption located on her hands and on her feet. Two months later she consulted for changes of her finger nails which appeared since 3 weeks. Her parents denied a nail trauma or fungal infection. The diagnosis of onychomadesis secondary to this HFMD was diagnosed. Physical examination revealed nail matrix arrest on her right index and right middle finger. The nail changes healed spontaneously without medication within two months. Practioners should be aware of this late complication to avoid unnecessary treatments and to recommend a simple follow-up.

Key words: Neonatal onychomadesis; Hand-foot-mouth disease; Onychomadesis

INTRODUCTION

Hand-foot-mouth disease (HFMD) is an acute infection caused most often by coxsackie A virus type 6 and enterovirus 71 frequently in children [1]. It generally starts with oral lesions after 4-6 days of incubation period [2].

CASE REPORT

A 2-year-old female child was referred to our department for an acute vesiculobullous eruption since two days with fever. Dermatological examination revealed a vesiculobullous eruption located on her hands (Fig. 1) and on her feet (Fig. 2). She also had some superficial erosions on her mouth. The diagnosis of hand-foot-mouth disease was assessed. She healed spontaneously within 4 days. Two months later she consulted for changes of her finger nails which appeared since 3 weeks. Her parents denied a nail trauma or fungal infection. On further quiery and since she suffered from hand-foot-mouth disease since two months, the diagnosis of onychomadesis secondary to this syndrome was diagnosed. Physical examination revealed nail matrix arrest on her right index and right middle finger (Fig. 3). The nail changes healed spontaneously without medication within two months.

DISCUSSION

HFMD is characterized by maculopapular and vesicular lesions especially on the hands, feet and mouth. Onychomadesis is the spontaneous separation of the nail plate from the matrix [1]. There are many etiologies responsible of the diagnosis of onychomadesis especially infections such as HFMD especially in children and attributable to coxsackie virus type A6. The first case was reported in 2000 in Chicago [3]. HFMD is considered to be the most common infectious disease in association with onychomadesis. Coxsackie A6 may be the major subtype associated with onychomadesis after HFMD. The nail changes vary from beau's lines to complete nail shedding. The median latency period between HFMD and onychomadesis is 40 days.

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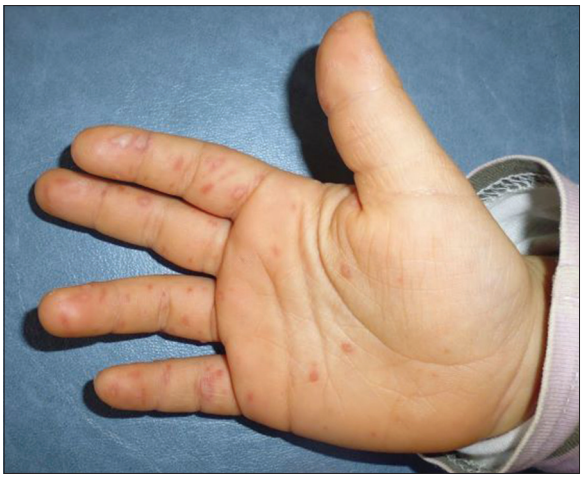

Figure 1: Vesiculobullous eruption on the right hand.

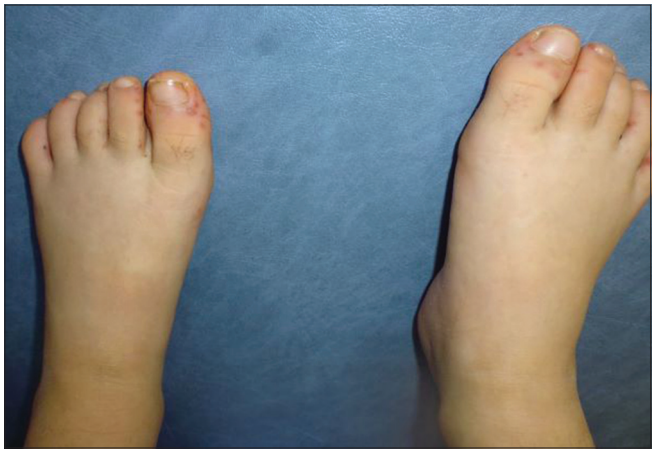

Figure 2: Vesiculobullous eruption on the feet.

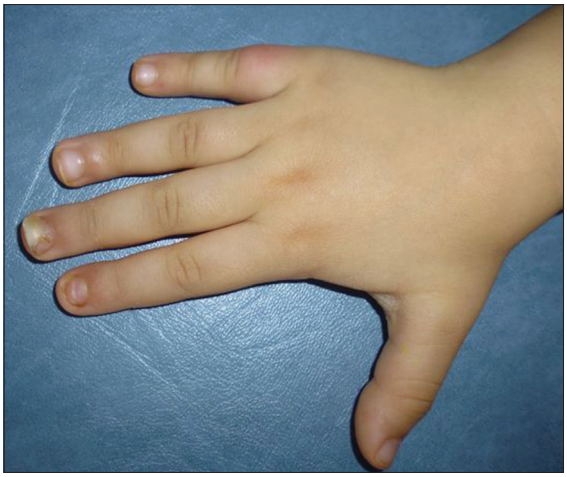

Figure 3: Onychomadesis on the nails of index and middle fingers of right hand.

A study from Taiwan reported that the incidence of onychomadesis in children with hand-foot-mouth disease was 5% [4,5]. This complication is considered even epidemic in Taiwan [2,6]. The mechanism of onychomadesis is still unknown. The difference in the turnover time between skin and nail could explain the delayed onset of nail changes after resolution of the systemic and cutaneous signs of HFMD [7]. Onychomadesis occurring after HFMD is temporary with spontaneous normal regrowth [8,9]. Indeed, there is no need for treatment and usually onychomadesis in those children diseappears spontaneously within 1 to 2 months [10].

CONCLUSION

In front of onychomadesis diagnosis in a child, a history of viral illness especially HFMD should be searched actively [11]. The diagnosis should be suspected especially in a well-appearing patient, absence of a known trauma. We should reassure the patient and his parents that it has a good prognosis and will heal spontaneously within one to two months [12]. Practioners should be aware of this late complication to avoid unnecessary treatments and to recommend a simple follow-up [13].

Consent

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

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Our Dermatology Online

Case Report

Stress associated median canaliform dystrophy of Heller in medical students more prominent on dominant thumb nail: A case series

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ABSTRACT

Median canaliform dystrophy of Heller is an unusual condition, presenting morphologically as a central or paramedian longitudinal groove with lateral projections, creating an appearance of 'inverted fir tree- like' pattern. Exact etiopathogenesis is unclear, however it has been proposed that Median Canaliform Dystrophy of Heller, is an acquired entity. Repetitive nail plate and cuticle trauma is a common association and treatment with oral retinoids have been hypothesized as the cause, however the etiology remains elusive for most affected individuals. Treatment is often unsatisfactory and prolonged, however topical 0.1% tacrolimus, 0.05% tazarotene and injectable triamcinolone acetonide have been tried with notable improvement. Psychiatric consultation should be sought when associated with obsessive – compulsive, impulse control or depressive disorders. We present a case series of three medical students, with stress associated Median Canaliform Dystrophy of Heller, typically more severe on right thumb nail in all three cases.

Key words: Stress; Medical student; Median nail dystrophy; Dominant thumb

INTRODUCTION

Median Canaliform Dystrophy of Heller, is a rare nail abnormality, presenting clinically as central or paramedian groove or split with multiple, transverse parallel lines, typically involving one or both thumb nails, however other nails can also be involved. Heller, recorded the first ever case of this disorder in 1928 [1]. The diagnosis is mostly based on Clinical features. Exact etiopathogenesis is elusive, however self inflicted trauma is implicated in most cases. Majority of cases are acquired but few cases with familial occurrence and following use of oral retinoids have been reported [2].

Male:Female ratio is 1:1 [3] and mean age of occurrence is 25.72 years [4]. The closest differential diagnosis to this condition is Habit Tic Deformity. Multiple treatment modalities have been tried with unsatisfactory outcome.

We report a case series of Median Nail Dystrophy of Heller in three medical students, with a common background of underlying stress related to exams and lesions predominantly on the right thumb nail.

CASE REPORTS

Case 1

A 24 years old, intern presented with single longitudinal groove with multiple oblique ridges running in a paramedian and outward manner, giving a 'fir tree – like' appearance on bilateral thumb nails since three years. Lesions were more prominent on right thumb nail. Lunula was enlarged in size than normal on bilateral thumb nails (Fig. 1). The median longitudinal groove extended from proximal nail fold upto distal nail edge. Cuticle was normal in bilateral thumb nails, with mild periungual scaling. No other finger nails were affected. No associated skin or mucosal lesions were present.

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Case 2

A 22 years old, male final year M.B.B.S. student, presented with similar complaints as that described for case 1 with additional findings of periungual hypopigmentation with superficial scaling and soggy appearance (Fig. 2).

Case 3

The third patient was 21 years old male, third year M.B.B.S. student, presented with similar signs and symptoms (Fig. 3). All the patients visited us due to cosmetic concern regarding the nails. There was a common background of underlying stress related to exams. With every semester exams the habit of nail picking/biting got aggravated and severity of nail involvement increased. There was no history of oral retinoid or other medication use, no history of contact with irritants or allergens. There was no systemic involvement. All routine investigations were normal. Nail dermoscopy, imaging studies and subungual scraping for KOH was done to rule out any underlying nail pathology. A diagnosis of Median Canaliform Dystrophy of Heller was made based on clinical evaluation. Psychiatric referral was done.

DISCUSSION

Median Canaliform Dystrophy of Heller, also known as Dystrophia unguis mediana canaliformis, nevus striatus unguis or soleonychia, presents clinically as longitudinal central or paramedian groove, with multiple lateral transverse projections, giving a pattern of 'inverted fir tree – like' appearance. In severe cases, the nail plate can split along the groove. Other features like enlargement and redness of lunula, thickening of proximal nail fold can be found. There is no sex predilection and mean age of presentation is 25.72 years [4]. Involvement most commonly is symmetrical and frequently involves the thumb, however other fingers and toes may be affected. In our case series there was predominant involvement of right thumb. This can be explained hypothetically because of involvement of dominant hand with recurrent Koebner phenomenon and relative ease of self inflicting trauma.

It is an acquired entity however Sweeney et al has reported familial clustering of cases in 2005 [3]. Exact etiopathogenesis is not fully understood, however

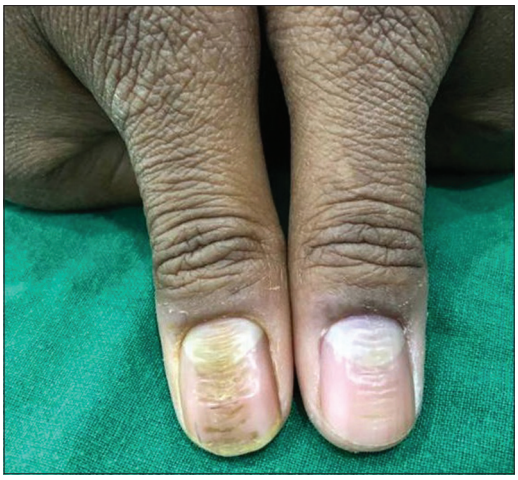

Figure 1: Single longitudinal groove with multiple oblique ridges running in paramedian and outward manner giving an 'inverted fir tree – like' appearance on both thumb nails, more prominent on right thumb nail in a 24 years male medical student. Size of Lunula enlarged on bilateral nails.

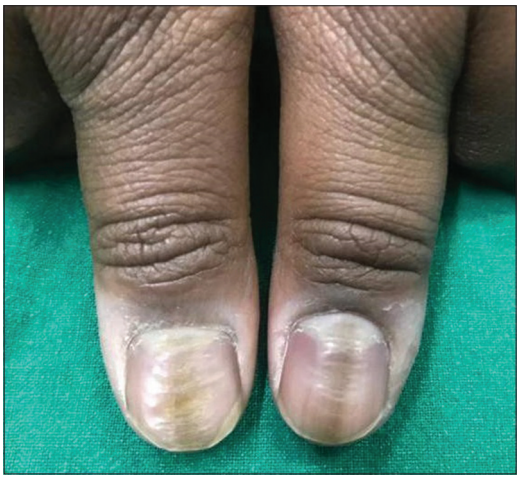

Figure 2: A single median longitudinal ridge with lateral projections, giving an 'inverted fir tree –like' pattern with enlarged lunula and periungual soggy appearance on both thumb nails, more prominent on right thumb nail, in a 22 years male medical student.

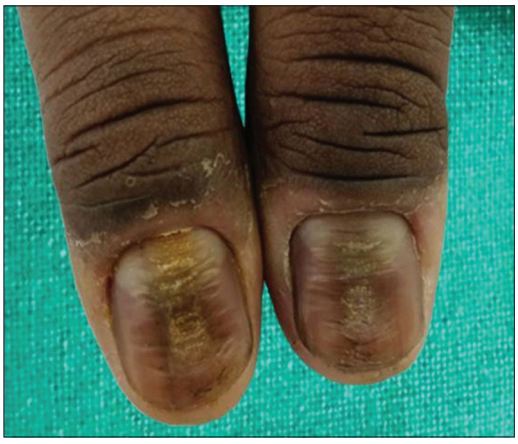

Figure 3: A single median longitudinal ridge with lateral projections, giving an 'inverted fir tree –like' pattern with enlarged lunula on both thumb nails more prominent on right thumb nail and bilateral mild superficial scaling, in a 21 years male medical student.

conditions causing temporary defect in nail matrix due to focal infection, discretization, self inflicted trauma to nail or nail bed or repetitive pushing down of cuticle or proximal nail folds, use of oral retinoids, have been thought to be the causative factors. Reason for formation of longitudinal groove can be attributed to absence of keratinocytic adhesions within nail matrix with dyskeratosis with splitting of nail plate due to weaker tensile strength [4].

The most significant differential diagnosis of MCD of Heller is Habit Tic Deformity. Habit tic deformity is caused by habitual or constant rubbing of the thumb's proximal nail fold and cuticle by the tip of second digit, resulting in longitudinal nail defects. Themain differentiating feature is normal cuticle in MCD of Heller,while cuticle is affected or completely lost in Habit Tic Deformity [5].

Most cases are poorly responsive to treatment. Topical application of tacrolimus (0.1%) and tazarotene (0.05%) [6], have been tried with notable improvement and acts by normalizing the process of keratinization with additional anti-inflammatory role. Satisfactory results have been seen with intralesional steroid injection using triamcinolone acetonide. Psychiatry consultation is indicated in cases of obsessive-compulsive, anxiety, depression or impulse-control disorders. Non-medical therapy includes covering the nail plate with nail wrap or tape, to avoid direct trauma to the nails.

CONCLUSION

The novelty of this case series lies in the fact, that all the three reported patients had aggravation of symptoms with stress related to examinations, predominantly involving dominant thumb nails. This is possibly the first case series reported to the best of our knowledge.

Consent

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

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Our Dermatology Online

Case Report

Onychomadesis secondary to autoimmune thyroid disease mimicking thyroid acropachy

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ABSTRACT

Onychomadesis has been described as proximal separation of the nail plate from the nail matrix due to drastic insult to the matrix that induces a total arrest of matrix activity. A vast variety of health conditions, mainly including infections and autoimmune diseases have been implicated in the etiology of onychomadesis. However, up to now no published data is available on the association of autoimmune thyroid disease with onychomadesis. Here, we present a case of autoimmune thyroid disease induced onychomadesis in a 85-year-old woman. Moreover, we highlighted a distinct feature of the patient in that nail findings of the patient exceptionally resemble thyroid acropachy, which is a very rare manifestation of autoimmune thyroid disease.

Key words: Onychomadesis; Autoimmune thyroid disease; Acropachy

INTRODUCTION

Onychomadesis is characterized by spontaneous detachment of the nail plate from the nail matrix, in which detachment begins at the proximal end of the nail bed, although not always, consequently leading to nail shedding. A vast variety of health conditions, mainly including infections and autoimmune diseases have been implicated in the etiology of onychomadesis [1,2]. It is well-known that thyroid diseases have significant cutaneous manifestations, some of which are distinctly linked with nails [3]. Thyroid acropachy is the utmost cutaneous manifestation of autoimmune thyroid disease, which is characterized by clubbing of fingers and toenails, swollen digits along with subperiosteal new bone formation [4-10]. Here, we describe a patient with onychomadesis associated with autoimmune thyroid disease, whom clinical features mimic those of thyroid acropachy. To our knowledge, this is the first case to be published in which the clinical findings favored the diagnosis of onychomadesis associated with autoimmune thyroid disease.

CASE REPORT

A 85-year-old woman visited our department with a history of nail shedding in her fingernails and deformation in her toenails. She told that a couple of weeks ago two of her fingernails and a small part of her left big toenail had lifted and subsequently shed with accompanying subtle pain. Her medical history revealed long-standing hypertension, for which she was receiving candesartan/hydrochlorothiazide for years. There was not any history of trauma or precipitating factors preceeding the nail findings. She denied any family history of similar lesions. Upon dermatological examination, we observed anonychia of left middle finger and right ring finger, also proximolateral quadrant of the left big toenail was seperated from the nail bed. All toenails except right 3-5th toenails were dystrophic with subungual hyperkeratosis (Figs. 1 and 2). A dusky erythema in distal parts of foot digits was also noticed (Fig. 1). Dermoscopic examination of toenails revealed subungual hyperkeratosis and purple to black pigmentation corresponding subungual hemorrhage in right 1st, 2nd and left 1-3rd toenails (Fig. 3). Mycological

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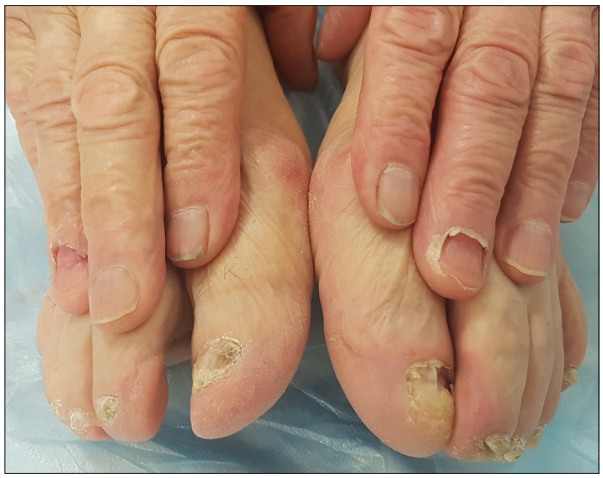

Figure 1: Anonychia of left middle finger and right ring finger, partial loss in left big toenail, subungual hyperkeratosis on toenails. Note the dusky erythema on distal parts of toe digits extending onto the toe pulp.

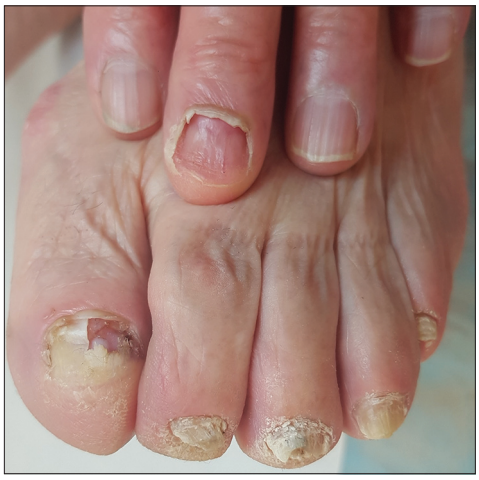

Figure 2: Closer view of left hand and foot. Note onychorrhexis of fingernails and subungual hemorrhages on toenails

examination of toenails was negative. Laboratory studies including biochemical panel, complete blood and differential counts, erythrocyte sedimentation rate, serum ferritin, folate, vitamin B12 and vitamin D levels were normal. The serum thyroid stimulating hormone level was 5.78mIU/L (normal range, 0.55 to 4.78) and anti-thyroid peroxidase (anti-TPO) was 80 IU/ ml (normal, <60 IU/mL). Anti-nuclear antibody, anti-double stranded DNA antibody, antibodies to saline-extracted antigens (ENA panel) and rheumatoid factor were negative. Plain X-ray radiographic examination of hand and foot were normal. The thyroid ultrasound showed a diffusely enlarged, hypo echoic gland. Thus, based on history and clinical and radiological findings, a diagnosis of onychomadesis associated with autoimmune thyroid disease was established. The patient was referred endocrinology department but lost follow-up after referral.

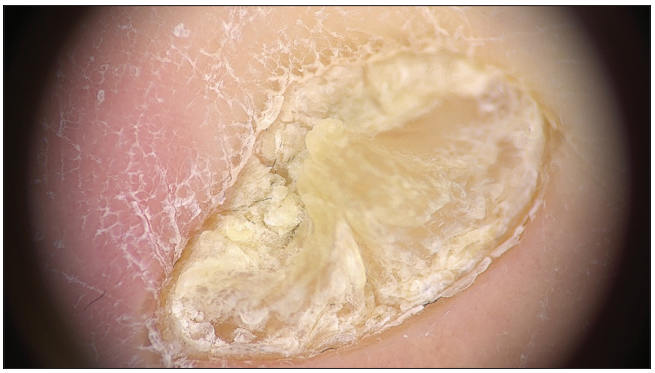

Figure 3: Dermoscopy of right second toenail (FotoFinderx20).

Informed consent was obtained from the patient.

DISCUSSION

Thyroid acropachy is an uncommon manifestation of autoimmune thyroid disease, characterized by clubbing of finger and toenails, swollen digits along with subperiosteal new bone formation. Other manifestations of autoimmune thyroid disease include thyroid ophthalmopathy and pretibial myxedema, which is also called as thyroid dermopathy. Thyroid acropachy is regarded as the insignificant manifestation of autoimmune thyroid disease, as it has been reported that about 4% of patients with thyroid ophthalmopathy have dermopathy, and that one of five patients with thyroid dermopathy has acropachy. Although the exact pathogenesis of autoimmune thyroid disease has not been fully understood yet, it is thought that genetic predisposition and environmental factors interact to produce an abnormal immune response to self-antigens. Since the musculoskeletal system is one of the main target tissues for thyroid hormones, autoimmunity against the tyhroid antigens expressed in the connective tissue cells is regarded to be the fundamental process contributing the development of acropachy, which eventually leads to increased glycosaminoglycan and fibroblast proliferation. Thyroid acropachy can be seen in all forms of autoimmune thyroid disease, thus clinically patients may be euthyroid, hypothyroid or hyperthyroid. But, the distinctive feature of thyroid acropachy is that, it represents the most extreme form of tissue damage caused by thyroid autoimmunity, since the presence of acropachy is known to indicate the severity of both ophthalmopathy and dermopathy. Usually, acropachy occurs in patients with long-term Graves' disease, in whom thyroid ophthalmopathy and dermatopathy have already been confirmed. It is suggested that there is a sequential presentation of extrathyroidal manifestations of autoimmune thyroid disease, in which acropachy develops at the last stage. On the other hand, isolated

case reports of acropachy have been documented in the literature [4-10].

Onychomadesis is considered as the drastic form of Beau's lines, which is defined as the detachment of the nail plate from the proximal nail fold as a result of transitory arrest in the activity of the nail matrix. Onychomadesis has been associated with a wide variety of clinical conditions, including major medical illnesses, infections and autoimmune diseases. Chemotherapeutics, antiepileptics, retinoids, lithium and antibiotics have been also implicated in the etiology of onychomadesis. Among the autoimmune diseases, pemphigus vulgaris is well-known to be associated with onychomadesis, indeed onychomadesis is the most common nail abnormality seen in pemphigus vulgaris [1,2]. Here, we described a patient with onychomadesis associated with autoimmune thyroid disease. As far as we know, there is not any report in the literature describing a causal relationship of onychomadesis with autoimmune thyroid disease. Takasu et al. reported a patient with TSBAb-positive hypothyroidism and onycholysis, which is also called as Plummer's nail [11]. Although clinically they are separate conditions, characteristic early finding of onychomadesis is symmetric proximal onycholysis [1]. All the potential etiological factors that could be implicated in the development of onychomadesis in our patient have been excluded. On the other hand, the induration and erythema in the distal parts of the feet (Fig. 1) point to the possible involvement of subcutaneous tissues, which suggests acropachy. However, a negative conventional radiograph, absence of fusiform soft tissue swelling, which usually involves the middle aspects of the digits, also digital clubbing rule out the diagnosis of acropachy. Moreover, although isolated cases of acropachy have been described, it is well-known that acropachy is almost always associated with dermopathy and ophthalmopathy [8].

Here, we report a case with autoimmune thyroid disease, of whom clinical manifestations imply thyroid acropachy, but indeed associated with onychomadesis. We highlight the importance of considering all the etiological factors while evaluating a patient with a nail finding. Since, a minor detail may be major indicator for a serious disease.

CONCLUSION

Here, we report a case with autoimmune thyroid disease, of whom clinical manifestations imply thyroid acropachy, but indeed associated with onychomadesis. We highlight the importance of considering all the etiological factors while evaluating a patient with a nail finding. Since, a minor detail may be major indicator for a serious disease.

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

Cutaneous mastocytosis mimicking hypertrophic scars: A case report

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ABSTRACT

Cutaneous mastocytosis are a group of disorders which are characterized by abnormal proliferation and accumulation of mast cells in the skin. We report a case of a 21 year old female who presented with few isolated lesions on the thigh which were initially misdiagnosed as hypertrophic scars by a general practitioner. However, following examination of the case by a dermatologist, a diagnosis of cutaneous mastocytoma was suspected and confirmed with histopathological examination.

Key words: Mastocytosis; Hypertrophic scar

INTRODUCTION

Mast cell is a type of granulocyte derived from myeloid stem cells. Once thought to be tissue resident basophils, mast cells have been shown to have a unique lineage. The mast cells have a diverse distribution inhabiting the skin, respiratory, gastrointestinal and genitourinary system [1]. Although best known for their role in allergy and anaphylaxis, mast cells are now known to have critical proinflammatory as well as immunoregulatory roles and are intimately linked with wound healing, angiogenesis and blood-brain barrier function [2]. Mast cells exert their functions by means of various medaitors like histamine, leukotrienes, chemokines, cytokines, chymase and tryptase among others.

Mastocytosis is a disorder characterized by abnormal mast cell proliferation and accumulation within various organs, most commonly the skin when it is called cutaneous mastocytosis. There are three main types of cutaneous mastocytosis: maculopapular cutaneous mastocytosis, solitary cutaneous mastocytosis and diffuse cutaneous mastocytosis [3]. Telengiectasia macularis eruptive perstans is regarded as a rare variant of cutaneous mastocytosis.

The clinical presentation of cutaneous mastocytosis is diverse with lesion morphology varying from macules, papules, plaques and nodules, size ranging from few millimeters to several centimeters, and colour differing from yellow-tan to red-brown. We report a case of cutaneous mastocytosis masquerading as hypertrophic scars.

CASE REPORT

A 21 year old female patient presented to the out-patient department (OPD) of the department of dermatology of our hospital with the chief complaints of few raised reddish brown to black lesions on the right thigh from 3 months. The lesions were associated with moderate to severe pruritus which would disturb the routine activities of the patient and mandate the use of over the counter antihistaminics for relief. The patient also gave history of non-specific diffuse pruritus which would occur occasionally and had a

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long history of many years. Rest of the history was unremarkable and there was no specific pointer to any other systemic involvement like gastrointestinal, cardiovascular, respiratory, etc. Local examination revealed the presence of two erythematous plaques and a linear erythematous plaques on the inner aspect of the right thigh (Fig. 1). The lesions were well defined with a regular hyperpigmented border. The nodules were approximately 1.5 cm in diameter and the plaque was approximately 5 cm along the long axis and 1 cm in width. The plaque had a brown black hue. The lesions were firm to hard on palpation and had been previously misdiagnosed as hypertrophic scar by some general practitioner. The surrounding skin was normal and no excoriations could be appreciated. Darier's sign was elicited over the lesions and the overlying skin turned red on stroking. The patient also had symptomatic dermographism which explained the diffuse pruritus that the patient complained of.

Laboratory investigations (CBC, LFT, KFT) done by the patient were within normal limits. A 5 mm punch biopsy was taken from the lesion and sent for histopathological examination which showed diffuse infiltration of the dermis by inflammatory cells with an unremarkable epidermis (Fig. 2). With higher magnification, collection of mast cells in the dermis alongside collections of eosinophils and lymphocytes could be appreciated (Fig. 3). Serum tryptase level was done in the patient and found to be within normal limits. A diagnosis of cutaneous mastocytosis was made in the patient.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

DISCUSSION

Cutaneous mastocytosis is a type of mastocytosis that primarily affects the skin. It is caused by KIT gene mutations, which are mostly sporadic and rarely inherited [4]. A diagnosis is generally suspected based on history and presence of typical lesions. Histopathological examination is generally diagnostic for cutaneous mastocytosis.

In this case, we came across a variable presentation of cutaneous mastocytosis. Even though a detailed history and examination made us suspect the diagnosis of cutaneous mastocytosis, examination by a non-specialist landed her with an ostensible diagnosis of hypertrophic scars. The clinical appearance of

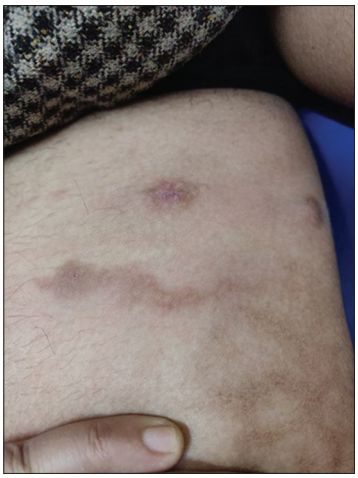

Figure 1: Mastocytoma: Two erythematous nodules and a single hyperpigmented plaque on the inner aspect of the thigh.

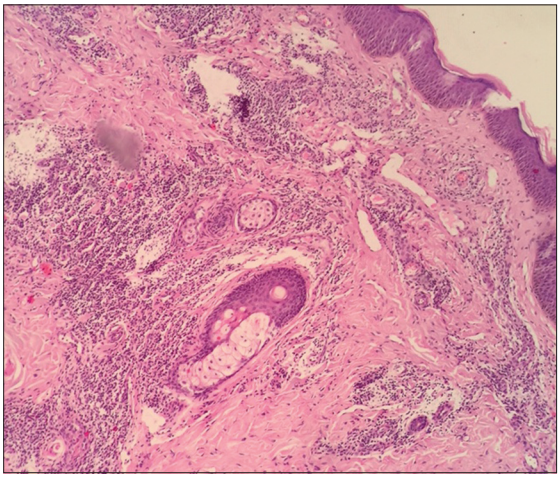

Figure 2: Photomicrograph showing aggregates of inflammatory cells extending into entire dermis with unremarkable epidermis. (100X magnification).

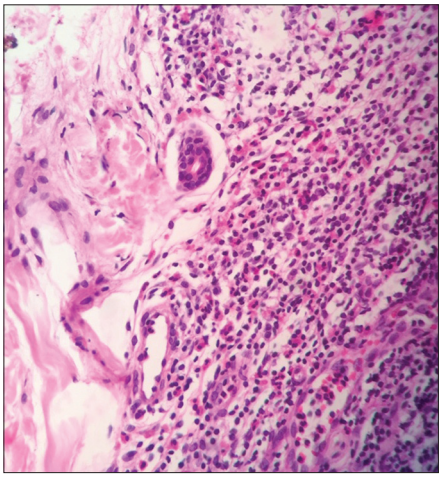

Figure 3: Collection of mast cells, eosinophils and lymphocytes in the dermis adjacent to the skin adnexae.

the lesions could fit into the diagnosis of cutaneous mastocytoma but the consistency of the lesions is said to be rubbery [5], unlike our patient whose lesions were rather firm in consistency.

Disorders masquerading as closely related or unrelated mimics can be a source of puerile inaccuracies on part of the treating physician and land the patient in great misery for the want of an appropriate diagnosis and proper treatment. A careful consideration of the patient history, a meticulous examination and a mind that leaves no possibility forsaken is of utmost importance in the clinical practice of diagnosis and treatment.

Consent

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

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Our Dermatology Online

Case Report

Elephantiasis neuromatosa

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ABSTRACT

Elephantiasis neuromatosa is usually associated with NF-1 mutation and sporadic cases are very rare. A 75-year-old woman presented with growing masses involving the left leg. A physical examination revealed an enlarged left leg with more than 30 huge, hard, and firm nodules below the knee. A biopsy specimen of a nodule showed a soft-tissue neurofibroma. The patient refused to undergo surgical de-bulking and was subsequently lost to follow-up. Our case had no personal or family history of neurofibromatosis type 1 and no other features of the disorder were recognized. There is agreement that, irrespective of the presence of NF-1 mutation, elephantiasis neuromatosa arises from a plexiform neurofibroma of the superficial and deep nerves ultimately leading to the elephant-like and grotesque appearance of the involved limb. Surgical de-bulking and limb amputation are needed in most severe cases.

Key words: Elephantiasis neuromatosa; Neurofibroma; von Recklinghausen phenotype; Lymphostasis

INTRODUCTION

Elephantiasis neuromatosa (EN) is characterized by abnormal soft-tissue hypertrophy and bone dysplasia that are associated with early and exaggerated bone growth of the affected leg along with the growth of infiltrating neurofibromas and lymphangiomatosis [1]. Thinning of bones, erosion of articular surfaces and periosteal dysplasia are other common features. A substantial proportion of cases are associated with neurofibromatosis type 1, i.e. the von Recklinghausen disease [1]. Sporadic patients have been reported even more rarely.

CASE REPORT

A 75-year-old woman had a one-year history of growing and painful masses involving the left leg. Previous history was remarkable for hypertension and chronic lymphedema of the lower limbs and her drug regimen consisted of ramipril and furosemide. A physical examination revealed an enlarged left leg with more than 30 huge, hard, and firm nodules below the knee. The nodules were up to 7 cm in maximum size, the overlying skin was thickened and pigmented, and no ulceration was seen (Figs. 1a and 1b). The right lower limb was normal. A biopsy specimen of a nodule of the left leg showed a soft-tissue neurofibroma (Fig. 2). The patient refused to undergo surgical de-bulking to alleviate the pain and improve the cosmetic appearance. She was treated conservatively and was subsequently lost to follow-up.

DISCUSSION

At presentation, the findings in this patient were highly reminiscent of EN, a rare and very impressive disorder first described by Virchow, and well illustrate the typical features of this enigmatic disorder [2]. The underlying pathophysiology as well as the mechanistic pathways of EN are not fully understood particularly in the very rare sporadic cases who do not have the classical von Recklinghausen phenotype and in whom no NF-1 mutation is found. There is agreement that, irrespective of the presence of NF-1 mutation, EN arises from a plexiform neurofibroma of the superficial and deep nerves. The unregulated proliferation of the perineural connective, fat, muscle tissue, and bone is thought to play a major role and accounts for the locally aggressive behavior of the tumor even though

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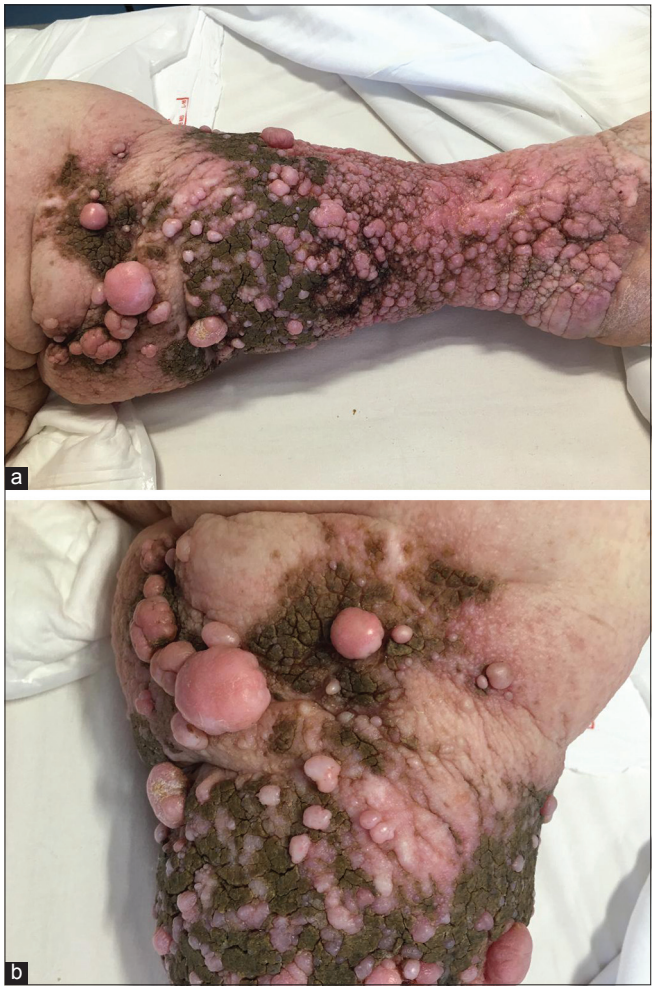

Figure 1: (a and b) Severe hypertrophy of the left leg with several huge, hard, and firm nodules below the knee. The greatest nodule was up to 7 cm in maximum size. The overlying skin appeared thickened and pigmented, with no ulceration.

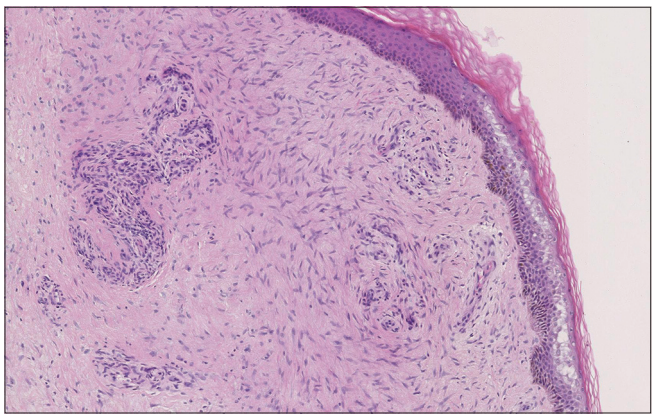

Figure 2: Histopathological examination (hematoxylin and eosin) of a sample from a nodule biopsy shows spindle cells arranged in short fascicles infiltrating the dermis and the underlying soft-tissues, a finding suggestive of a massive neurofi broma.

there is no evidence of malignancy [3]. Ultimately, the unchecked growth of the neurofibroma and the paralleling exaggerated soft-tissue hypertrophy and bone dysplasia lead to the elephant-like and grotesque appearance of the involved limb. The disfiguring features of EN are usually limited to the lower third of the affected leg however the chest, buttocks and the limb roots can be also involved. Chronic lymphostasis, lymphedema, and the dysplasia and hyper-proliferation of the lymphatic vessels have been proposed to play a mechanistic role and consequently patients with chronic lymphedema and lymphostasis are at increased risk of developing EN as compared to healthy subjects [4]. This hypothesis fits well with the clinical presentation of our patient and her history of chronic lymphedema.

Most patients with EN have the NF-1 mutation [1]. Our case had no personal or family history of neurofibromatosis type 1 and no other features of the von Recklinghausen disease, such as "café au lait" spots, iris Lisch hamartomas, axillary and inguinal freckling, and skeletal abnormalities, were recognized. Filariasis, lymphangitis, cellulitis, and scleroderma are often advocated when first facing a patient with EN. However, a long-held dogma suggests that elephantiasis nostras verrucosa is the most important differential diagnosis for EN patients. Elephantiasis nostras verrucosa results from chronic venous stasis that triggers the appearance of chronic changes in areas of dependent edema such as hyperkeratosis, papillomatous plaques, loosely adherent crust and cobblestone-like nodules, erythema and skin ulcers [5].

Patients with EN may have infiltration of the subcutaneous fat and muscle compartments, which can cause severe muscle atrophy and functional impairment. Entrapment of the main limb veins and arteries is common and this can be an important cause of severe and potentially life-threatening bleeding. Ulceration and infection are other clinically relevant complications in the course of EN. Surgical de-bulking and limb amputation or disarticulation are needed in most severe cases of EN [6].

CONCLUSION

This patient presented with gross EN and massive gigantism of her left leg. The limb enlargement was extremely disfiguring and resulted in severe disability. In most cases, EN is a rare clinical manifestation of the von Recklinghausen disease and sporadic cases not associated with the NF-1 mutation are even more rare.

Consent

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

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Our Dermatology Online

Case Report

Granulocyte-Colony stimulating factor induced early psoriasis - a case report and literature review

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ABSTRACT

Human Recombinant Granulocyte colony-stimulating factor is a hematopoietic growth factor; most commonly known to be used for chemotherapy induced neutropenia for the mobilization of peripheral blood stem cells. A case of 43 years old lady, post radical mastectomy for breast cancer and one cycle of chemotherapy was encountered with the development of massive psoriasis like eruptions all over the body including the scalp with adherent silvery scales after 10 days of administration of granulocyte colony stimulating factor with failure of remission even after months of treatment. Clinical signs of psoriasis were seen positive. Munro micro abscess was also noted in the Biopsy. Patient was treated as adverse drug reaction with immediate cessation of G-CSF administration. The rash improved significantly with no new appearances. However, during follow up, island of patches persisted on certain areas, and soon after there was second round of massive eruption without the drug administration. It is very unusual for a drug reaction to not heal after the cessation of the drug. Moreover, since there was second round of sudden massive eruption without the drug, it was clearer that it was not a drug reaction. Rather, the clinical signs and the biopsy were suggestive of early psoriatic presentation.

Key words: Granulocyte colony stimulating factor; G-CSF; Psoriasis; Adverse drug reaction; Neutropenia

INTRODUCTION

Granulocyte colony-stimulating factor (G-CSF) is a hematopoietic growth factor (HGF) that stimulates the production and function of granulocytic cells mostly neutrophils [1]. The incorporation of human recombinant G-CSF as a therapeutic tool has allowed an exogenous stimulation of hematopoietic precursors in order to increase the number of circulating neutrophils [2]. These agents are used frequently to promote leukocyte recovery and reverse resultant myelosuppression after high dose chemotherapy. They have made a substantial clinical impact especially in the management of cancer patients. As every coin has two sides, there have been reports of various adverse effects both cutaneous and systemic. Therefore, we here have a case of initial drug eruption induced by G-CSF administration in a patient with breast cancer, which was later recognized to be early psoriasis.

CASE REPORT

Patient, female, 43 years old, post radical mastectomy and one cycle of chemotherapy presented to the outpatient department of our hospital with extensive erythema, maculopapular rashes and desquamation for two weeks. She had undergone one cycle of chemotherapy (docetaxel 140mg, cyclophosphamide 1140mgdl, q21d) according to the TC regimen with necessary adjuvant therapy. On the tenth day after chemotherapy, the patient developed bone marrow suppression for which the patient was given recombinant Human granulocyte colony-stimulating factor (G-CSF). On the same day of the administration of G-CSF, the patient developed a

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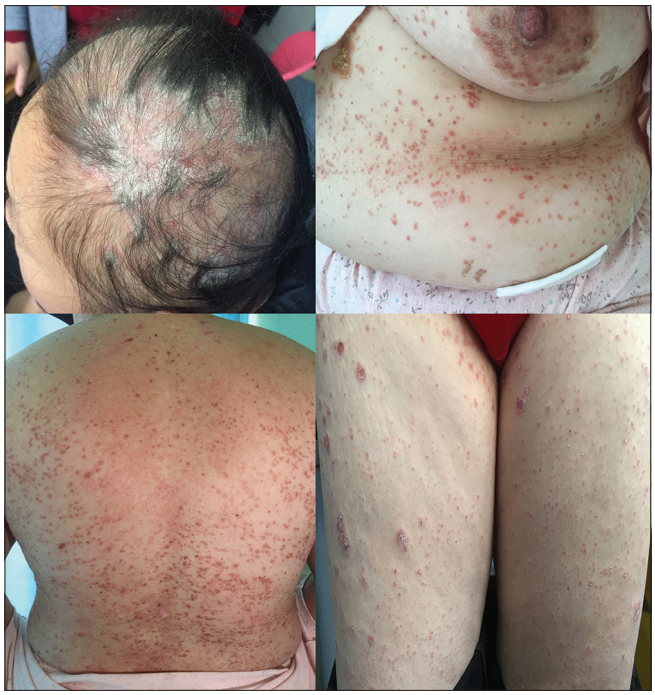

Figure 1: Erythematous maculopapular rashes and patches with silvery white scales over the scalp, abdomen, back and thighs at presentation.

red rash on the right side of her armpit, which spread to the chest and buttocks, and gradually spread over the whole body including the scalp. Numerous small miliary rashes to large erythematous patches covered with adherent silvery white scales were noted (Fig. 1) with no pruritus or pain. Her lesions were extensive and were increasing rapidly. Newly appeared fresh red rashes as well as faded brown maculopapular rashes, covered with silvery white scales could be observed on the trunk and limbs with positive Film phenomenon and dot bleeding sign (Auspitz sign). Thick white scaly patches were seen on the scalp with fine demarcation extending outside the hairline with scarce hair (Fig.1). The patient had no other significant past medical history and no systemic abnormalities were detected. Biopsy showed hyperkeratosis of the epidermis, parakeratosis, and neutrophil infiltration in the stratum corneum with Munro micro abscess formation, mild spongiotic changes in the epidermis and mild perivascular infiltration in the superficial dermis (Fig. 2). After the comprehensive analysis of patient's medical history and ongoing chemotherapy it was termed as G-CSF induced drug eruption.

She was then treated with anti-allergic drugs in combination with topical therapies, which showed significant improvement of her rashes with no new eruptions. On follow up after two months, the

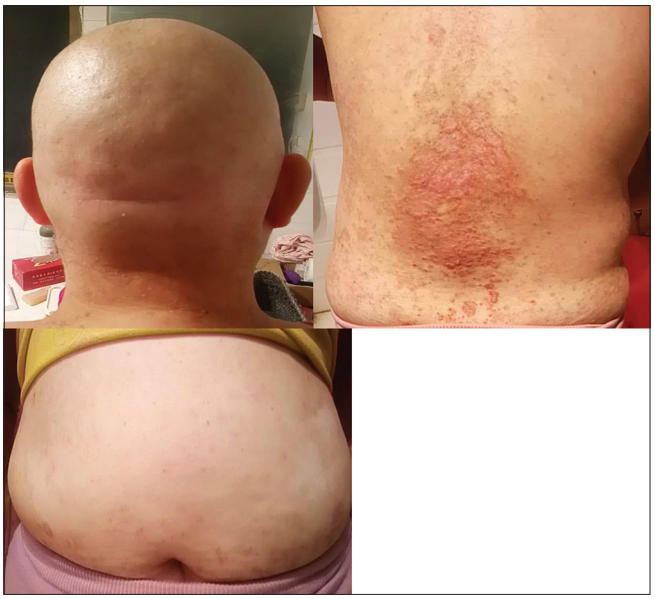

Figure 2: Complete remission of lesions over the scalp and abdomen. Residual maculopapular rashes and island of patches over the back after 2 months during follow up.

rashes on her scalp, abdomen and extremities had completely cleared but islands of patches persisted on her back with large erythematous maculopapular rashes without scales (Fig. 3). Therefore, the patient was under simultaneous treatment for her cancer and the rashes. But again after 4 months of initial eruption she had second round of sudden extensive eruption all over her body (Fig. 4). The lesions varied from small red maculopapular rashes to large scaly patches with adherent silvery scales similar to the first episode of eruption. Auspitz sign and film phenomenon were seen positive. Patient however refused to do another biopsy and insisted on supportive management.

Since the second time had no any aggravating factors and the clinical manifestation was favorable for psoriasis. Finally, after overall analysis of the case, the final diagnosis was made as psoriasis induced upon the administration of G-CSF 4 months ago, the initial drug eruption being the early psoriatic presentation.

DISCUSSION

Psoriasis is one of the most common chronic inflammatory skin disorder predominantly characterized by accumulation of Th1-type T cells and neutrophils, rigorous epidermal proliferation and differentiation, and enhanced epidermal production

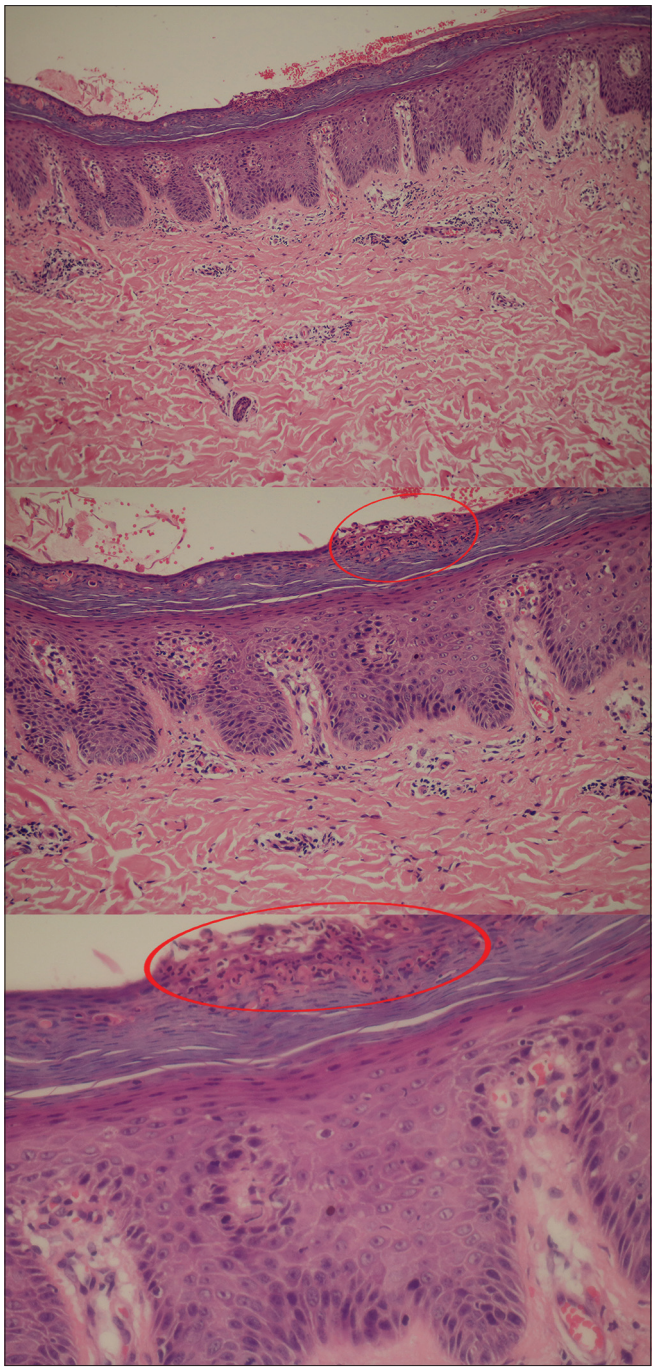

Figure 3: Biopsy (Hematoxylin and Eosin stain, 20x, 40x and 100x) showing hyperkeratosis of the epidermis, parakeratosis, and neutrophil infiltration in the stratum corneum with Munro microabscess formation(circled), mild spongiotic changes in the epidermis and mild perivascular infiltration in the superficial dermis.

of antimicrobial peptides [3]. Granulocyte colony stimulating factor (G-CSF) is a cytokine that is commercially available as a result of recombinant DNA technology [4,5]. Human recombinant G-CSF was used for the treatment of neutropenia induced by chemotherapy in the presented case. In this case the first lesions were seen on the 10th day of administration

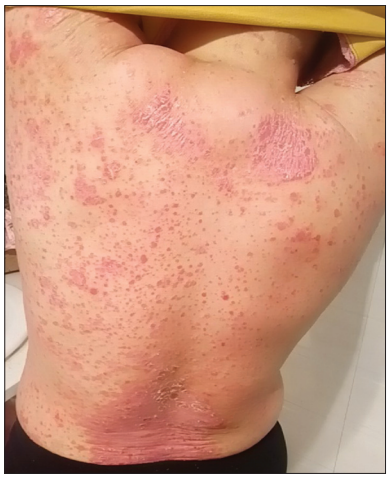

Figure 4: Second round of extensive eruption.

of G-CSF after first cycle of chemotherapy. Within this short period of time, the patient had developed erythematous macules and patches with silvery white scales all over the body including the scalp, with positive film phenomenon and Auspitz sign. These signs clinically suggested Psoriasis but the biopsy and Reflectance Confocal Microscopy reports suggested otherwise. Although biopsy reported the presence of Munro micro abscess and hyperkeratosis, other characteristic features of psoriasis were not found. As the lesions had developed quickly and patient had no prior history of psoriasis or any other cutaneous inflammatory disease, we can argue that this might be an early presentation of psoriasis due to which the biopsy and RCM were negative showing only mild proliferation and inflammation. Also, the failure of remission of the rashes and extensive recurrence of the rash again after few months despite continuous treatment indicates that it is not merely a simple drug reaction. This also suggests that it can be an early presentation of psoriasis.

A very similar case was reported in 1989 [6] which also described psoriasiform eruption triggered by recombinant granulocyte macrophage colony stimulating factor (rGM-CSF) and exacerbated by G-CSF in a patient with breast cancer. The patient however had complete remission of the lesions and no relapse was noted. This is one of the earliest reported cases of G-CSF induced cutaneous eruption. The major difference with our case is that the patient did not have complete remission of her lesions even after 2 months, which makes it fairly arguable whether this case is a drug eruption or early psoriasis. No reports are found stating the induction of the disease Psoriasis itself with G-CSF.

Later, in 1997 a case was reported stating the worsening of psoriasis after treatment with G-CSF in a patient with small-cell lung cancer. Also, they stated that the withdrawal of G-CSF therapy coincided with the improvement of psoriasis in the patient [7].

However, in later years very few reports of psoriasis like eruption were reported in the literature. Rather other forms of G-CSF induced drug eruptions were reported such as generalized erythematous and indurated papules and plaques with mild epidermal spongiosis and dermal infiltrate of enlarged plump macrophages [8], granulomatous dermatitis [2,9] with enlarged histiocytes clinically manifesting as painful edematous nodules with high fever similar to Sweets syndrome, and cases of G-CSF induced Sweet syndrome reported by Kenneth et al in 1999 and White et al in 2005 [10,11]. It has also been reported that G-CSF stimulates the proliferation of myeloid leukemic cells. Yamashita et al states that although there were no leukemic cells in the peripheral blood or bone marrow, eruptions containing leukemic cells were observed. They explain that those leukemic cells might have responded to hG-CSF and proliferated in the skin [12].

According to a study which analyzed the cytokine profile of this cytokine induced psoriasis like eruption and psoriasis [13], the Polymerase Chain Reaction and immunohistology of G-CSF induced dermatitis resembled psoriasis with regard to epidermal hyperparakeratosis and accumulation of lymphocytes in the upper dermis. This was however different with our patient who showed neutrophil infiltration in the stratum corneum, mild spongiotic changes in the epidermis with perivascular infiltration in the superficial dermis.

High concentrations of G-CSF in the skin is said to induce the production of cytokines by resident cells, including other colony-stimulating factors and interleukins. Activation of macrophage function could stimulate the production of tumor necrosis factor-a, which stimulates keratinocyte-derived monocyte chemotaxis and activating factor. Activated monocytes could further trigger the inflammatory reaction by producing interleukin- 1 and tumor necrosis factor-a like in the pathogenesis of psoriasis which may be the reason for the induction of the psoriatic lesions after its administration.

Although the role of G-CSF in the pathogenesis of psoriasis has not been established, there are reports in which G-CSF could have been related to the induction or exacerbation of psoriasis. In all the cases reported about psoriasis like eruption, the common point is the eruptions of brand-new lesions and worsening

CONCLUSION

The lesions following G-CSF-induced leukocytosis are characterized by a lymphocytic inflammation and cytokine pattern similar to that detected in active psoriatic lesions and share many of the cellular and molecular changes that are similar to the psoriatic epidermis. Therefore, we speculate that the pattern of skin changes induced by G-CSF, a cytokine involved in the host defense against bacterial infections, is partially overlapping with the induction of cutaneous immune functions that characterize psoriasis and this can be termed as a key pathogenic factor in the induction of psoriasis. Also, the genetic variation of the population can be an important factor for the induction of the psoriasis like eruptions in the patients since not everyone receiving it develops the reaction. Gene polymorphism could be significant to explain the variants in the induction of the disease to G-CSF and should be researched for the better and clearer explanation of this phenomenon. Not many cases have been reported with the association of G-CSF with psoriasis or psoriasis like eruptions. However, the ones, which were found reported in the literature, were also mostly done in the early 90s. So, since the administration of this human recombinant granulocyte colony-stimulating factor has become so common in clinical practice there should be more research and study regarding its adverse cutaneous reactions as they can be life threatening too if not recognized prior to worsening of the patient.

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Our Dermatology Online

Case Report

Beta-blocker bisoprolol induced psoriasis

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ABSTRACT

A number of beta-adrenoceptor blocking drugs have been reported to be upon the most common causative agents for drug-induced psoriatic lesions. Apparently this adverse reaction appears after several months of continuous therapy. In our case psoriasis eruption is associated with bisoprolol (B1-blocker) therapy in a man without previous skin lesions and history of psoriasis. The biopsy demonstrated psoriasiform dermatitis with spongiosis and parakeratosis. The pathogenic mechanisms to be discussed are the pharmacological effects on the epidermal beta-adrenergic adenylate cyclase-cyclic AMP system and on the excessive release of lysosomal enzymes.

Key words: Bisoprolol; Beta-adrenoceptor blocking drugs; Psoriasis eruption; Drug eruption; Drug- induced psoriatic

INTRODUCTION

Adverse drug reactions constitute a significant public health problem, and, therefore, identifying relevant drug interactions is a critical step for prevention. Many reports in the literature outline the more or less prominent role of drugs in initiating, triggering, or aggravating psoriasis lesions [1-4].

Since their introduction, beta-blockers have been increasingly prescribed in the treatment of cardiovascular diseases such as angina pectoris, arrhythmia, hypertension as well as non-cardiovascular indications like essential tremor, migraine headache prophylaxis, and infantile hemangioma [3-5]. Beta-blockers are classified as non-cardioselective and cardioselective, according to their capacity to interact selectively with ß1- and ß2-adrenergic receptors. Side effects are well reported for several organ systems. The integumentary system constitutes one of the rarest areas which may be affected by these agents.

Adverse cutaneous reactions induced by beta-blockers imitate different polymorphic skin disorders which are related to the wide extent of intracellular transduction pathways and signals they influence. The reported clinical cutaneous symptoms include classical dermatoses such as psoriasiform and papulosquamous eruptions, lichenoid, eczematous, exfoliative eruptions, and hyperkeratosis of the distal extremities [6].

Extracutaneous organ manifestations associated with beta-blockers represent characteristic symptom complexes like the oculomucutaneous syndrome and the pseudolupus erythromatosus syndrome [7]. Fibrinous peritonitis may be a lethal side effect. The drug induced LE syndrome is clinically difficult to distinguish from the idiopathic SLE.

Therapy with beta-blockers may result in a de novo induced psoriasiform eruption on clinically uninvolved skin in a known case of psoriasis, aggravation of a pre-existing psoriatic tendency or in precipitation of the disease in persons without family history of psoriasis or in predisposed individuals [8]. Even cases who became resistant to conventional anti-psoriatic therapy are reported [6]. An induction period before

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the occurrence of clinical manifestation is characteristic, which is usually of an approximately 1 year duration, but may vary [7]. All these facts make it difficult for clinicians to comprehend the causal relation and therefore often lead to a misdiagnosis. The mechanisms by which beta-blockers might induce or exacerbate psoriasis are largely unknown, but there may be two major pathogenetic mechanisms causing the cutaneous reactions: heterogeneous immunological stimulation and the pharmacological effect of adrenergic beta-blockers on the adenylate cyclase AMP system in epidermal cells.

In this context we would like to present a case report highlighting the importance of considering beta-blockers as potential cause of polymorphic cutaneous eruptions.

CASE REPORT

We present a case of a 57- year male farmer referred to the dermatology clinic, Medical University of Graz, Austria, with some patches of eczematous dermatitis over the trunk (Fig. 1). These eruptions were thought to be induced by the anti-gout medication allopurinol, a substance that inhibits the action of xanthine oxidase, which he has been using uneventfully for several years. The skin biopsy showed spongiotic dermatitis. Therefore allopurinol therapy was withdrawn immediately. The patient improved well and the rush subsided. But after 20 days he was hospitalized again due to a sub-erythrodermatic eruption with partial symmetrical papulo-squamous lesions on his face and trunk. In addition, dystrophic hyperkeratosis of the palms, nails and soles were accompanied by severe itching.

A diagnosis of sub-erythrodermatic psoriasis was made, and we raised the question of a beta-blocker induced psoriasiform eruption. This suspicion was indorsed by the patient's history, his clinical presentation and the results of the histological examination. The biopsy specimen of the right thigh demonstrated psoriasiform dermatitis with spongiosis and parakeratosis. His history revealed an approximately two year period consumption of Rivacor® (bisoprolol, ß1 selective) due to arterial hypertension before the onset of cutaneous symptoms. No previous skin lesions and history of psoriasis could be elicited. Laboratory results showed high IgE levels, 21% eosinophils in the differential blood count, positive antinuclear antibodies test and LE cells. The beta-blocker medication was discontinued, and an ACE Inhibitor was prescribed. Topical bethametason therapy was added, and as a result the cutaneous symptoms were ameliorated. The amount of total ANA titer decreased (1:160). At the follow-up control after 4 weeks we saw a partial remission of the suberythrodermatic skin condition and the hyperkeratotic lesions. Rechallenge with bisoprolol was refused by the patient and thus not pursued.

DISCUSSION

Many cases of cutaneous, mucous and dermal appendage side effects of non-selective (alprenolol, carvedilol, nadolol, oxprenolol,pindolol, propranolol) [8] as well as selective beta-blockers (acebutolol, atenolol,cetamolol, metoprolol, practolol) have been published.

Because psoriasis is a very complex disease and its activity is often unpredictable, clinical studies on adverse drug effects in psoriasis have been difficult to conduct [1]. Heng et al. [9] have shown distinct clinical and histopathological features of beta-blocker induced psoriasiform eruptions which differentiate this syndrome from psoriasis. The psoriasiform lesions induced by beta-blockers are characterized as (generalized) erythematous papulosquamous plaques with less erythema and scaling than seen in psoriasis. The trunk and extremities are symmetrically affected without involving the face. The histopathology findings reveal an intradermal and predominantly perivascular mixture of mononuclear cells, neutrophils and eosinophils.

There are two major theories which explain the underlying pathomechanism; Lymphocytes, macrophages and neutrophils expose membrane beta-adrenergic receptors, depressed cAMP levels through blocking these receptors via beta-blockers are

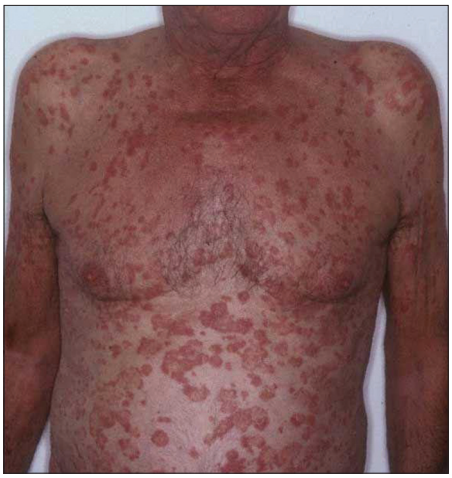

Figure 1: Psoriasisform rash with well-demarcated erythematous scaly plaques in the trunk 2 years after beginning of therapy with bisoprolol.

associated with enhanced proliferation, motility and activity of lymphocytes, neutrophils and cells of the macrophage Langerhans cell series [9-12]. Released lysosomal enzymes by these cells are responsible for the presence of basal keratinocyte herniations and the related hyperproliferation and psoriasiform eruptions Epidermal cells are mainly ß2 adrenergic receptor carriers. Located on the membrane, adenylate cyclase converts ATP into cAMP. It is generally accepted that cyclic AMP plays a key role in keratinocyte proliferation and differentiation. Decreased intracellular AMP levels lead to a higher proliferation and reduced cell differentiation, whereas AMP reduction results in a decrease of mitotic and metabolic activity [13].

Thus blocking the beta-receptors in the skin leads to a decrease in intracellular calcium and intra-epidermal cyclic AMP. This decrease, in turn, results in an increased epidermal cell proliferation. The reason why beta-blockers of the newer generation (ß1 selective) affect ß2 receptors in epidermal cells is related to cross- reactions between the different beta-blocker subtypes.

Other theories related to beta-blocker induced cutaneous side effects include impaired lymphocyte transformation and delayed hypersensitivity Type (IV hypersensitivity). Immunoreactions are thought to be associated with psoriasiform and lichenoid lesions which histologically show the pattern of a lichenoid drug eruption. This hypothesis is supported by in vivo (positive patch test) and in vitro tests [7].

Beta-blocker induced eruptions can mimic a wide range of cutaneous lesions thus delaying diagnosis. Although the clinical presentation resembles psoriasiform skin lesions microscopic imaging shows in most of the cases a monomorph histology with acanthosis, focal hyperkeratosis, mixed dermal infiltration and lichenoid drug reaction secondary to beta-blockers [14].

Latency periods for beta-blockers vary from several days to 12 months (48 weeks) on average. They are shorter in cases of de novo pustular psoriasis and in the exacerbation of pre-existing psoriasis. The reasons for these variations remain unknown and imply the influence of individual, genetic, and racial background [2]. An induction period of two years as seen in our case was previously reported in the literature [7]. Medication history should always be considered in terms of unexplainable skin eruptions, and an adequate substitution of the offending beta-blocker agent should be initiated. After withdrawal of the beta-blockers the psoriasiform eruptions usually clear up in nearly 50 % of the cases [7].

The exacerbation of a pre-existing psoriasis after bisoprolol initiation was previously reported [15]. With our patient we mention the first case of a de-novo induced psoriasifrom eruption due to bisoprolol in a patient with no history of psoriasis.

Consent

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

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Our Dermatology Online

Case Report

Coexistence of tuberculous gumma with tuberculosis verrucous cutis (TBVC) in an immunocompetent female

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ABSTRACT

Tuberculous gummas and tuberculosis verrucosa cutis (TBVC) generally manifest in two extreme poles across the cell mediated immunity spectrum of cutaneous tuberculosis. The present case report refers to a 43 year old female with subcutaneous soft to firm non-tender, minimally fluctuant nodules & abscesses over digits of B/L hands and few well defined verrucous plaques over lateral aspects of bilateral soles. Ziehl-Neelsen stain did not demonstrate any acid fast bacilli. On histopathologic examination it was diagnosed as Tuberculous gumma with Tuberculosis Verrucosa cutis as per clinical diagnosis and its coexistence in a single individual is unique. The patient was treated with anti tubercular drugs (ATD) & responded well.

Key words: Cutaneous tuberculosis; Tuberculous gumma; Tuberculosis verrucous cutis (TBVC); Immunocompetent

INTRODUCTION

Cutaneous tuberculosis constituting a small fraction about 1.5% of all forms of extra pulmonary tuberculosis, manifests as different clinical types across the cell mediated immunity spectrum. The clinical manifestations like lupus vulgaris, tuberculosis verrucosa cutis (TBVC), scrofuloderma, tuberculous gumma, tuberculous chancre, miliary tuberculosis, papulonecrotic tuberculid and lichen scrofulosorum may be dependent on the route of infection (endogenous or exogenous), the immune status of the patient and previous sensitization with tuberculosis [1]. Tuberculous gummas, also called metastatic tuberculous abscesses, are usually seen in malnourished children and in immunocompromised states, as result of hematogenous dissemination of tubercle bacilli from an underlying focus and occur during periods of lowered immunity [2]. It usually presents as one or multiple non-tender subcutaneous nodules, which slowly soften, or cold abscesses with fluctuant swelling. Whereas TBVC results from direct inoculation of the bacilli into the skin of previously infected patients having intact immunity. It manifests as a large verrucous plaque with finger like projections at the margins. Co-existence of different types of cutaneous tuberculosis has been described in various literatures in the form of scrofuloderma with tuberculosis verrucosa cutis [3], lupus vulgaris with tuberculosis verrucosa cutis, papulonecrotic tuberculid with lichen scrofulosorum and lupus vulgaris with papulonecrotic tuberculid [4]. Interestingly, we came across a rare presentation in a 43 year immunocompetent female presenting with both subcutaneous skin abscesses in multiple sites (low immunity) along with verrucous plaques over B/L feet (high immunity), proven histopatholigically as TB gumma and TBVC respectively.

CASE REPORT

A 43 year old female presented to us with chief complaints of multiple painless swellings over digits of B/L hands for 4 weeks. On examination, there were multiple subcutaneous soft to firm non-tender, minimally fluctuant nodules &

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abscesses of size about 3*3 cm^2 with overlying intact skin, mild erythema and no surface change (Fig. 1). On further examination, we found few well defined verrucous plaques over lateral aspects of bilateral soles which was persisting since 2 months (Fig. 2). We sent samples from both lesions for histopathological study. Routine blood investigations were within normal limits, except raised ESR (68cm/hour). Except for episodic mild raise of temperature (99-100F) patient had no other systemic complaints. There was no evidence of any immunosuppression or lymphadenopathy. Radiological investigations for bony involvement were negative. Mantoux test was positive with 15 mm induration at 48 hours. Gram stain and Ziehl-Neelsen stain for acid fast bacilli were negative. PCR for Mycobacterium tuberculosis was negative. HP study from the nodules showed multiple granulomas composed of epitheloid cells, histiocytes, lymphocytes and Langhan's type of giant cells with small areas of caseous necrosis involving reticular dermis and subcutaneous tissue (Figs. 3a and 3b). The verrucous lesions on HP study revealed mildly hyperkeratotic epidermis with well-defined granulomas composed of epitheloid cells and Langhan's type of giant cells without any necrosis (Figs. 4a and 4b). A diagnosis of Tuberculous gumma with Tuberculosis verrucosa cutis was made and ATT was started.

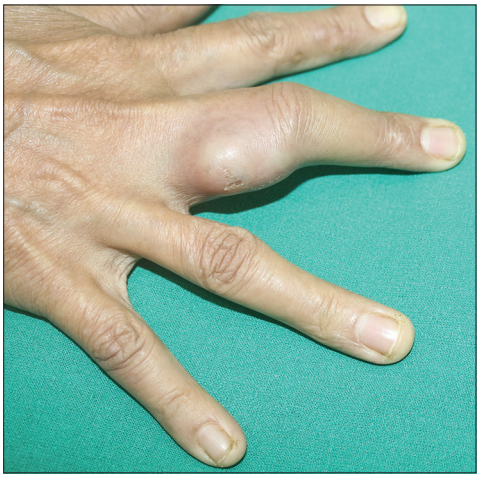

Figure 1: A skin coloured, soft to firm, fluctuant nodule on the right middle finger.

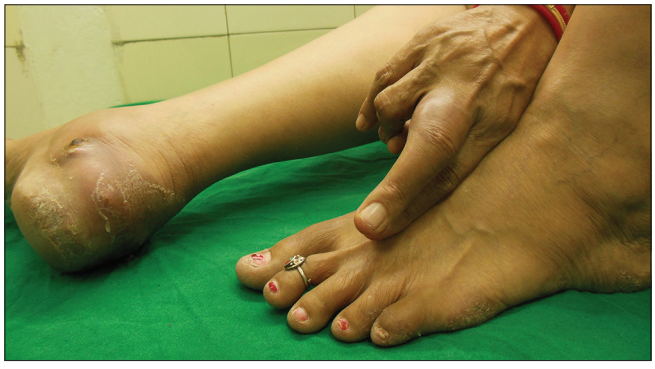

Figure 2: Irregular warty plaques with scaling over lateral aspect of bilateral soles.

DISCUSSION

Tuberculosis verrucosa cutis (TBVC) is warty form of cutaneous tuberculosis and was first described as "Prosecutor's wart" by Rene Laennec. It is caused by exogenous inoculation mostly due to trauma in presensitized persons with moderate to high degree of cell mediated immunity. Clinically, TBVC lesions are mainly distributed over the trauma prone areas like extremities and present as a slowly growing, asymptomatic papule/nodule to a firm verrucous plaque. Histopathologically well formed classical tubercular granuloma with pseudoepitheliomatous hyperplasia of epidermis is seen. But caseous necrosis is a rare finding [5]. Tuberculous gumma, also known as metastatic tubercular abscess is a rare form of cutaneous TB, caused by hematogenous spread of the bacilli from a primary underlying focus during periods of lowered immunity. Gumma presents clinically as cutaneous and subcutaneous nodules and/or abscesses, which are nontender and fluctuant, forming undermined ulcers on rupturing. Epitheloid

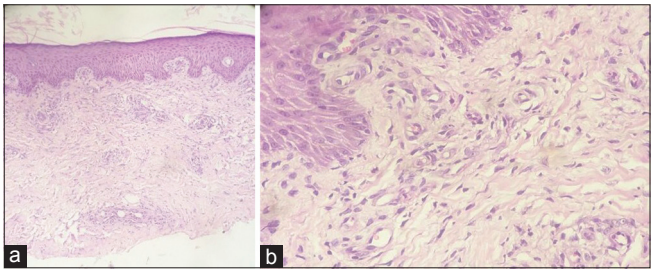

Figure 3: (a) Multiple granulomas and focal collection of inflammatory cells in the dermis [H&E, x4], (b) Multiple granulomas composed of epitheloid cells, histiocytes, lymphocytes, Langhan's type of giant cells with small areas of necrosis [H&E, x40].

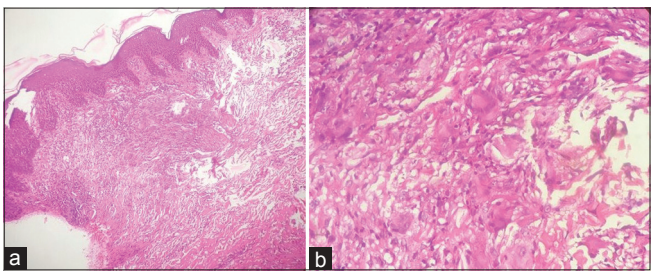

Figure 4: (a) Hyperkeratosis, acanthosis and dense inflammatory infiltrate with giant cells in the dermis [H&E, x4], (b) Well defined granulomas composed of epitheloid cells & Langhan's type of giant cells without any necrosis [H&E, x40].

cell granulomas with extensive areas of caseous necrosis are histopathological findings of tuberculous gumma. Since, tuberculous gumma spreads hematogenously from an underlying focus in an immounocompromised patient, almost all patients presenting with gumma have systemic tubercular involvement as well as some form of immunosuppression [6]. But our patient presented without any systemic involvement or immunosuppression. Co-existence of various types of cutaneous TB has been reported in literature including Scrofuloderma with TBVC and Scrofuloderma with TB gumma [3,4]. To the best of our knowledge simultaneous occurrence of TB gumma and TBVC in a single patient (which occupy two extreme poles in the immunological spectrum of cutaneous TB) has not been reported till date. Hence we, report this rare case of co-existence of TBVC and TB gumma in an otherwise immunocompetent patient with no other systemic involvement.

CONCLUSION

Simultaneous occurrence of TB gumma and TBVC are extremely rare findings in an immunocompetent indivisual.

Consent

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

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Our Dermatology Online

Case Report

Concomitant erythema induratum of Bazin and papulonecrotic tuberculid: A rare manifestation

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ABSTRACT

The tuberculids represent a group of disorders resulting from hypersensitive immune reactions within the skin due to hematogenous dissemination of *Mycobacterium tuberculosis* or its antigens from a primary source. Erythema induratum of bazin, papulonecrotic tuberculid and lichen scrofulosorum are classified as true tuberculids. Tuberculids are rare manifestation and simultaneous occurrence of two tuberculids in one patient is even rarer. We report a case of 25 year lady presenting with erythema induratum and papulonecrotic tuberculid simultaneously. Though no source of active infection was found, her lesions were found to be consistent with the diagnosis clinicopathologically and resolved with antitubercular treatment. Concomitant occurrence of two tuberculids in one patient is a rare manifestation and when this has been reported, the commonest combination appeared to be erythema induratum of bazin and papulonecrotic tuberculid, similar to our case, which resolved with antitubercular treatment.

Key words: Erythema induratum of bazin; Papulonecrotic tuberculid; Rare; Simultaneous; Occurrence

INTRODUCTION

The tuberculids represent a group of disorders resulting from hypersensitive immune reactions within the skin due to hematogenous dissemination of *Mycobacterium tuberculosis* or its antigens from a primary source, occurring in a patient with strong antituberculous cell-mediated immunity. There are three main clinical manifestations of cutaneous tuberculids: lichen scrofulosorum, papulonecrotic tuberculid (PTN) and erythema induratum of Bazin (EI) [1]. The diagnosis of tuberculid may be uncertain when there is an atypical clinical presentation, inconsistent circumstantial evidence, and lack of direct evidence [2]. We report a rare case in which two tuberculids, EI and PTN, occurred simultaneously in the same patient.

CASE REPORT

A 25 years female, previously healthy presented with multiple painful reddish raised solid lesions on both the lower limbs for 1 months. She also developed multiple asymptomatic solid and fluid filled lesions which broke down to form ulcer on upper abdomen, back and both the arms of same duration. She was not suffering from cough, malaise or weight loss but complains of fever which was not documented. She had no past history of tuberculosis (TB), however was living with a family member who suffered from pulmonary tuberculosis.

On cutaneous examination, multiple, tender, erythematous to dusky red,well defined, coin shaped, indurated subcutaneous nodules was present distributed symmetrically over the bilateral lower limb, measuring approximately (1 cm^2 - 3 cm^2) in size on both calves, shins, left thigh, and right dorsum of foot, some of these had begun to ulcerate (Fig. 1). She also had few vesicles and multiple dusky red papules, some with central necrosis, few scattered and some linearly arranged, discrete, with brownish colored crusts and erythematous border of size 0.5×0.5 cm^2 presenton right upper quadrant of abdomen, chest, back and

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both upper limbs (Fig. 2). There was no evidence of lymphadenopathy. Her systemic examination was unremarkable.

Her routine investigations (hemoglobin, complete blood count, liver function tests, and renal function tests, urine rme) were normal with erythrocyte sedimentation rate of 20 mm/hr. Chest X-ray and abdominal ultrasonography examination were normal. Serology for HIV, HbsAg, anti HCV, VDRL was negative. Examination of tuberculin test site revealed indurated plaque (24 × 24 mm) and multiple erythematous papules at the periphery of the positive tuberculin reaction.

Three biopsy sample were obtained from the characteristic lesion of both eruptions comprising of vesicle, ulcer and nodule. A biopsy specimen of a nodular lesion from the lower leg revealed large area of necrosis involving both septa and lobules with aggregates of histiocytes and necrosis of blood vessel wall (Fig. 3). However, the biopsy specimen of the ulcer and vesicle lesion from the left arm and abdomen respectively showed focal necrosis of dermal collagen with surrounding epithelioid histiocytes, fibrinoid necrosis of vessels with extravasation of red blood cells with perivascular lymphohistiocytic infiltration in the dermis (Fig. 4). These findings were consistent with erythema induratum and papulonecrotic tuberculid, respectively. Acid-fast bacilli were not found in the skin biopsy specimens and PAS stain was negative for fungal element. In view of clinicopathological features, she was started on standard antituberculous regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months followed by 4 months of isoniazid and rifampicin. The lesion completely reduced with post inflammatory hyperpigmentation, and atrophy within 4 months of treatment. At the end of 6 month, no recurrence was noted.

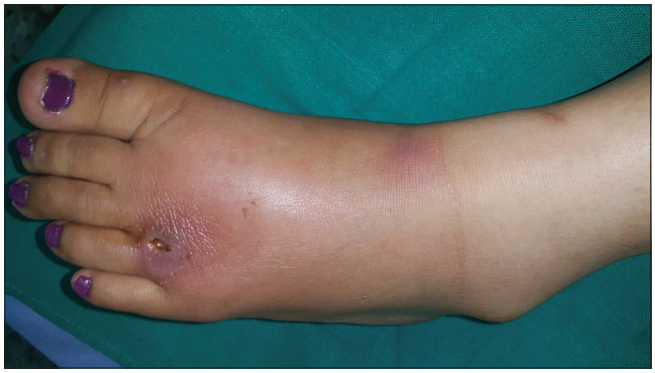

Figure 1: Erythema induratum of bazin.

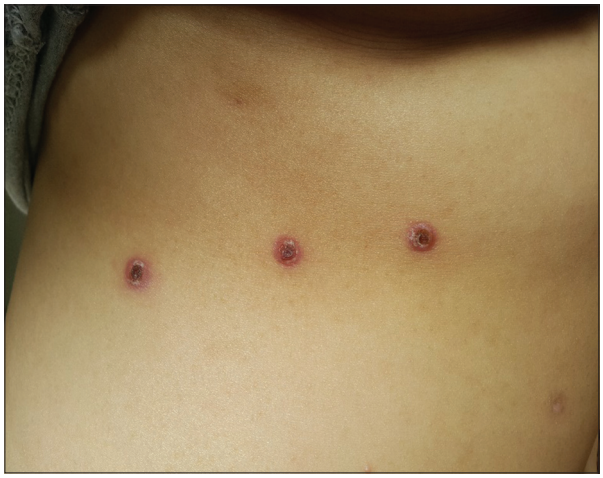

Figure 2: Papulonecrotic tuberculid.

DISCUSSION

The term tuberculid was coined by Darier in 1896 [3]. Erythema induratum of bazin, papulonecrotic

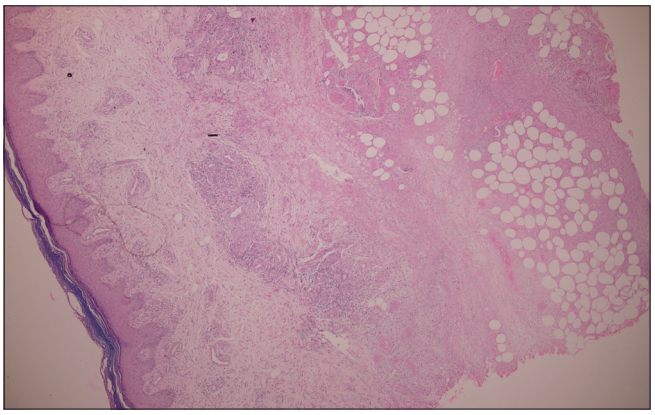

Figure 3: Erythema induratum. (H&E; X40 magnification) showing epidermis, dermis and subcutis. The necrosis of subcutaneous lobules and thickening of septa are evident in this magnification.

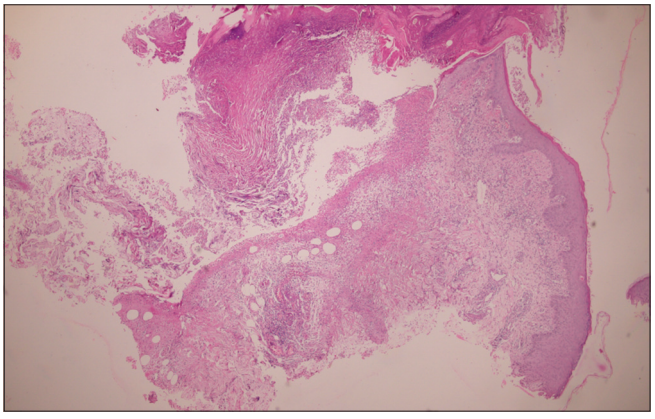

Figure 4: Papulonecrotic tuberculid. Low power view (H&E; X40 magnification) showing ulceration and necrosis.

tuberculid and lichen scrofulosorum are generally classified as true tuberculids, i.e., skin manifestations of TB in which no organisms can be demonstrated on acid-fast bacteria (AFB) stain or on culture of the skin lesions [4]. EI have a chronic recurrent course and female preponderance which is presents as persistent nodules or plaques usually sited on the lower third of the calf. The lesion may ulcerate and heal with depressed scar. Histologically a vasculitis affecting small and medium-sized vessels is seen producing a dermal granuloma with epithelioid and giant cells and fat atrophy [5]. PNT occurs as crops of symmetric, small, erythematous, inflammatory papules which have an acral and extensor surface predilection. Lesions may undergo central ulceration and heal spontaneously within weeks, leaving varioliform scars and pigmentation. Microscopically, wedge-shaped area of necrosis is seen with underlying vasculitis and granulomatous infiltrate [4,5].

CONCLUSION

Our patient had both papulonecrotic tuberculid and erythema induratum simultaneously. The clinical and pathological features were entirely consistent with both diagnoses. Her Mantoux test was strongly positive. Although no source of active infection was found this is not unusual. It has been suggested that the failure to detect mycobacteria is a result of rapid destruction of organisms in hypersensitive individuals [6]. The occurrence together of two tuberculids is extremely rare but when this has been reported previously the commonest combination appeared to be PTN and EI as seen in our patient [4].

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Our Dermatology Online

Case Report

About a rare case of lupus panniculitis of difficult diagnosis at the Borgou/Alibori Departmental UHC (Benin)

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ABSTRACT

We report an unusual case of lupus panniculitis or Kaposi-Irgang disease, of difficult diagnosis. A 40-year-old woman without particular pathological history had consulted in the Service of Dermatology of the Departemental CHU Borgou/Alibori for nodular and painful lesions of the trunk and the thoracic members having begun in the right breast and evolved for eight continuous months. The dermatological examination discovered on the trunk and the thoracic members, nodular hurts under an erythema skin, painful at the palpation; of diameters varying between one and five centimeters. Anatomical examination and immunohistochemistry helped to retain the diagnosis of lupus panniculitis and the patient was given Prednisone orally in degressive doses. Skin lesions regressed after three months. Anatomical-clinical confrontation is essential to retain a positive diagnosis of rare skin diseases such as panniculitis lupus.

Key words: Lupus panniculitis; Deep biopsy; Lymphocytic infiltrate; Benin

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Our Dermatology Online

Case Report

A propos d'un cas rare de panniculite lupique de diagnostic difficile au CHU Departemental Borgou/Alibori (Benin)

Christiane Koudoukpo[1], Christelle Ahomadégbé[2], Marie-Claire Ballé[1], Fabrice Akpadjan[3], Bérénice Dégboé[3], Romulus Takin[2], Nadège Agbéssi[1], Luc Brun[1], Hugues Adégbidi[3], Félix Atadokpèdé[3]

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RÉSUMÉ

Nous rapportons un cas inhabituel de panniculite lupique ou maladie de Kaposi-Irgang, de diagnostic difficile. Une femme âgée de 40 ans sans antécédent pathologique particulier avait consulté dans le Service de Dermatologie du CHU Départemental Borgou/Alibori à Parakou pour des lésions nodulaires douloureuses du tronc et des membres thoraciques ayant débuté au sein droit depuis huit mois sur un mode continu. L'examen dermatologique découvrait sur le tronc et les membres thoraciques, des lésions nodulaires sous une peau érythémateuse, douloureuses à la palpation; les diamètres de ces lésions variaient entre un et cinq centimètres. L'examen anatomopathologique et l'immunohistochimie ont permis de retenir le diagnostic de panniculite lupique et la patiente a été soumise à la Prednisone par voie orale, à doses dégressives. Les lésions cutanées ont régressé au bout de trois mois. Des conseils diététiques liés à une corticothérapie au long cours ont été prodigués. Une confrontation anatomo-clinique est indispensable pour retenir un diagnostic positif des dermatoses rares comme la panniculite lupique.

Mots clés: Panniculite lupique; Biopsie profonde; Infiltrat lymphocytaire; Bénin

INTRODUCTION

La panniculite lupique ou maladie de Kaposi-Irgang est une forme clinique rare du lupus érythémateux chronique [1,2]. La panniculite est constatée dans plusieurs maladies infectieuses, vasculaires, systémiques, de cause physique, pancréatique, ou par déficit en 1-antitrypsine, et rarement dans le lupus où elle représente 1 à 3% [1,3]. La panniculite lupique est considérée de nos jours comme un état précancéreux du lymphome T pléomorphe hypodermique [4]. Nous rapportons le cas d'une patiente atteinte de panniculite lupique dont l'examen anatomo-pathologique, en l'occurrence l'étude immunohistochimique a été d'un grand apport au diagnostic qui peut être erroné sans ces outils car la présentation clinique n'est pas la plus spécifique de la maladie lupique.

OBSERVATION

Une femme âgée de 40 ans sans antécédent pathologique particulier, avait consulté le 15 mai 2018 dans le Service de Dermatologie du CHU Départemental Borgou/Alibori à Parakou (Bénin) pour des lésions nodulaires du tronc et des membres thoraciques. A l'anamnèse, ces lésions non prurigineuses, auraient débuté au sein droit il y a 8 mois, sur un mode continu. Il s'agirait de lésions ponctiformes localisées au début sur le sein gauche; elles auraient augmenté de taille puis étendues progressivement au tronc et aux membres thoraciques. A l'inspection, les

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lésions étaient érythémateuses avec discret phénomène de peau d'orange (Fig. 1). A la palpation, elles étaient douloureuses, sous cutanées et nodulaires, de diamètres variant entre un et cinq centimètres, siégeant sur le tronc et les membres thoraciques (Fig. 2). Les sérologies rétrovirale et hépatique B et C étaient négatives. Le bilan immunologique (anticorps anti-ADN natif, anti-Ro/SS-A) était négatif mais le dosage des fractions du complément (C3 et C4) n'a pu être réalisé. Des prélèvements biopsiques cutanés profonds réalisés en zones nodulaires (dos, sein gauche et bras droit) ont révélé:

- au faible grossissement, la présence d'un infiltrat lymphocytaire nodulaire intralobulaire (Fig. 3);
- au fort grossissement des lymphocytes en amas au sein des lobules adipeux, accompagnés de quelques macrophages et d'un foyer de nécrose adipocytaire à type de cytostéatonécrose (Fig. 4).

L'examen anatomopathologique conclut à une hypodermite lymphocytaire nodulaire faisant discuter un lymphome T panniculite-like ou une panniculite lupique. L'étude immunohistochimique a montré des lymphocytes T CD3+/CD8- accompagnés de quelques lymphocytes B réactionnels CD20+ (Fig. 5) permettant d'éliminer le lymphome T panniculite-like. Le diagnostic de panniculite lupique a été retenu et la patiente a été mise sous Prednisone 1mg/kg/jour pendant trois semaines puis à doses dégressives. Les lésions cutanées ont régressé partiellement au bout de 3 mois (Fig. 6). Des conseils diététiques liés à une corticothérapie au long cours ont été prodigués.

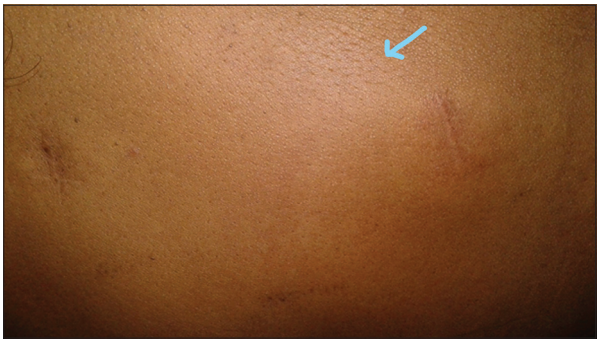
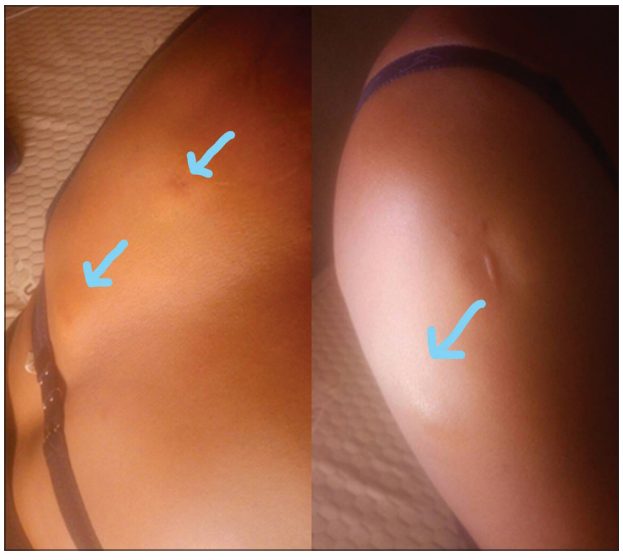


Figure 1: Erythème avec discret phénomène de peau d'orange en regard d'une lésion nodulaire du dos.



Figures 2: Lésions nodulaires de dimensions 3 x 5cm de grands diamètres du dos et du membre thoracique droit.

DISCUSSION

La panniculite lupique encore appelée " lupus érythémateux profond " est une forme anatomo-clinique rare du lupus érythémateux chronique, souvent associée à un lupus érythémateux systémique dans 10%

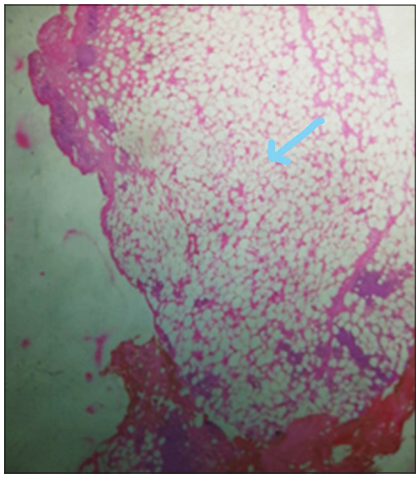


Figure 3: Infiltrat lymphocytaire nodulaire, intralobulaire.

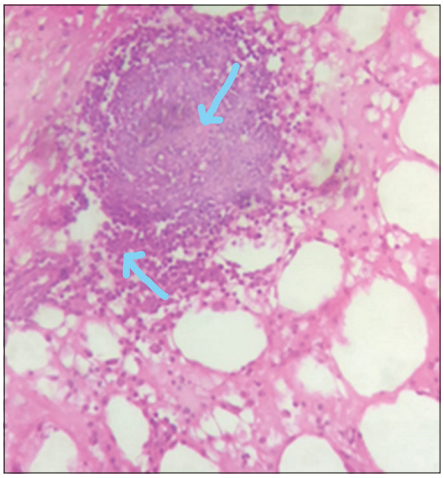
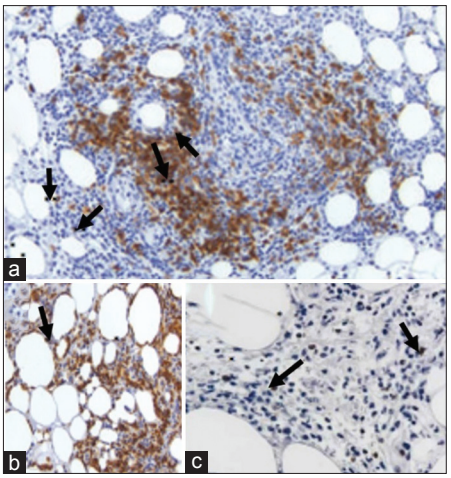
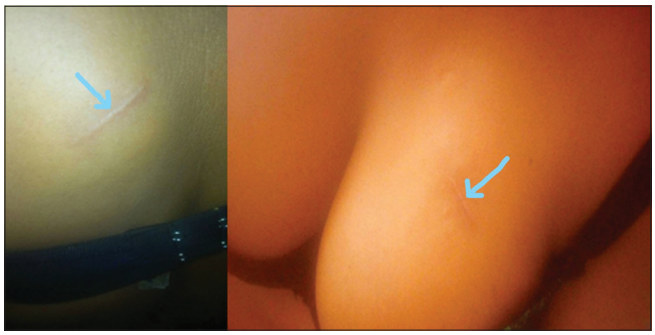


Figure 4: Lymphocytes groupés en amas au sein des lobules adipeux, accompagnés de quelques macrophages et de foyers de nécrose adipocytaire à type de cytostéatonécrose.



Figures 5: Immunohistochimie: (a) Lymphocytes B de type réactionnel (CD20+); (b) Lymphocytes T CD3+; (c) Lymphocytes T CD8-; x40.



Figures 6: Bonne évolution clinique des lésions au dos et au sein gauche après prélèvements biopsiques et corticothérapie.

des cas [1,3]. Le diagnostic repose principalement sur l'intégration des données cliniques et histologiques. Les nodules de panniculite lupique peuvent être isolés ou plus souvent s'intégrer dans une maladie lupique connue, en général de bon pronostic [5,6]. Dans le lymphome, des signes généraux sont plutôt associés tels que la fièvre, les frissons, l'asthénie et l'amaigrissement dans plus de 50% des cas et la présence dans 25% des cas, d'adénopathies et/ou d'hépato-splénomégalie [7,8]. Sur le plan biologique, les examens biologiques les plus importants sont immunologiques avec l'identification globale d'anticorps antinucléaires, de ses composantes (anti-ADN natif, anti-Ro/SS-A et La/SS-B, Sm, RNP) et éventuellement la recherche d'une activation du système du complément ainsi qu'une recherche d'anticorps antiphospholipides [9,10]. L'examen histologique nécessite une biopsie large et profonde, à lame de bistouri, comprenant l'hypoderme où se situe l'infiltrat intéressant les lobules graisseux, mimant une panniculite lobulaire. Il permet d'éliminer les principaux diagnostics différentiels que sont le lymphome T panniculite-like et la vascularite urticarienne [11,12]. On observe habituellement dans le lupus profond, un épidermotropisme lorsque l'épiderme est représenté mais il peut-être quasi-absent avec atteinte du derme profond, comme dans le lymphome T panniculite-like, égarant le diagnostic [13,14]. Dans le lupus, il existe aussi habituellement des dépôts de mucine, la présence de centres germinatifs réactionnels, de foyers de cellules B ou de nombreux plasmocytes, de cellules dendritiques plasmocytoïdes ainsi que de cellules MxA, la présence d'une bande lupique en immunofluorescence directe (IFD) cutanée et l'absence de réarrangement clonal du T-cell receptor (TCR) diagnostic [15,16].

L'étude immunohistochimique permet en général de lever l'équivoque. Dans la maladie lupique, comme dans notre cas, les lymphocytes T sont de phénotype CD3+/CD8-. Dans les lymphomes, ils sont de phénotypes CD3+/CD8+/CD56-/CD30- TCR alpha-bêta avec expression des protéines cytotoxiques comme le granyme B, et présence d'un trou phénotypique CD2, CD5 et/ou CD7 [17,18].

La difficulté diagnostique reste toutefois accrue par l'existence d'authentiques associations entre le lupus et le lymphome, et par la possible coexistence d'aspects histologiques des deux sur différents champs du même prélèvement biopsique [19].

Certains auteurs [19,20] suggèrent que ces 2 pathologies appartiendraient à un même spectre. Le diagnostic de lymphome doit être envisagé devant un lupus profond et, inversement, qu'un lupus systémique soit recherché dans la surveillance des patients atteints de lymphome sous-cutané et panniculite-like. L'évolution clinique du lupus profond se fait vers le développement de cicatrices dystrophiques inesthétiques malgré un traitement bien conduit. L'autre hantise reste, comme soulignés par certains auteurs [19,20], une évolution de la maladie lupique vers le lymphome.

CONCLUSION

La panniculite lupique est inhabituelle, de diagnostic parfois difficile avec le lymphome qui est en l'occurrence, aussi bien un diagnostic différentiel, qu'une phase évolutive de la maladie. Une bonne clinique avec des tests immunologiques adéquats et une biopsie cutanée profonde et large avec une étude immunohistochimique permettent de faire un diagnostic de précision. L'évolution est souvent

favorable mais le challenge reste dans une surveillance rigoureuse de ces sujets à risque de développer un lymphome.

Consent

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

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Our Dermatology Online

Case Report

Unrecognized lupus vulgaris, revealed by its treatment

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ABSTRACT

A 49-year-old woman, without medical or family history, presents since 6 months ago an erythematous-squamous, papular plaque at the centro-facial level that increased very progressively. The physical examination was normal including pleuro-pulmonary, abdominal and osteo-articular examination. Everything was evolving in a context of apyrexia and conservation of the general state. During her hospitalization, the cutaneous biopsy found a granuloma with epitheliod and giant cells without caseous necrosis. The tuberculin IDR was negative. The search of Koch bacillus was negative in the cutaneous samples and sputum. TPHA/VDRL and HIV serologies were normal. The bacteriological and mycological examination of the biopsy fragment was negative. The expert gene to identify Mycobacterium tuberculosis was negative and also the smears to research leishmania bodies were negative. Despite the absence of diagnosis evidence, an anti-tuberculosis treatment; 2RHZE/4RH regimen, was prescribed and a spectacular amelioration was noted during and many months after the end of the treatment. So, the response to the treatment was the only diagnosis evidence for the lupus vulgaris.

Key words: Granuloma; Cutaneous tuberculosis; Infection disease of skin

INTRODUCTION

Cutaneous Tuberculosis (TB) is uncommon; it represents 2% of extra-pulmonary localizations and often poses diagnosis problems. Lupus vulgaris(LV) is a form conventionally linked to the reactivation of an endogen focus. We report an observation of unrecognized LV, revealed by its treatment.

CASE REPORT

A 49-year-old, housewife, of low socioeconomic status, from Marrakech, without particular pathological history, presents over 6 months an erythematous squamous papular plaque at the centro-facial level that had been growing progressively.

At her admission, there was an erythematous, ulcerated placard, 10 × 8.5 cm, recovered with crust and oozing on which was many fold flubbydermic micronodules brown-yellowish at vitro-pressure, giving to lesion an lupoid aspects (Fig. 1a).

Otherwise, the rest of the clinical examination was normal including pleuro-pulmonary, digestive and osteo-articular examination. Everything was evolving in a context of apyrexia and conservation of the general state. Cutaneous biopsy found a granuloma with epitheliod and giant cells without caseous necrosis (Figs. 2a and 2b).

The tuberculin IDR was negative. The search for Koch's bacillus was negative on cutaneous samples and sputum. The TPHA/VDRL and HIV serologies were negative. Bacteriological, mycological examinations of the biopsy fragment were negative. The expert gene to identify Mycobacterium tuberculosis was negative and also the smears to search leishmania bodies were negative. The pulmonary radiography, the abdominal and pelvic echography was normal.

The diagnosis of cutaneous leishmaniasis was initially evocated despite the negativity of the cutaneous smear and the patient was treated with metronidazole 750 mg per day for 3 months but without any improvement.

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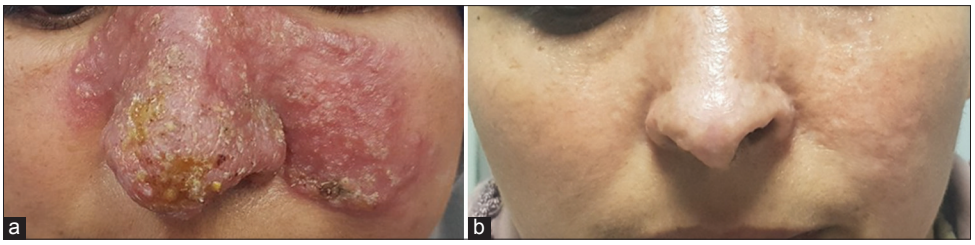

Figure 1: An erythematous squamous papular plaque at the centro-facial level (a), regression of the lesion after 6 months of antituberculous treatment (b).

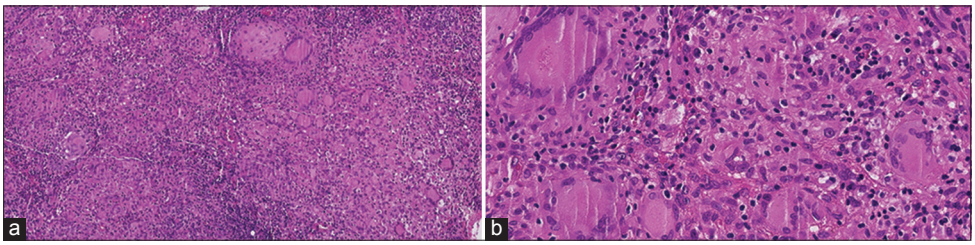

Figure 2: Granuloma structures (hematoxylin and eosin * 20) (a), infiltration in the subcutaneous tissue, granuloma arrows indicate multinuclear giant cells (hematoxylin and eosin * 40) (b).

LV was also evoked in front of the origin of the patient, the lupoid aspect at the vitro pression as well as the granulomatous aspect in the histology. The patient was treated with an anti-tuberculosis treatment with 2RHZE/4RH(first 2 months of isoniazid, rifampicin, pyrazinamide, ethambutol quadruple treatment plus 4 months of isoniazid and rifampicin combination). After the end of the treatment, a complete disappearance of the lesion was noted (Fig. 1b).

DISCUSSION

TB is uncommon and much less frequent than the other localization of Tuberculosis disease [1] LV represents the most common form in the Western countries. It affects the female sex more frequently [2]. Its favorite localization is the face, especially the nose and cheeks. It is almost single, rarely multiple [3,4]. The diagnosis of certainly of the LV remains difficult. In our context, the culture and methods of rapid detection of *Mycobacterium tuberculosis* by genomic amplification (PCR) are not available; it is usually in front of many epidemiological, clinical, paraclinical arguments, that the diagnosis is often retained. Indeed, the Mycobacterium tuberculosis is rarely found at the direct examination and at the culture [5,6].

Clinically, LV can be confused with cutaneous leishmaniasis, leprosy, tertiary syphilis…; thus, the diagnosis can be even more difficult in the presence of a tuberculoid granuloma without caseous necrosis in the histology, which can be observed in many non-tuberculous dermatoses [7].

The therapeutic decision must take into account mainly the epidemiological and clinical arguments, especially the existence of lupomas at the vitro- pressure test at the periphery of every dermatosis which extends very slowly, paraclinically by a positive tuberculin IDR, histology and a pulmonary radiography evocative and especially a rapid evolution under antituberculosis allowing to retain the diagnosis [8].

However, the response to the specific anti-tuberculosis treatment may be the only evidence to the diagnosis of TB as in our case [9].

CONCLUSION

The Lupus vulgaris is an etiology to consider ahead of an old cutaneous lesion in our country where the prevalence of cutaneous tuberculosis remains high despite the negativity of the etiological assessment.

Consent

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

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Our Dermatology Online

Case Report

Cutaneous leishmaniasis in Nepal: an emerging public health concern

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ABSTRACT

Cutaneous leishmaniasis, a vector borne protozoan infection of skin manifests as chronic nodulo-ulcerative growth in skin. In Nepal, cutaneous leishmaniasis, the most common form, supposed to be rare is gradually rising as an emerging public health concern. These days, a number of imported and native patients are being reported from different parts of Nepal. Since, it's less endemic here; there is high chance of being treated as other diseases. Here, we report a series of cases of cutaneous leishmaniasis, who presented in the outpatient department of dermatology, TU Teaching Hospital in the year 2015-2016 and was treated with meltifosine.

Key words: Cutanoeus leishmaniasis; Miltefosine; Nepal; Public health

INTRODUCTION

Cutaneous leishmaniasis (CL) is vector borne parasitic infection. A 'classical' lesion starts as a papule or nodule at the site of inoculation. CL is caused by different species of Leishmania but L. major is the common reported cause in Nepal [1,2]. It is transmitted by a bite of infected female sandfly of the genus phlebotomus in the old world and the genus Lutzomyia in the new world. The disease is prevalent in 98 countries and responsible for increasing health problems [3,4]. About a million cases of CL reported in the last 5 years and 310 million people at risk. Because of labor migrants, refugees and cause of international travel, cases are also being seen in new regions [5]. First reported case of CL in Nepal was in 2006 which were imported from gulf countries. But now, there is increasing number of reports of natives of CL from far-western and central part of Nepal [6-9]. Here we report three cases of CL.

CASE REPORT

First case

It's a case of 40 years housewife native in Kathmandu who presented with asymptomatic non-healing small nodule at the philtrum with swelling of the central part of upper lip of 1 year duration (Fig. 1). She denied history of recent travel, fever, weight loss, pain or ulceration. Investigations were normal. Acid fast stain of slit skin smear and sputum were negative. Biopsy revealed multiple granulomas composed of lymphocytes, histiocytes with amastigotes. LD bodies were seen in Giemsa stain. Patient was treated with oral miltefosine 50 mg three times a day for 28 days with improvement.

Second case

A 27 years old patient from Chitwan presented with multiple non-healing wound over the upper and lower extremities for 4 months. Patient had recently returned from Saudi Arabia. Initially the lesions started from right arm as painless eruptions which became pustular, gradually broke up into an ulcer and few of which heal with scarring. There were number of lesions involving both the lower limbs, upper limbs and abdomen. Examination revealed multiple erythematous plaques over right and left thighs, arms, forearm, measuring 1x1 cm to 4x3cm with surface ulceration and crusting (Fig. 2). Histopathological examination revealed dermal

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aggregates of mixed inflammatory cells including nuclear polymorphs, lymphocytes, histiocytes, plasma cells.

Third case

A 52 years old male from Ilam, a labour worker, returnee from Saudi Arabia, attended with non- healing wound over the extensor aspect of right leg, forearm and abdomen for 2 months. Local examination revealed large erythematous plaque with superficial crustations. There were verrous plaque in the right leg in linear pattern (Fig. 3). Biopsy specimens showed dense granulomatous reaction with multinucleated gaint cell, epithelioid cells and LD bodies (Fig. 4). Patient was treated similarly with oral miltefosine 50 mg three times a day for 28 days. Comparative tabulate form of all the cases is given in Table 1.

DISCUSSION

Cutaneous leishmaniasis is an emerging public health problem in Nepal [4]. From 2006 AD of first reported case of CL to present context, there are increasing number of cases being reported from different parts of country [6-9]. Previously, majority patient had history of travel to gulf countries but recently a studies denies such history in majority of patients [9].The geographic distribution of our cases of CL evaluated reflects travel and immigration patterns; two of the patients were returnees from Saudi Arabia, however, one of them

Table 1: Profile of Patients

Case	1	2	3
Age	40	27	52
Sex	Female	Male	Male
Address	Kathmandu	Chitwan	Ilam
Duration of Disease	1 year	4 months	2 months
Occupation	Housewife	Cook	Labor worker
Foreign travel	No	Saudi Arabia	Saudi Arabia
Site of lesions	Philtrum	Thigh, arm, forearm	Leg, forearm, abdomen
Biopsy	Confirmed	Confirmed	Confirmed
Treatment	Miltefosine	Miltefosine	Miltefosine

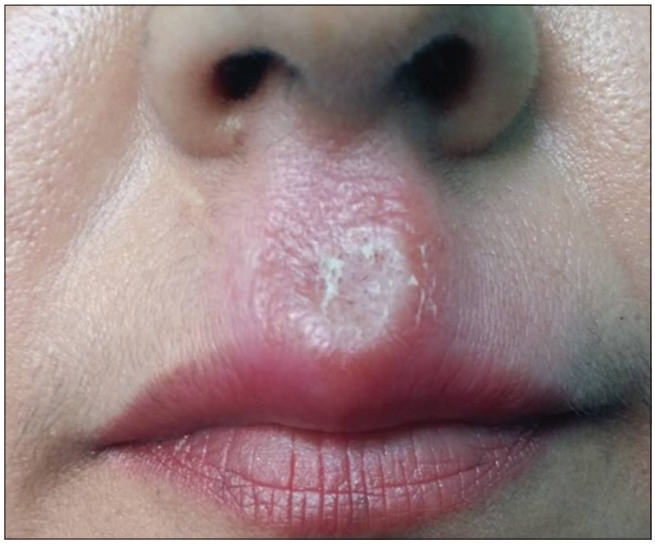

Figure 1: Lesion in the philtrum.

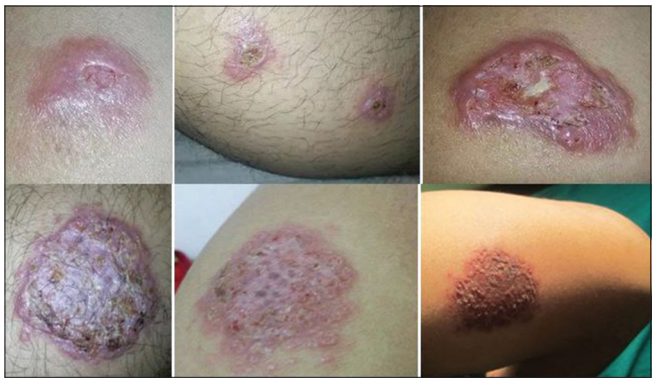

Figure 2: Different stages of lesions of case 2.

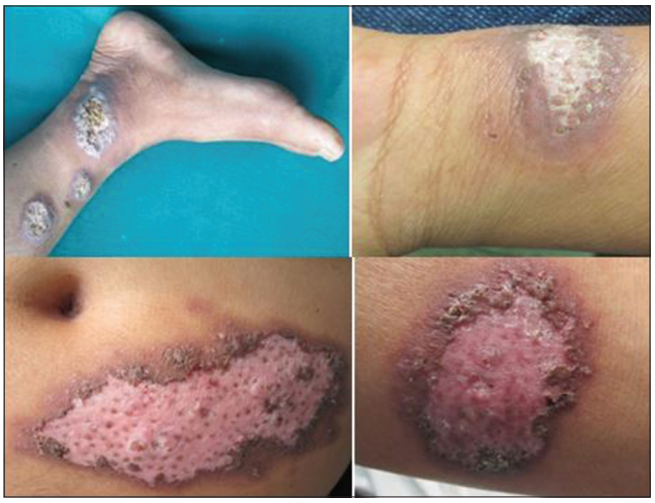

Figure 3: Different stages of lesions of case 3.

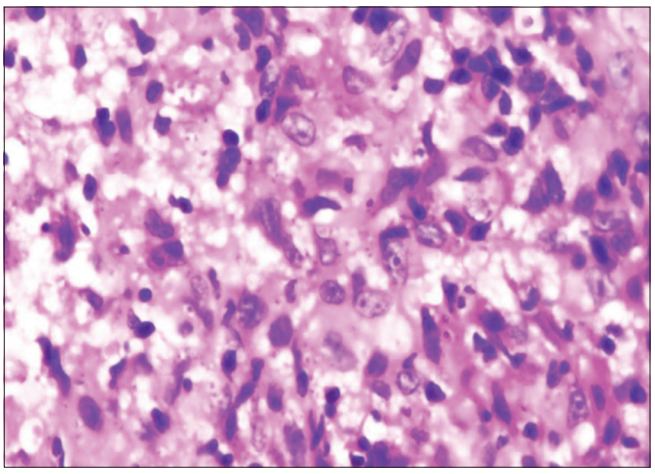

Figure: 4 LD bodies.

denies any travel outside Nepal, similar to case being reported.

Diagnosis of cutaneous leishmaniasis is history and clinical examination, confirmed by demonstration of amastigotes in Giemsa stained smears from infected skin by FNAC, presence of leishmanial granulomas in the dermis in H and E specimens, growth of promastigotes in Nicolle-Novy- macNeal (NNN) culture medium or Leishmanial DNA by PCR [10].

After the recent report of the native cases, there is serious concern of increasing number of CL cases in days to come. However, because of non-endemicity of CL in Nepal and heterogeneous presentation, it can easily be missed clinically and reported cases could be the tip of iceberg with a number of cases underreported and undiagnosed. Many different therapeutic interventions, including topical, systemic and non-pharmacological treatments, have been described. Systemic treatment with pentavalent antimonials is indicated for problematic sores like involvement of mucosa or cartilage, sores on the lower leg or over a joint, sores where scarring would be disabling or disfiguring. Oral miltefosine, available free of cost by Nepal government, was used in our cases with good improvement.

CONCLUSION

Though, cutaneous leishmaniasis is rare in Nepal, it's time to be highly alert about its possibility in every chronic nodulo-ulcerative lesion for proper and timely treatment to reduce the morbidity associated with it.

Consent

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

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

Our Dermatology Online

Case Report

Subcutaneous granuloma annulare

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ABSTRACT

Granuloma annulare (GA) is a benign granulomatous skin disease. Subcutaneous granuloma annulare is a rare variant in adults, predominantly affects women and typically involves hands. Differential diagnosis should be made with rheumatoid nodules, which frecuently pose a challenge because of the clinical and histological resemblance. Histopathologically, subcutaneous granuloma annulare is a necrobiotic non-infectious granuloma surrounded by chronic inflammatory infiltrate. Treatment is not standarised, although topical or intralesional stereoids and surgery are used.

Key words: Granuloma annulare; Subcutaneous granuloma annulare; Rheumatoid nodules; Intralesional steroids

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Our Dermatology Online

Case Report

Granuloma anular subcutáneo

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RÉSUMÉ

El granuloma anular (GA) es una enfermedad cutánea granulomatosa poco frecuente, de carácter inflamatorio y benigno. La variante profunda o subcutánea es infrecuente en adultos y cuando se localiza en manos debe distinguirse de los nódulos reumatoideos, con los que tiene importantes similitudes clínicas e histológicas. Histológicamente, el GA profundo presenta formación de granulomas en empalizada localizados en dermis profunda y tejido celular subcutáneo. El tratamiento no está estandarizado, aunque se sugieren los corticoides tópicos o intralesionales, así como la cirugía.

Palabras clave: Granuloma anular; Granuloma anular subcutáneo; Nódulos reumatoideos; Corticoides intralesionales

INTRODUCTION

El granuloma anular profundo es una variante de granuloma anular poco frecuente en adultos, que suele afectar a mujeres de mediana edad. Se presenta como nódulos indoloros color piel, de predominio en miembros inferiores, manos o cuero cabelludo. Es fundamental hacer el diagnóstico diferencial con los nódulos reumatoides cuando las lesiones se localizan en las manos, ya que son entidades que clínicamente pueden ser indistinguibles.

CASE SYNOPSIS

Mujer de 54 años con antecedentes personales de hipotiroidismo en tratamiento con levotiroxina. Acudió a la consulta por lesiones asintomáticas de años de evolución localizadas en el dorso de la mano derecha. La paciente negaba clínica sistémica o articular asociada; así como lesiones cutáneas en otras localizaciones. Se trataba de nódulos eritematosas que medían entre 1 y 2 cm aproximadamente (Fig. 1). Tenían una superficie lisa y polilobulada, consistencia firme y no estaban adheridas a planos profundos. Las lesiones se localizaban en la superficie dorsal de la mano derecha sobre las articulaciones metacarpofalángicas e interfalángicas. La biopsia de la lesión mostró degeneración del colágeno formando granulomas, rodeados en algunas zonas de histiocitos en empalizada (Figs. 2a y 2b), con discreto aumento de mucinas. Se realizó una analítica que incluía reactantes de fase aguda (VSG y PCR), ANA y factor reumatoide (FR) que fue normal. La ecografía cutánea puso de manifiesto unas lesiones hipoecoicas localizadas en dermis y tejido celular subcutáneo, bien delimitadas y polilobuladas, próximas al periostio sin infiltración ósea (Fig. 3a). Las lesiones no mostraban flujo en modo Doppler (Fig. 3b).

Se realizó el diagnóstico de granuloma anular profundo o subcutáneo y se realizó tratamiento intralesional con 1 ml de betametasona distribuido por las tres lesiones con importante mejoría de las mismas. Tras seis meses de seguimiento, la paciente se encuentra estable sin aparición de nuevos nódulos.

DISCUSSION

El granuloma anular (GA) es una enfermedad cutánea granulomatosa poco frecuente, de carácter

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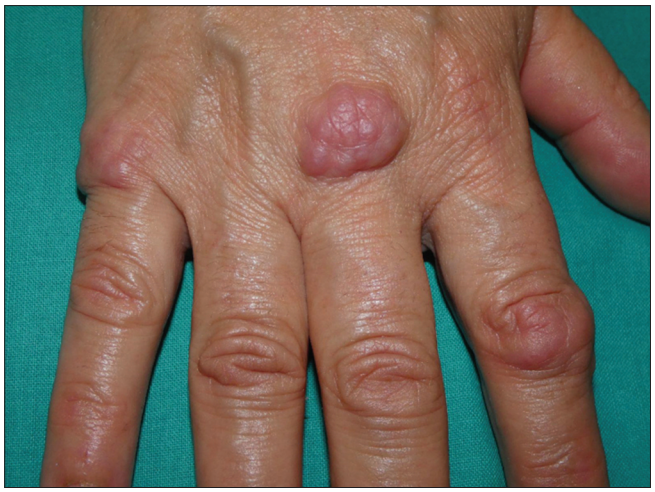

Figura 1: Nódulos eritematosos polilobulados de superficie lisa.

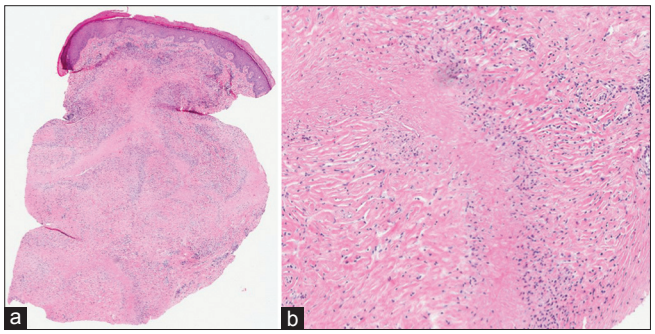

Figura 2: (a) A pequeño aumento se observan varios focos de colágeno degenerado a distintos niveles de la dermis (H&E, x10) (b) Detalle de uno de los focos de colágeno degenerado rodeado de histiocitos.

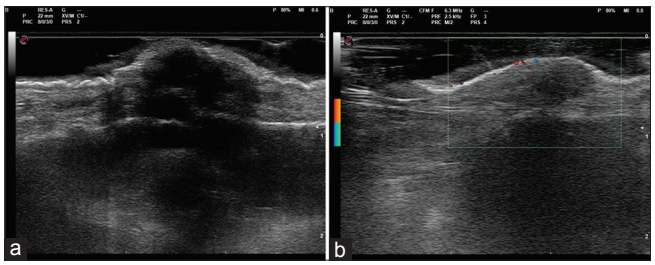

Figura 3: (a) Lesiones hipoecoicas localizadas en dermis y tejido celular subcutáneo, bien delimitadas y polilobuladas, próximas al periostio sin infiltración ósea (b) Ausencia de flujo en modo doppler.

inflamatorio y benigno. Se trata de una entidad de etiología desconocida y autolimitada, pero con recurrencias frecuentes. De entre las variantes de GA descritas, el GA profundo o subcutáneo ocupa el tercer lugar en frecuencia tras el GA localizado y el GA diseminado [1,2]. Característicamente, el GA profundo afecta a niños sanos menores de 5 años, y con menos frecuencia a adultos jóvenes [1-5]. El granuloma anular profundo o subcutáneo se presenta como nódulos indoloros color piel, de predominio en miembros inferiores, manos o cuero cabelludo [1-3]. El GA profundo es infrecuente en adultos y cuando se presenta suelen ser mujeres de mediana edad con lesiones localizadas en manos próximas a las pequeñas articulaciones [5]. En estos casos es fundamental hacer el diagnóstico diferencial con los nódulos reumatoides, entidades que clínica e histológicamente pueden ser indistinguibles. Otros cuadros que se deben incluir en el diagnóstico diferencial son paniculitis, necrosis grasa, granulomas infecciosos o reacciones a cuerpo extraño entre otros, en función de la historia clínica de la lesión [1,2,4,5]. Histológicamente, el GA profundo presenta formación de granulomas en empalizada localizados en dermis profunda y tejido celular subcutáneo. Típicamente tiene un mayor grado de necrobiosis y depósitos de mucina que las formas clásicas de GA, pero menos necrobiosis que la presente en nódulos reumatoideos [1,2,4]. Se ha visto que el GA profundo y los nódulos reumatoideos (NR) comparten características histológicas. Así, Mesara et al. describieron el término "nódulo seudorreumatoideo" para referirse a lesiones que clínica e histológicamente se asemejan a NR en pacientes sin datos de artritis reumatoide u otras enfermedades sistémicas [2,4-6]. Las publicaciones en relación al tratamiento de esta patología tienen una evidencia pobre, ya que en su mayoría de tratan de casos sueltos o series cortas de casos. El abanico de opciones es amplio, e incluye tanto tratamientos tópicos como sistémicos, pero es frecuente la persistencia o recurrencia de las lesiones. En el caso del GA profundo, la primera línea incluye los corticoides de alta potencia tópicos o intralesionales [5]. La alterantiva quirúrgica se reservaría para las lesiones yuxta-articulares que provoquen impotencia funcional [2].

CONCLUSION

El GA profundo es una variante infrecuente de GA. Cuando las lesiones se localizan en manos de mujeres de mediana edad, debe hacerse el diagnóstico diferencial con los nódulos reumatoides, para lo que nos debemos apoyar tanto en la negatividad del FR, como en la ausencia de clínica articular y en la histología.

Consent

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

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Our Dermatology Online

Clinical Image

Ophthalmic rosacea in a patient with Takayasu disease

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Rosacea is a chronic dermatological disease that may affect the ocular structures up to 6-72% [1] of all cases with important visual consequences for affected patients. Therefore, an early diagnosis associated with adequate treatment is important [2].

The aim of this study is to report an original observation of ophthalmic rosacea in a patient with Takayasu disease.

We report the case of 49-year-old women with Takayasu disease treated by methotrexate 20mg/day who consulted for eye redness, tearing, and decreased visual acuity. The ophthalmological examination revealed a visual acuity (VA) of 9/10, keratoconjunctivitis + blepharitis (Fig. 1). He was diagnosed with ocular rosacea and treated with doxycycline and topical tacrolimus cream.

Ocular rosacea includes multiple ophthalmic manifestations ranging from inflammation of the eyelid margin and blepharitis to serious corneal affectations. An early diagnosis associated with adequate treatment visual allows avoiding sequelae.

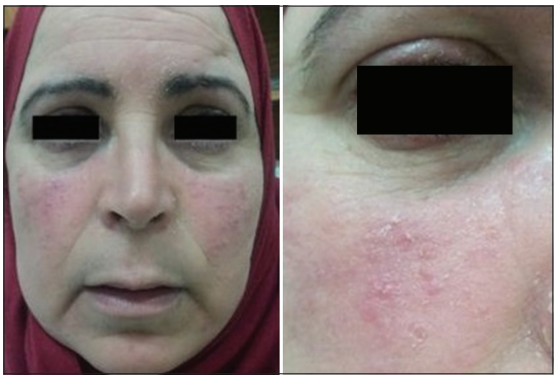

Figure 1: Blephartis and conjonctivitis in patient with rosacea.

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Clinical Image

Extramedullary plasmacytomas and prognostic implications in multiple myeloma

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Multiple myeloma is a malignant proliferation of monoclonal plasma cells and is often confined to the bone and bone marrow. When the disease affects organs besides the bone or the bone marrow is called extramedullary plasmacytoma [1].

We describe the case of a 68-year-old male, with an IgG lambda multiple myeloma under second-line therapy with bortezomib, thalidomide and dexamethasone after lack of response to first-line treatment, presenting to dermatology department due to the recent development of an erythematous-violaceous nodule of 1,2 cm of diameter on the left flank (Fig. 1), an occipital subcutaneous mass with 5 x 5 cm (Fig. 2) and 4 subcutaneous nodules on the forehead (Fig. 3), between 1,5 and 2 cm of diameter. Lesions were asymptomatic and had grown rapidly in size over weeks. Skin biopsy revealed a dermal and subcutaneous nodular proliferation of immature plasma cells, morphologically and immunohistochemically consistent with cutaneous plasmacytoma. Cranial and maxillofacial computed tomographies were requested, revealing spontaneously dense regular masses at the parietal, right paramedian, frontal and right malar regions, with a lytic infiltrative aspect causing irregularity of the cortical bone and diploe (Fig. 4). The patient died 2 months later from extensive and rapid extra-medullary progression.

Cutaneous plasmacytomas can occur primarily in the skin, without involvement of the bone marrow, or secondarily, from the dissemination of multiple myeloma or plasma cell leukemia [2]. Secondary cutaneous plasmacytomas occur by direct extension from underlying bone lesions or by hematogenic spread. Typically these lesions present as cutaneous or subcutaneous nodules or masses and can be erythematous-violaceous or normochromic [1,2]. There are frequently multiple lesions, of smooth and raised surface, more commonly on the trunk, extremities and face [2]. These lesions occur late in the course of the disease and dictate a poor prognosis,

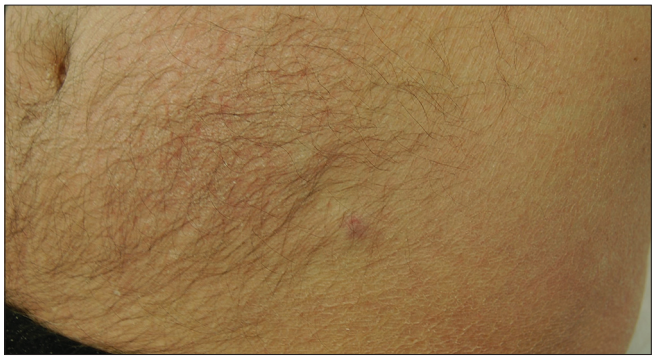

Figure 1 : Erythematous-violaceous nodule on the left flank.

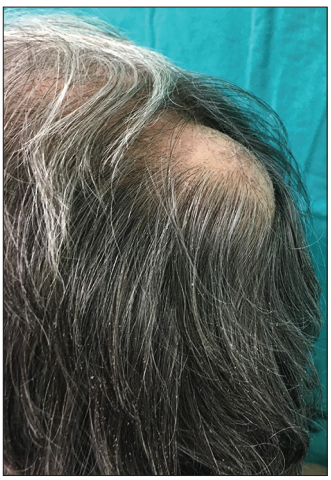

Figure 2: Normochromic subcutaneous mass on the occipital region.

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DOI:10.7241/ourd.20201.23

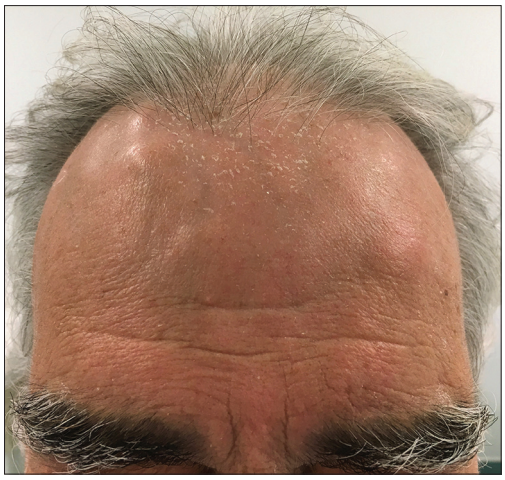

Figure 3 : Frontal subcutaneous nodules.

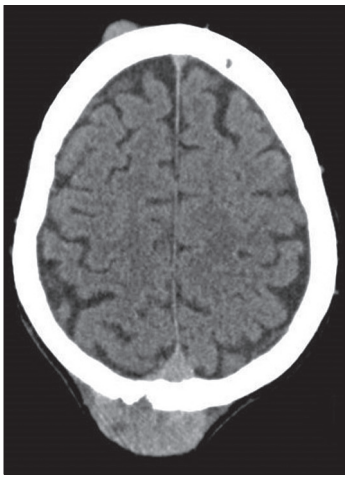

Figure 4: Computed tomographic aspect of the extracranial subcutaneous masses.

with 50% of the patients dying within 6 months after diagnosis [2,3].

Consent

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

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

Our Dermatology Online

Clinical Image

Median canaliform dystrophy of Heller at thumb level

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Child 12 years old, having a tic history of cuticle regrowth of thumbs bilaterally. No history of use of oral retinoids or other drugs, or history of contact with irritants or allergens was present. No nail disorder or psychiatric disorder in the family. Consult for bilateral nails lesions. On examination, a single medial longitudinal groove with transverse furrows from the medial side on either side achieving a fir appearance present on both thumbnails, above, the right thumbnail (Fig. 1). The medial groove extended from the proximal fold to the distal edge of the nail. The Lunula seemed to be enlarged in size. No skin lesions present elsewhere. The systemic examination was without particularity. The diagnosis of median nail dystrophy has been made on a clinical basis. The patient was advised not to bite their nails. A psychiatric consultation was recommended; advice was offered to the patient. The evolution was good after 6 months.

Median canaliform dystrophy (MCD) of Heller is a rare entity characterized by a midline or a paramedian ridge or split and canal formation in nail plate of one or both the thumb nails. It is an acquired condition resulting from a temporary defect in the matrix that interferes with nail formation [1]. The condition is diagnosed based on its clinical features. It results from a temporary defect in the nail matrix, following dyskeratinization or focal infection, or due to self-inflicted trauma to the nail plate, nail matrix or nail bed [2]. A few cases have been attributed to oral retinoid use also [3]. Presents with small cracks or fissures that extend laterally from the central canal or split towards the nail edge giving the appearance of an inverted fir tree or Christmas tree, usually symmetrically affecting the thumb nails mainly [4]. Treatment of median nail dystrophy includes injectable triamcinalone acetonide, topical 0.1% tacrolimus, and tazarotene 0.05%, which is many a times challenging for a dermatologist. Psychiatric opinion should be taken when associated with the depressive, obsessive-compulsive, or impulse-control disorder [1].

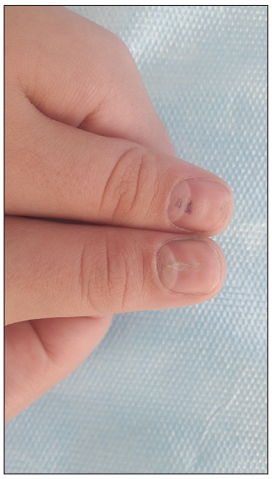

Figure 1: Heller medial canaliform dystrophy at the bilateral thumb.

Consent

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

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

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Our Dermatology Online

Clinical Image

Simple anonychia congenita

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A 10-year-old male presented with absence of all nails since birth (Fig. 1a and 1b). On examination, there was absence of all finger nails and toenails. No abnormality of the bone and teeth was present. Radiography of both hands and feet showed no abnormality. The patient had normal intelligence. There was no family history. Based on the clinical features and history, a diagnosis of congenital nonsyndromic simple partial anonychia was made.

Anonychia (absence of nails) is a very rare congenital or acquired anomaly. It may occur as a single feature or as part of a syndrome. Nonsyndromic anonychia has been reported in either partial or total forms. Simple anonychia means congenital absence of the nails without any other coexisting major congenital anomaly, and is extremely rare [1]. It is caused due to frameshift and nonconservative missense mutation in the exon 2 of R-spondin 4 gene present on chromosome 20p13, which affects the highly conserved first furin-like cysteine-rich domain that plays a crucial role in nail morphogenesis, resulting in absence of nails [2].

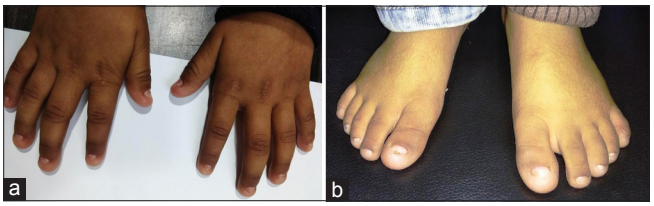

Figure 1: (a and b) Complete absence of all fingernails and toenails.

Treatment remains masterly inactivity or artificial nails.

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Letter to the Editor

Shark island pedicle flap for large reconstruction of the upper lip

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Sir,

The principle of an ideal upper lip reconstruction include repair of all subunits disrupted by the lesion, restoration of dynamic motion, sensation, oral sphincter competence and minimization of distortion and disfigurement [1-3]. The "shark" island flap is optimized for reconstruction of large defects of the upper lip without significant muscle involvement in a single stage procedure.

Two cases are reported where the same procedure is used to remove a basal cell carcinoma involving part of the cutaneous upper lip. The skin around the lesion is outlined locating the incision in the sub-nasal fold, the lateral philtrum, the vermilion margin and the melolabial fold, comprising entirely the upper lip subunit. A V-flap with a shark-like shape is also outlined on the cheek lateral to the defect (Figs. 1a and 2a). Local anesthetic solution with a concentration of 2% mepivicaine + adrenaline 1:100.000 is injected into the dermis around the defect and the lateral donor site. The lesion is incised as planned and removed (Fig. 1b). Deep incisions are made in the superior and inferior limbs of the flap, up to the sub-dermal plane, followed by medially adequate undermining of the surrounding skin. Once the flap is properly dissected, it is advanced to close as much defect area as possible with minimal deviation of the philtrum and anchored superiorly and inferiorly with subcutaneous stitches. As soon as the initial defect area has been covered, the rest of the secondary defect is closed by direct approximation of the free margins with a direct suture (Figs. 1c and 2c). Adequate follow-up time is given for complete and proper recovery (Figs. 1d, 2c and 2d).

When the upper lip defect to cover is large, flaps may have the drawback of causing deformation on natural folds as well as distortion on the nostrils and the vermilion. In this case the subcutaneous island flap is a good option for upper lip restoration allowing: great skin mobility from the medial cheek, reconstruction of an entire lip sub-unit with cosmetically, functionally and topographically similar skin, lateral advancement of tissue without significant philtrum deformation or up-down-words pulling causing facial asymmetry. This technique is successful because the flap maintains vitality thanks to a wide subcutaneous pedicle and it naturally slides into the defect combining movements of advancement and rotation.

Optimal results in a single- staged procedure are obtained, allowing preservation of the cosmetic subunit of the

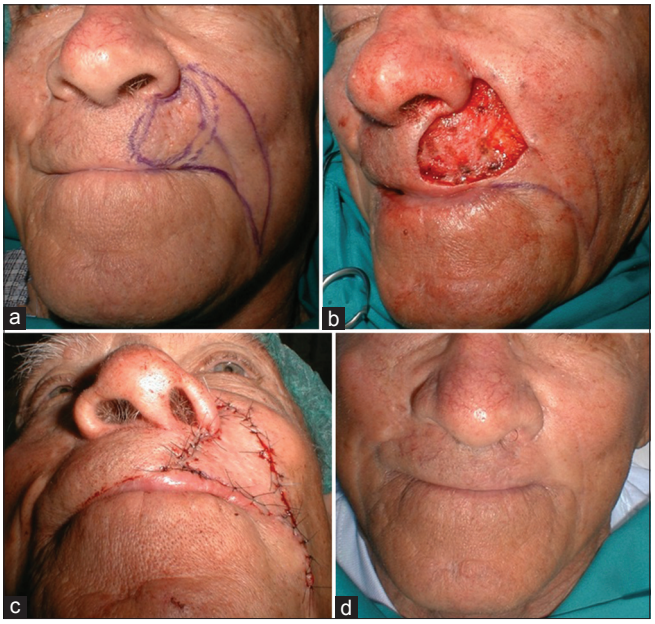

Figure 1: Case 1. (a) Pre-surgical planning of incisions. (b) Surgical defect. (c) Immediate post-operative picture (d) Six months follow-up picture.

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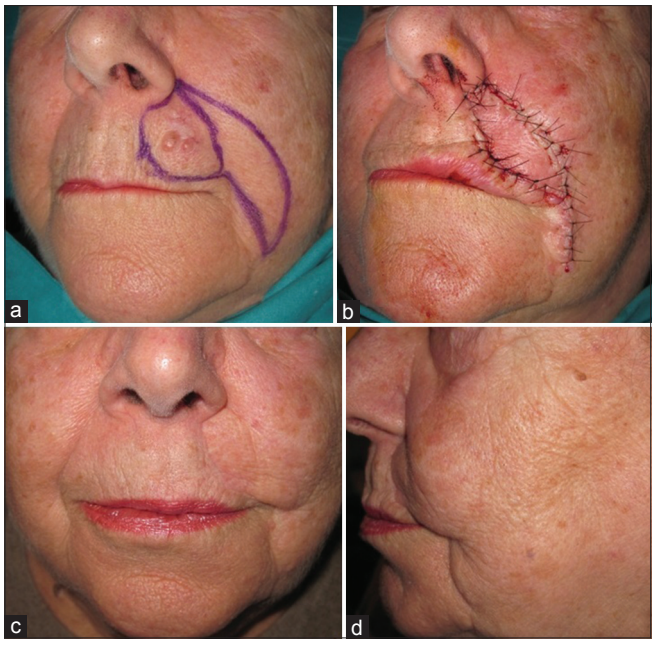

Figure 2: Case 2. (a) Pre-surgical planning of incisions. (b) Immediate post-operative picture (c-d) Nine months follow-up picture.

upper lip with minimal postoperative distortion of the philtrum which is completely recovered within weeks.

Consent

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

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Letter to the Editor

Lymphomatoid papulosis associated with Hodgkin lymphoma

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Sir,

Lymphomatoid papulosis (LyP), a recurrent spontaneous regressing papulonodular skin eruption with a chronic course, is one of the CD30-positive lymphoproliferative disorders (LPDs), among which are primary cutaneous anaplastic large cell lymphoma (ALCL) and borderline cases. LyP is known to increase the risk of malignant lymphoma, such as mycosis fungoides, ALCL, and Hodgkin lymphoma (HL) [1-3]. HL is characterized by CD30-positive Hodgkin/Reed-Sternberg (HRS) cells and is rare among the East Asian population [4]. Herein, we report a Japanese case of LyP associated with HL.

A 79-year-old Japanese man with a history of HL in complete remission by chemoradiotherapy 10 years prior presented with a 7-mm-sized asymptomatic reddish nodule on his left eyelid for over 3 months (Fig. 1a). He also had scattered reddish papules on his trunk (Figs. 1b and 1c), which had waxed and waned for about 10 years. A skin biopsy from the eyelid showed atypical lymphoid cell proliferation in the dermis (Figs. 2a and 2b), and these atypical cells had HRS-like features with bilobed nuclei and abundant cytoplasm (Fig. 2c). Immunohistochemical staining revealed that the tumor cells were positive for CD3, CD4, and CD30 (Fig. 2d) and negative for CD8, CD15, CD20, PAX, and ALK. A biopsy specimen from the trunk lesion exhibited perivascular cell infiltration with large lymphoid cells (Figs. 2e - 2g) with the same immunohistochemical staining pattern. Retrospectively, the lymphoma cells in the lymph node diagnosed as HL were positive for CD15, CD30, and PAX and negative for CD3, CD4, CD8, CD20, and ALK. PET-CT imaging was negative for nodal and visceral lesions. These findings led to a definitive diagnosis of LyP for scattered skin lesions. The nodule on the eyelid was resected as it had remained unchanged for over 4 months. No recurrence was observed at the site of excision on the eyelid, and the nodules on the trunk have been stabilized with topical corticosteroid treatment for 2 years.

CD30-positive LPDs and HL both express CD30 and they could be the differential diagnosis of one another. The current consensus is that HL cells are derived from germinal center B cells and have the immunophenotypic features of CD15 and PAX positivity, whereas the ALCL cells are negative for both [5]. As skin infiltration in HL is rare and usually occurs adjacent to an enlarged lymph node, the scattered multiple nodules in the present case were not indicative of specific HL-associated skin lesions. Although patients with LyP have a good prognosis, they have been reported to have an increased risk of developing lymphoid malignancy. LyP may be preceded with or followed by a malignant lymphoma in 10–20% of the patients [1-3]. HL is the one of the most common diseases associated with lymphomas reported in western countries; however, LyP associated with HL has not yet been reported in the Japanese population. The multiple cutaneous nodules in the present case with spontaneous regressing course were diagnosed as LyP, and the persistent nodule on his

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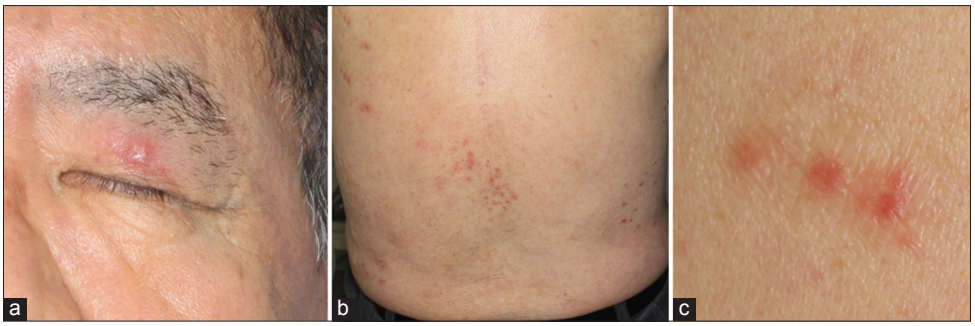

Figure 1: (a) The patient had a 7-mm-sized asymptomatic reddish nodule on his left eyelid at the first visit. (b and c) The patient also had scattered reddish papules on his trunk (lesions on the back and at close-up view, respectively).

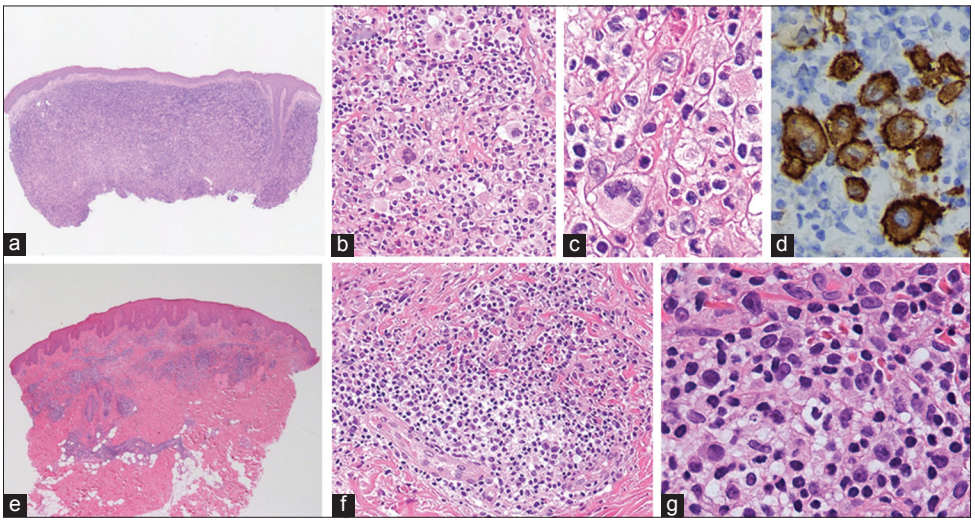

Figure 2: (a) The punch biopsy specimen from the eyelid showed diffuse and dense cell infiltration in the dermis (hematoxylin-eosin [HE], at scan magnification). (b and c) The tumor cells have large nuclei and abundant cytoplasm and some tumor cells have HRS-like figures with bilobed, double, or multiple nuclei (HE, ×100 and ×400, respectively). (d) The atypical lymphoid cells were CD30 positive (immunostaining for anti-CD30 antibodies, ×400). (e) The punch biopsy specimen from the trunk showed nodular perivascular cell infiltration (HE, at scan magnification). (f and g) The lymphoid cells with large nuclei scattered in the inflammatory cell infiltration (HE, ×100 and ×400, respectively).

eyelid as a borderline lesion that are likely associated with an HL history.

Consent

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

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Letter to the Editor

Giant basal cell carcinoma

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Sir,

We report a 65-year-old man who was evaluated for a large cutaneous tumor which was neglected by the patient. There was no history of arsenic exposure or to X-radiation. On physical examination, he had a large vegetating tumor with a wide central ulceration and pigmented border measuring 10x7 cm and located on his lower left abdomen (Fig. 1). A dermoscopy of the lesion revealed arborizing telangiectasia and ovoid nests (Fig. 2). A skin biopsy of the tumor was performed revealing large tumor nests with a smooth palisaded borderconsistent with nodularbasal cell carcinoma. Hence, giant basal cell carcinoma was confirmed and the patient underwent computed tomography scans which didn't reveal any metastases. He had a wide local resection of the tumor and is now free of the disease.

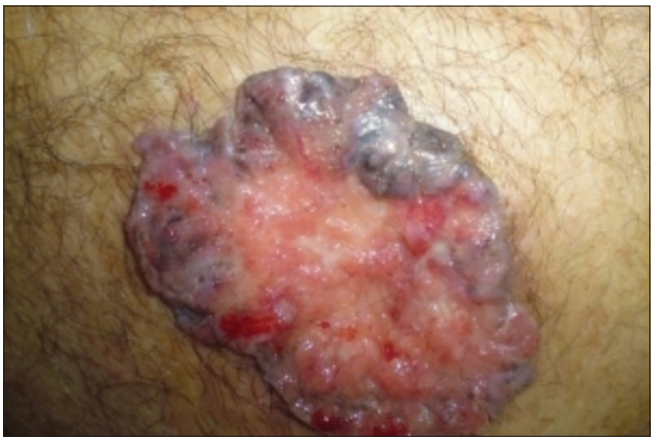

Figure 1: Large vegetating tumor with a wide central ulceration and pigmented border measuring 10x7 cm located on his lower left abdomen.

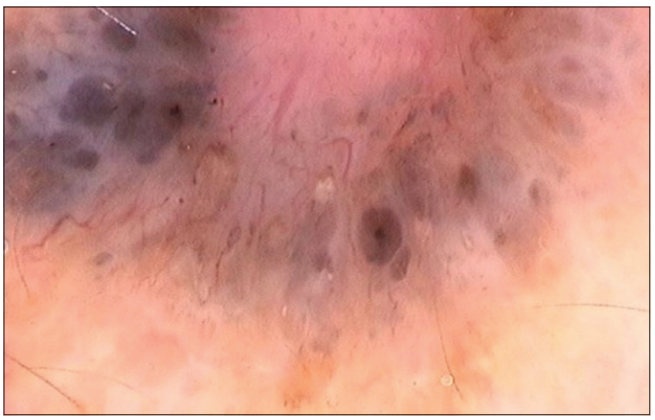

Figure 2: Arborizing telangiectasia and ovoid nests (Foto Finder, FotoFinder Systems GmbH, Bad Birnbach, Germany; original magnification: ×50).

Giant basal cell carcinoma (BCC) is a rare and agressive variant of basal cell carcinoma which is the most common skin cancer in humans [1-4]. It occurs mainly on the sun shielded trunk.Giant basal cell carcinoma is defined by the American joint committee on cancer as a tumor larger than 10 cm in diameter [1]. Only 1% of all basal cell carcinomas achieve this size. This case is being reported since basal cell carcinoma in our case was giant and located on the trunk. Only 10% of all basal cell carcinomas are located on the trunk and 80 to 85% occur on the head and neck. Neglect is responsible for one third of the case of giant basal cell carcf. Some authors have suggested that Giant basal cell carcinoma is cigarette smoking-related in more than 50% of the cases [5].Giant BCC could sometimes show an aggressive behavior [6-7]. Giant BCC is a rare variant that infiltrated dermis and frequently involves extradermal structures [6]. They may lead to metastasis and death. Metastatic location includes regional lymph nodes, bones, liver and lungs [1]. Metastasis appears 9 year after the diagnosis of Giant BCC and the survival period is less than 1 year [5]. Giant BCC should be treated aggressively and closely monitored. Treatment relies mainly on surgery with wide local excision usually followed by reconstruction with skin grafts or free flaps [6].

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Giant BCC is rarely reported in the literature. It is mainly located on the trunk. Treatment relies mainly on surgery.

Consent

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

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Letter to the Editor

Chancriform penile cutaneous leishmaniasis

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Sir,

Cutaneous leishmaniasis (CL) is endemic in Tunisia, particularly in the central and northern parts of the country. CL is more frequently seen on exposed body areas such as the face, eyelids, forehead, hands, wrists and, occasionally, the legs. The involvement of the penis is unusual.

A 42-year-old man from southern Tunisia presented to the dermatology department with a 2 month history of asymptomatic and persistent ulcer on his penis. He was taking no medications. The patient's general medical and specific sexual history was unremarkable. Physical examination showed a 2 x 1,5 cm ulcer with a slightly indurated base and raised infiltrative borders on the glans, adjacent to a second 0,5 cm ulceration (Fig. 1). The rest of the examination was unremarkable. Smears, taken from both lesions, showed Leishmania amastigotes. Polymerase-chain-reaction (PCR) assay identified *Leishmania Major*. The diagnosis of chancriform CL was confirmed. No regional lymph nodes were noted.

The patient was treated with meglumine antimoniate intramuscular (60 mg/kg/day) during three weeks; with complete cicatrization of the lesions and indelible scars.

Our observation was specific by the unusual localization of the CL and by the clinical form. The involvement of the penis is rare, although there are a few previous reports [1,2].

The peak of nocturnal activity of Phlebotomus and the habit of sleeping naked may explain the emergence of cases of CL in the genital area [3]. A more detailed anamnesis in our patient revealed an insect bite on the glans some weeks prior to the ulceration.

Cutaneous leishmaniasis should be considered for lesions that do not heal for a long time in individuals who live or travel to regions that have a high risk of CL, no matter whether lesions are located in covered or non-covered areas.

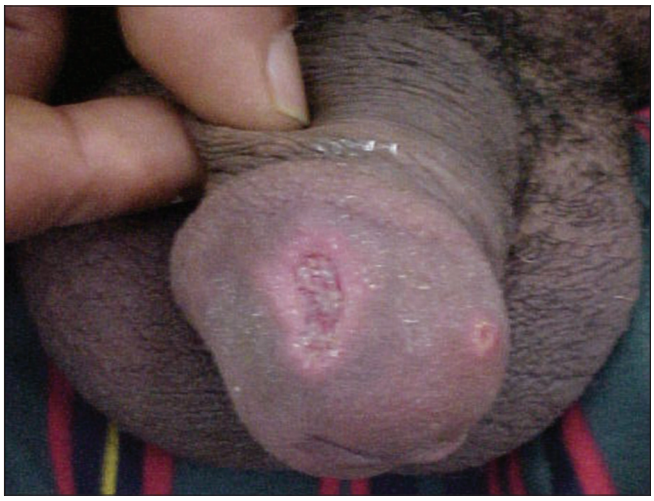

Figure1: Figure 1: Two ulcerations with a slightly indurated base and raised infiltrative borders on the glans.

Consent

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

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Letter to the Editor

A vesicating dermatitis from a blister beetle, in the neck of Septuagenarian Saudi male

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Sir,

A 72 years old Saudi male presented with an itchy and mildly painful skin lesion on the left side of the neck after being contacted before 2 days by a blister beetle while sleeping at night.

On examination, there is a well demarcated skin lesion, which has 'burnt' appearance, with streaks of hyperpigmentation at its lower border (Fig. 1).

The patient was able to identify the insect responsible, which is photographed in (Fig. 2).

He responded to topical steroid and an oral antihistamine.

The nature of this lesion and general instructions to avoid its recurrence were also given to the patient.

Blister beetle dermatitis is a sort of an irritant contact dermatitis. It is also known as dermatitis linearis, or paedrous dermatitis (PD). It is caused by chemical substances (Cantharidin, Pederin, Pseudopederin or Pederone), released from some beetles when crushed, pressed or come in contact with the skin [1-3]. The beetles do not bite or sting.

The lesion may take 1-2 days to develop but usually appear in the morning following a sleep.

As occurred in our case, the lesion usually affects the head and neck area.

There are approximately 250 known species of Paederus beetles. Most of these beetles contain vesicant fluid.

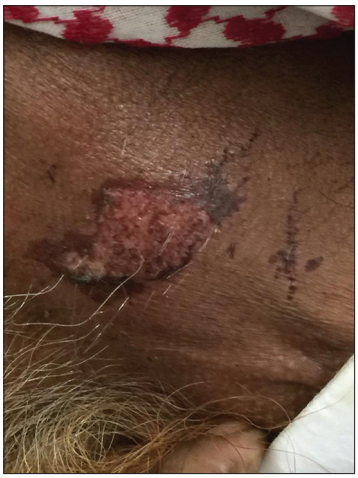

Figure 1: A 'burnt skin' appearance of the lesion with streaks of hyperpigmentation from dripping of irritant beetle fluid.

Figure 2: The type of beetle involved in the skin lesion.

Examples of species, belonging to genus Paederus, involved in PD include Paederus fuscipes, *P. irritans*, *P. sabacus*, and *P. himalayicus*.

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We could not have access to identify the exact species in this case, as there are no nearby entomological centers.

PD may cause extensive ulcerations but systemic symptoms do not usually occur.

Farmers and workers living outdoors are mostly at risk but people living indoor can be also affected.

The condition is not rare but seems to be under-reported. A series of 37 and 46 cases have been published [1,2].

PD takes a seasonal preference being maximum between May to July.

Tenderness of the affected area is thought to be an important clinical sign for PD.

With a proper history the diagnosis is not difficult but differential diagnoses may include burns by liquids, herpes simplex, herpes zoster, allergic or irritant contact dermatitis, bullous impetigo and phyto photo dermatitis.

Simple preventive measures can be undertaken based on the behavioral pattern of this nocturnal beetle which is known to breed in damp places, with high humidity.

Measures which were proved to be effective include;

- The housing of the workers in the farms is preferably not to be inside the agricultural land or near decaying garbage.
- Farmers are advised to use proper clothing or mosquito nets during the sleep.
- Regular spraying of the farms with insecticides such as a combination of Baygon (carbamate group) and Malathion (organophosphorus group).
- Avoiding resting in open areas close to paddy fields and neon or fluorescent lamps during night time, and proper use of insect repellants.
- Health education to the people about the condition and how to prevent it and the ways to deal with it.

Consent

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

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Letter to the Editor

A case of twenty nails dystrophy on atopic dermatitis

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Sir,

The twenty nails dystrophy is a very rare nail abnormality. It may be primitive genetic or secondary to multiple dermatological or systemic diseases. Atopic dermatitis is an etiology so rare that reported. We present a rare case of this 11-year-old boy, with no notable pathological history, from a non-consanguineous marriage who had consulted for dystrophy of the fingernails and feet that had started in infancy. The dermatological examination showed signs of atopic dermatitis with cutaneous xerosis, hyperpigmentations of the neck and folds, eczematids and a second lower palpebral fold of Dennie Morgan, without any signs of lichen, psoriasis, alopecia areata, ichthyosis, bullous dermatitis, or anything else (Figs. 1-3). The parasitological samples were sterile three times. Biological exploration in search of a systemic or systemic cause was negative. The nail biopsy was proposed but refused. The diagnosis of syndrome of dystrophy of twenty nails secondary to atopic dermatitis was retained. The boy was put under a mini bolus of corticosteroid treatment at a rate of 2 mg/kg three days a month with the start of whitening of the nails during the three-month control.

The twenty nails dystrophy is a dermatosis of the child par excellence. Most often it is idiopathic genetic, the main dermatoses and systemic diseases associated are: alopecia areata, psoriasis, lichen, atopic dermatitis, amyloidosis, chemotherapy, hemopathies, ichthyosis vulgaris, the deficit IgA, IPEX syndrome, pemphigus vulgaris, incontinentia pigmenti, primary biliary cirrhosis and sarcoidosis. The diagnosis is easy clinically and assisted by histology which remains non-mandatory. Apart from the etiological treatment, the symptomatic treatment is uncodified and uses oral or intralesional corticosteroids, calcipotriol, tazarotene, retinoids, immunosuppressants... the prognosis depends on the causal condition [1-5]. Atopic dermatitis is a possible

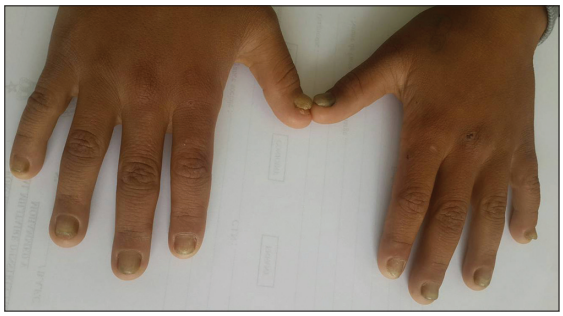

Figure 1: Twenty nail dystrophy on hands in a child with atopic dermatitis.

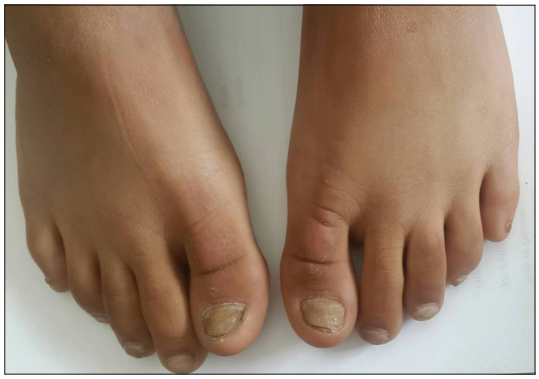

Figure 2: Twenty nail dystrophy on the feet in a child with atopic dermatitis.

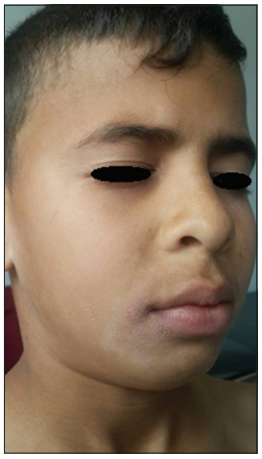

Figure 3: Atopic dermatitis of the face (eczematids, sign of Dennie Morgan, paleur and hyperpigmentations).

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cause of the twenty-nail dystrophy syndrome that must be kept in mind before this syndrome.

Consent

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

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Letter to the Editor

A rare case of Conradi-Hunermann-Happle syndrome

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Sir,

Conradi-Hunermann-Happle Syndrome is a rare type of chondrodysplasia punctata that presents with ichthyosis, asymmetry of limbs, short stature, and less frequently cataracts, ichthyosiform erythroderma, epiphyseal stippling and craniofacial defects [1,2]. It is X linked dominant disorder with mutation in the gene emopamil binding protein (EBP) located on short arm of X chromosome. EBP gene encodes 8-7 sterol isomerase which is involved in the cholesterol biosynthesis [3]. In this report, a case of a 9-years-old girl diagnosed with Conradi-Hunermann-Happle syndrome with a typical clinical picture is reported.

A 9 years old female presented to the Out Patient Department with 7 years history of generalized linear and swirling pattern of hyperpigmentation along with dry, thickened skin and coarse, lusterless hair. The patient was born at full term with normal delivery and unremarkable family history. Her mother gave a history of red scaly skin at birth that resolved by 1 year of age. The patient's father and mother had non-consanguineous marriage. Parents and the two siblings were healthy.

Dermatological examination revealed hyperkeratotic plaques with thick adherent scales and accentuation of skin markings over the extremities and buttock (Fig. 1). Bilaterally symmetrical brown linear streaks were present on upper and lower limbs. Atrophoderma was present on back and limbs. She displayed short stature, palmoplantar hyperkeratosis and dystrophy of nails. Thinning of bilateral eyebrows with flat nasal bridge was present (Fig. 2). Hair was coarse and lusterless with patchy alopecia. Bone and ocular findings were normal.

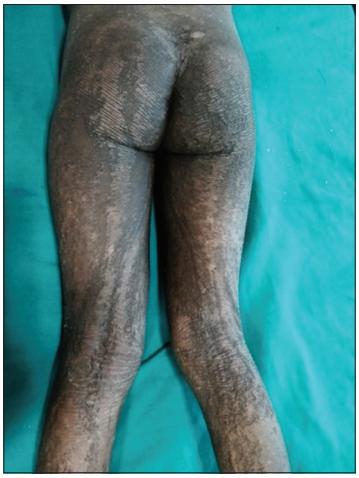

Figure 1: Hyperpigmented and hyperkeratotic plaques along the lines of Blaschko over the buttocks and lower extremities.

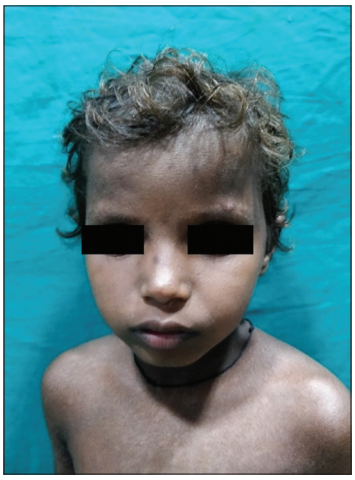

Figure 2: Sparse lusterless hair over the scalp and eyebrows with depressed nasal bridge.

The patient underwent biopsy which showed thick laminated orthokeratosis, and acanthosis of stratified

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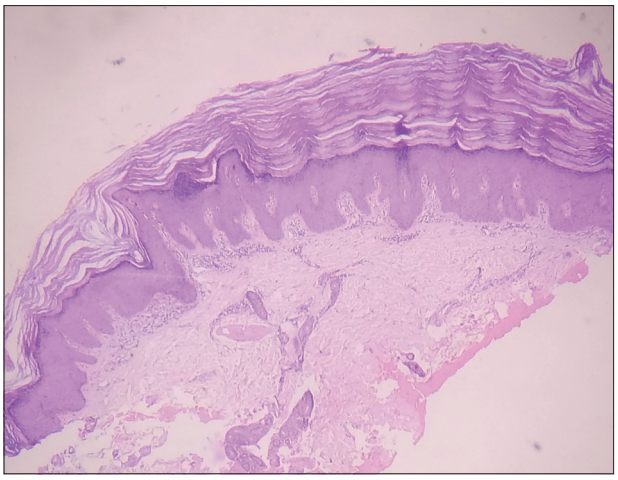

Figure 3: Histopathology from the hyperkeratotic plaque showed thick lamellated orthokeratosis, acanthosis and sparse lympho-histiocytic infiltrate in the dermis (H&E, 10X).

squamous epithelium with lymphohistiocytic infiltrate and few pilosebaceous units in the dermis (Fig. 3). X-ray of the spine and limbs were normal.

Conradi-Hunermann-Happle Syndrome presents with hyperkeratotic lesions on erythematous base with linear or blotchy ichthyosis in the lines of Blaschko. It resolves to leave linear or whorled pattern of atrophoderma and pigmentary abnormalities. Patients also present with asymmetry of limbs, short stature, coarse hair and less frequently with cataracts, epiphyseal stippling and craniofacial defects [1,4]. It is a rare genetic disorder that occurs almost exclusively in females, though small number of affected males are reported [5]. It shows increased disease expression in successive generations [6]. Therefore, genetic counselling, diagnostic DNA and prenatal diagnosis should be offered.

Diagnosis is based on dermatological, ophthalmic, radiographic and biochemical investigations. Clinical diagnosis can be confirmed by a sterol analysis of plasma or tissue in which levels of 8-dehydrocholestrol and 8(9)-cholestenol are elevated [3].

Our patient presented with some features typical of chondrodysplasia punctata such as short stature, erythroderma at birth, atrophoderma, ichthyotic and hyperkeratotic skin. Diagnosis was made based on clinical and histopathological features. Biochemical and molecular analysis could not be done due to financial constraints of the patient. This case is reported because of the rare nature of the disease and the classical presentation.

Consent

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

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Letter to the Editor

Dermoscopic features of spider angioma in a healthy child

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Sir,

We report a 7-year-old boy presented to our department for a newly appearing lesion of the cheek. He had no past medical history and there was not a history of trauma preceding the onset of the cutaneous lesion. Dermatologic examination revealed an erythematous small lesion with small vessels radiating from the center to the periphery located on the left cheek (Fig. 1). Dermoscopy revealed a vascular pattern with small telangiectasia and a stellate network (Fig. 2). The telangiectasias disappeared when pressure was applied with the dermoscope's glass (Fig. 3). The diagnosis of spider angioma was retained. An abdominal examination didn't reveal hepatomegaly or splenomegaly. Laboratory tests excluded the diagnosis of hepatitis, hepatic deficiency or cirrhosis. The patient was scheduled for a treatment with pulsed dye laser for his small vascular lesion.

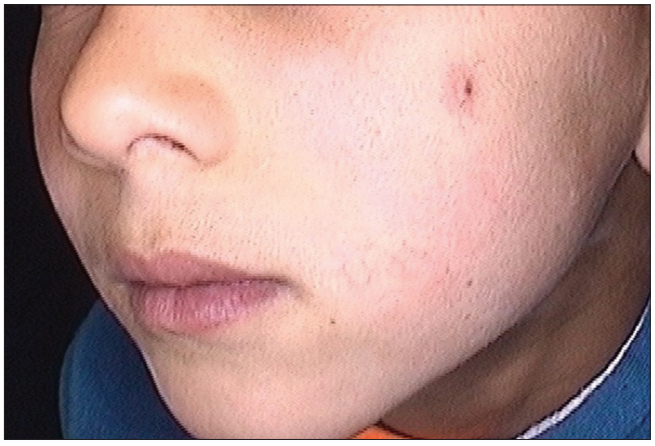

Figure 1: Small spider angioma on the left cheek in a child.

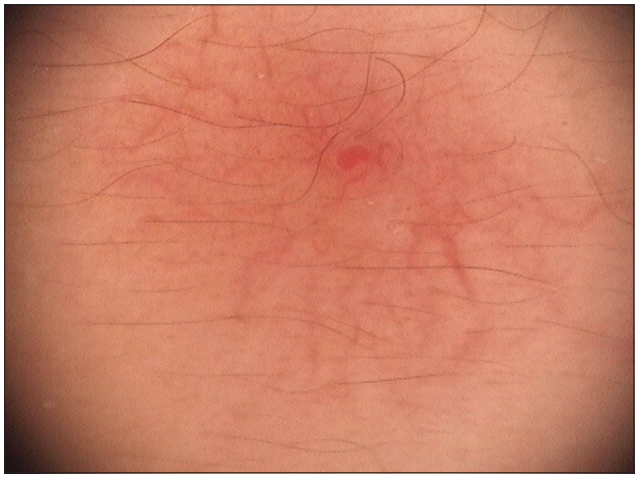

Figure 2: An arteriole in the central region that radiated out in numerous small vessels that resembled the legs of a spider.

Spider angiomas are lesions that appear as red spots, shiny, with numerous microvascular radiations which pale when pressure on a central spot is temporarily applied [1-2]. This condition was frequently associated with hepatic abnormalities [3]. Spider angiomas also called nevus araneus are lesions that appear as bright red small shiny lesions with numerous microvascular radiations which pale when pressure on a central spot is temporarily applied [1-3]. These lesions are made of small vessels radiating from center to peripheric zone. They are called spider angiomas because of their characteristic appearance resembling spider crotch. Nevus araneus has a small central artery that could pulsate. Several dilated vessels radiate from the central area. Compression of the central arteriole caused the entire lesion to blanch, and it quickly refilled once the compression was released. This pattern of blanching and refilling characterized spider angiomas [4]. The exact

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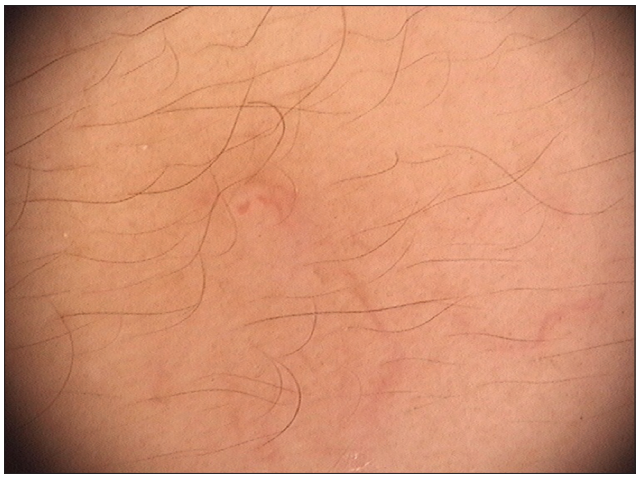

Figure 3: Compression of the central arteriole caused the entire lesion to blanch.

cause of spider angioma is not known. They may be present in physiological situations, such as in pregnancy, in children, in women under oral contraceptives, but are commonly associated with chronic liver diseases. Most frequent involvement sites of spider angiomas are the face, chest and arms. In our patient, the lesion was located on the face. Treatment of spider angiomas is not necessary. For cosmetic reasons, they could be treated using a fine electrolysis needle or with pulsed dye laser. However, sometimes spider angiomas may recur after treatment [3-5].

Spider angioma is a condition frequently associated with hepatic abnormalities. It can occur in children and has no pathologic signification. Dermoscopy could be helpful for the diagnosis of this facial vascular lesion.

Consent

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

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Our Dermatology Online

Historical Article

Dermatology Eponyms – sign –Lexicon (W)

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ABSTRACT

Eponyms are used almost daily in the clinical practice of dermatology. And yet, information about the person behind the eponyms is difficult to find. Indeed, who is? What is this person's nationality? Is this person alive or dead? How can one find the paper in which this person first described the disease? Eponyms are used to describe not only disease, but also clinical signs, surgical procedures, staining techniques, pharmacological formulations, and even pieces of equipment. In this article we present the symptoms starting with (W) and other. The symptoms and their synonyms, and those who have described this symptom or phenomenon.

Key words: Eponyms; Skin diseases; Sign; Phenomenon

WALCHEREN SIGN

Malarial fever in Holland [1].

WARTENBERG'S SIGN

In ulnar nerve paralysis due to leprosy, the little finger assumes the position of constant abduction secondary to paralysis of adductor digiti minimi and is considered the earliest sign of ulnar nerve affection [2].

WAX DOLI SIGN

Bagginess of the eyelids and bloated faces that give the patient an appearance of a wax doli. A sign of myxoedema. Also known as Marshalls sign [3-5].

GEOFFREY MARSHALL

British physician.

WEGENER'S SIGN

Invasive granulomatous lesion destroying the bridge of the nose and affecting the sinuses. Granulomatosis with polyangiitis is characterized by the main violation of the upper and lower respiratory tract and kidney AND Is considered a systemic vasculitis of medium-sized and small blood vessels [6,7].

FRIEDRICH RUDOLF GEORG WEGENER

German pathologist, 1907-1990 (Fig. 1). Friedrich Wegener worked in Breslau (Poland) when he first described the condition that carries his name.

After World War II Friedrich Wegener was suspected of being a war criminal. He was interned by the Allies but was later cleared of the charges and "denazified". As early as in 1932, eight months before Hitler came to power, he joined the S.A (Sturmabteilung) and became a member of the Nazi party on May 1, 1933. According

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to documents found by Alexander Woywodt in the Bundesarchiv, Wegener in 1938 became SA Sanitäts-Obersturmbannführer [8,9].

After the outbreak of the war, Wegener worked as a military pathologist in Lodz (Poland), where he also held a position in the Gesundheitsamt.

WEGNER'S SIGN

Growth arrest lines found in the upper extremities in an infant with congenital syphilis. Growth arrest lines show an enhanced zone of provisional calcification (radiopaque band) which is associated with osteoporosis immediately below the dense zone. The growth arrest line may be smooth or serrated [10]. A serrated appearance is known as Wegner's sign.

WEIL'S SIGN

Severe leptospirosis (Figs. 2a and 2b); also called Landouzy's sign and Fiedler's sign. Leptospirosis is an infectious disease caused by the pathogenic spirochete Leptospira interrogans. There is a large range of clinical manifestations in leptospirosis, and infected people can present with asymptomatic illness, self-limited systemic infection or severe and potentially fatal disease [11-14]. The severe form is characterized by jaundice, acute kidney injury (AKI) and hemorrhage, and is mainly caused by the serovars Icterohaemorrhagiae, Copenhageni and Lai. There are also severe forms of the disease that occur without jaundice or renal failure, such as hemorrhagic pneumonitis.

ADOIF WEIL

German physician, 1848-1916 (Fig. 3). Adolf Weil studied at Heidelberg, receiving his doctorate in 1871, and completed his education in Berlin under Ludwig Traube and Friedrich Theodor von Frerichs, and at Vienna under Ferdinand von Hebra, Moriz Kaposi and Leopold von Schrötter-Kristelli. From 1872 to 1876 he was Frerichs' assistant, and was habilitated for internal medicine, becoming ausserordentlicher professor in 1876. In 1886 he was called to Dorpat as ordentlicher professor of clinical medicine. Already in 1887 he had to resign from his teaching duties because of tuberculosis of the larynx, also abandoning his scientific activities. For some years he practiced in the winter in Ospedaletti and San Remo, in the summer in Badenweiler, and in 1893 settled Wiesbaden, where he died in 1916.

He was professor of medicine at Tartu, Estonia, and Berlin. He described four cases of the disease which he had observed in Heidelberg [15].

WEIR-MITCHELL'S SIGN

The term erythromelalgia (Fig. 4), specific to the myeloproliferative disorders, refers to the occlusion of

Figure 1: Friedrich Rudolf Georg Wegener.

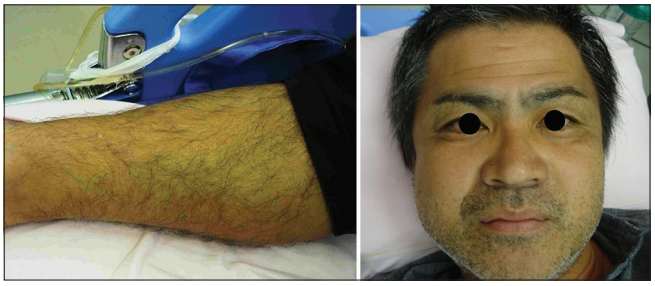

Figure 2: Weil's sign.

Figure 3: Adolf Weil.

the microcirculation by platelets and is characterized by redness, congestion, and painful burning sensations of the extremities. Symptoms are characteristically relieved by cold or elevation of the extremity [3,16-18].

SILAS WEIR MITCHELL

American neurologist and writer known for his discovery of causalgia, 1829-1914 (Fig. 5). He studied at the University of Pennsylvania in that city, and received the degree of M.D. at Jefferson Medical College in 1850. During the Civil War he had charge of nervous injuries and maladies at Turners Lane Hospital, Philadelphia, and at the close of the war became a specialist in neurology. In this field Mitchell's name became prominently associated with his introduction of the rest cure, subsequently taken up by the medical world, for nervous diseases, particularly neurasthenia and hysteria. His medical texts include Injuries of Nerves and Their Consequences (1872) and Fat and Blood (1877). Mitchell's disease (erythromelalgia) is named after him. He also coined the term phantom limb during his study of an amputee. Silas Weir Mitchell discovered and treated causalgia (today known as CRPS/RSD), a condition most often encountered by hand surgeons. He is considered the father of neurology as well as an early pioneer in scientific medicine. He was also a psychiatrist, toxicologist, author, poet, and a celebrity in America and Europe. His many skills and interests led his contemporaries to consider him a genius on par with Benjamin Franklin. His contributions to medicine and particularly hand surgery continue to resonate today [3].

WEREWOLF SIGN

Individuals are completely covered in hair except for their palms and soles. A sign of congenital hypertrichosis lanuginose [19,20].

WERLHOF'S SIGN

Purpura haemorrhagica [3,21,22]. Also known as Werlhoff's sign.

PAUL GOTTLIEB WERLHOF

German physician, 1699-1767 (Fig. 6). He studied medicine at the University of Helmstedt under Lorenz Heister and Brandanus Meibom, who was the son of Heinrich Meibom. After completing his studies, he practiced medicine in Peine for four years, and in 1725 moved to Hannover, where he became one of the more influential physicians in Europe. In 1740 was appointed

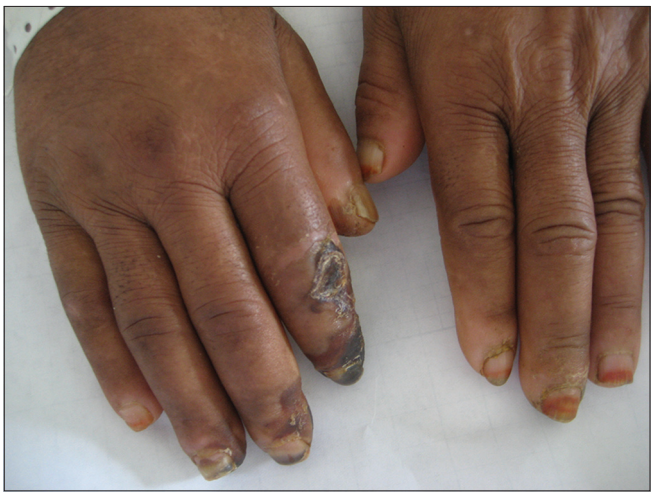

Figure 4: Weir-Mitchell's sign.

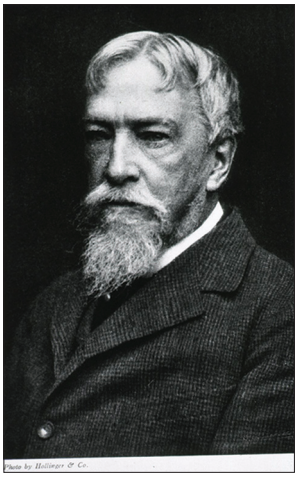

Figure 5: Silas Weir Mitchell.

Figure 6: Paul Gottlieb Werlhof.

Königlicher Leibarzt, physician to Hannover royalty. In 1735, Werlhof presented the first description of idiopathic thrombocytopenic purpura (ITP), a bleeding disorder. In addition to his reputation as a physician, Werlhof was highly regarded as a poet, and was a good friend of anatomist Albrecht von Haller, who was also an accomplished poet. Werlhof composed his poems and hymns in German, while his medical treatises were written in Latin. Among his written works were a 1732 treatise on fevers called Observationes de febribus, and a collection of poetry titled Gedichte [23].

WESSELSBRON SIGN

Muscle pain, fever, super sensitive skin with possible maculopapular rash. Caused by the mosquito-borne zoonotic Wesselsbron fever flavivirus [24].

WEST NILE SIGN

Fever and rash, with respiratory and flaccid paresis caused by brain swelling. Caused by the zoonotic West Nile fever flavivirus. Can be mosquito or food borne, and has also been associated with transplants of fluids and tissues [25].

WESTBERG'S SIGN

White spot disease, morphea alba (Fig. 7) [26,27].

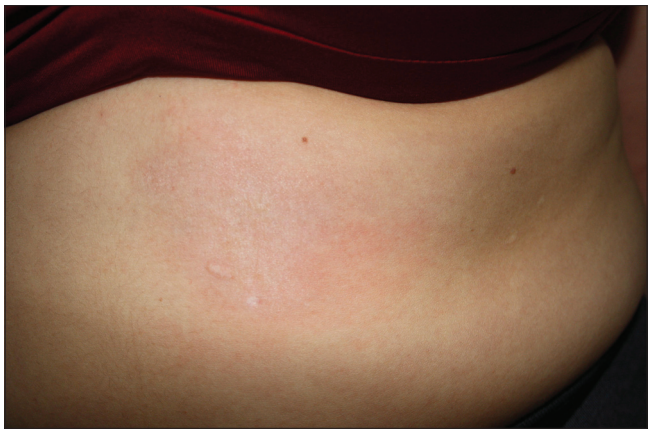

Figure 7: Westberg's sign.

FREDRICH WESTBERG

19th century German physician.

WET LEAVES SIGN

The odor of Mycobacterium tuberculosis [28-30].

MIKHAIL AFANASICVICH BULGAKOV

Russian physician, 1891-1940 (Fig. 8). Writer whose doctor stories are based on his experience as a rural physician in a small village called Nikolskoye in the province of Smolensk. Nikolskoye was his first assignment after studying medicine at Kiev University. After 18 months in Nikolskoye, he went on to specialize in venereology in Kiev. Shortly thereafter, he gave up a career in medicine for writing. All his life he was sceptical to the Soviet system and used his satire against the regime. He worked on his main work, The Master and Margarita, from 1928 until his death. The novel was not published in his lifetime [31].

Figure 8: Mikhail Afanasicvich Bulgakov.

WHALE'S FLIPPER SIGN

Obliteration of the concavity of the palm which makes the large hand look like a whale's flipper. A sign of middle palmar space infections [32].

WHITE HAIRY TONGUE SIGN

The tongue and oral mucous membranes are covered in a white fur or plaque. An indication of an oropharyngeal infection with *Candida albicans* [5,33].

WHITE LEPROSY SIGN

Leukoderma, a pathologic process with the result of a deficiency in the normal pigmentation of the skin (Fig. 9). Also know by many colloquial appellations

in the Indian subcontinent as *sufaid-korh*, *cham ba*, *phoolyree*, *buras*, *cabbore*, *kuf tam*, and leopard pattern [34,35].

WHITE'S SKIN SIGN

Keratosis follicularis (Fig. 10). Also known as Darier disease, Darier–White disease, Dyskeratosis follicularis [36-38].

JAMES CLARKE WHITE

American dermatologist, 1833-1916 (Fig. 11). At the age of 16 he entered Harvard and in 1853 began his medical education at Tremont Medical School which had a semi-official connection with Harvard. He served a term as house pupil at the Massachusetts General Hospital, and received his M.D. in 1855. A European postgraduate tour, during which he worked under Oppolzer, Sigmund, and Hebra, was completed in 1857.

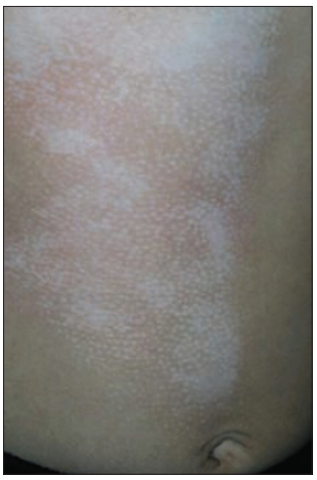

Figure 9: White Leprosy sign.

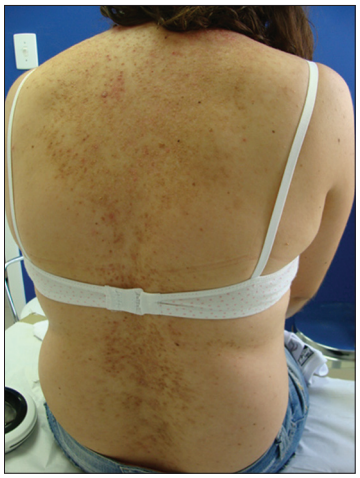

Figure 10: White's skin sign.

After an early interest in toxicology and chemistry, White turned to dermatology exclusively, and in 1863 became Professor of Dermatology at Harvard. He was the first President of the American Dermatological Association, and the first to describe keratosis follicularis, also known as "Darier-White Disease" [36].

WHITE-SPOT SIGN

Degeneration of the papillary and reticular layers of the skin marked by the formation of white bead-like spots; morphea guttata. Also know as Westberg's sign.

WICKHAM SIGN

Also know as Wickham's striae (Fig. 12). There are delicate white or grey lines that course the surface of a papule of lichen planus [39]. The lines may be seen only at the periphery of a papule, but usually they form a network across the entire papule. They are most pronounced in fully developed lesions that tend to be aggregated.

Figure 11: James Clarke White.

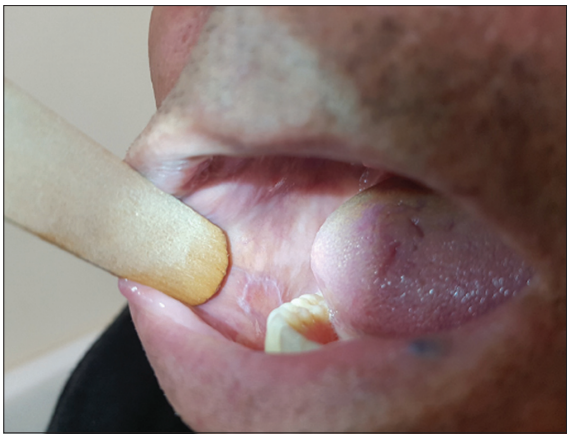

Figure 12: Wickham sign.

LOUIS FRÉDÉRIC WICKHAM

French physician and pathologist (1861-1913), (Fig. 13). In 1895, Louis-Fédéric Wickham described whitish streaks, now known as Wickham's striae, on the surface of lichen planus papules [40]. He received his education at Paris and obtained his doctorate in 1890. He then turned to the study of dermatology, worked several years at the Hôpital Saint-Louis, and in 1897 became Médecin at the Hôpital Saint Lazare. From 1905 he concerned himself with radium research, and occasioned the establishment of the Laboratoire Biologique du Radium. His work concerns the treatment of angiomas, celoids, carcinomas of the skin, and other dermatoses, and on the effect of radium on visceral carcinoses. In 1888 he was commissioned to report on the methods of teaching dermatology in England. He designed a multibladed knife for scarification treatment of lupus vulgaris.

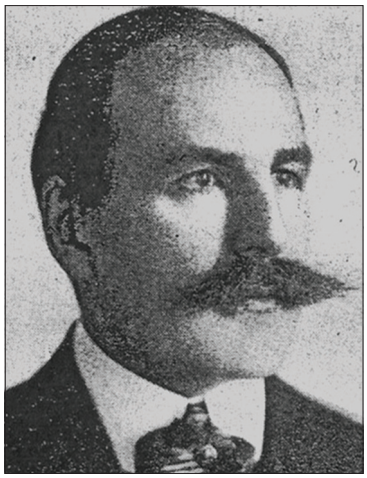

Figure 13: Louis Frédéric Wickham.

WIDY SIGN

Hairs that showed a deposit of melanin pigment at its distal end [41].

Figure 14: Robert Willan.

WILLAN'S SIGN

Psoriasis circinate [42,43]. Also called Willan's lepra. When in psoriasis the eruption involves only a limited extent of space, the epidermic scales may become loosened and fall off, leaving bright-red, slight elevated spots or we notice only a partial desquamation especially in the middle of single circular patches, giving rise to psoriasis orbicularis (lepra Willani or psoriasis laepreformis) [44].

Figure 15: Robert Willan grave.

ROBERT WILLAN

English physician, 1757-1812 (Figs. 14 and 15). A 1780 graduate in medicine from the University of Edinburgh, spent most of his professional life in London. He worked at the Carey Street Public Dispensary, which was also staffed mainly by such graduates from Edinburgh as Thomas Bateman, Richard Bright, and Thomas Addison. Willan's major dermatology works can be categorized into two groups: an introduction of the first classification of skin diseases, and the correct clinical descriptions of many diseases. Both were based predominantly on morphologic features rather than on the etiologic or pathophysiologic characteristics of a disease. Between 1798 and 1808, Willan published a four-part work, Cutaneous Diseases, in which he developed a classification of skin diseases according to the form of their pathologic products. Willan was also the first to recognize the importance of illustrations in the description of skin disorders and to create the

first atlas of skin diseases containing color pictures [45]. Willan divided all cutaneous disorders into nine orders: papulae, squamae, exanthemata, bullae, pustulae, vesiculae, tubercula, maculae, and dermal excrescences. For the first time in history, a physician with access to patients with abundant cutaneous problems scrutinized individual spots with the intention of recording every shade and detail. Willan was the first to give a comprehensive medical account of psoriasis, erythema nodosum, a skin symptom of sarcoidosis,12 herpes simplex and herpes zoster lesions of the skin,13 and Schönlein-Henoch purpura, ichthyosis hystrix,14 and ichthyosis.

Grounded on Willan's famous principals of skin disease, dermatology was recognized as its own specialty within the field of medicine in 1884 [46].

WILLAN'S CHEEK SIGN

Lupus vulgaris of the cheek (Figs. 16a and 16b). Lupus vulgaris is the oldest forms of cutaneous tuberculosis described in the medical literature and were known as the king's evil. The word 'Lupus', meaning wolf, was given to the lesion because of the ulcerating and devouring character of the lesion. Lupus vulgaris is a form of reinfection tuberculosis of the skin occurring in patients with moderate to high degree of immunity, originating from an underlying tuberculosis focus of the skin. However, it may also result through exogenous inoculation. Lupus vulgaris at the site of BCG vaccination has also been reported [47].

WILLARD'S SIGN

Lupus vulgaris (Figs. 17a and 17b). Lupus vulgaris is the most common type of cutaneous TB often presents as an asymptomatic, slow growing plaque on the face. Approximately 1%-2% of all cases of tuberculosis are cutaneous tuberculosis [48,49].

WILSON'S SIGN

Dermatitis exfoliative [50].

SIR WILLIAM JAMES ERASMUS WILSON

English dermatologist and philanthropist 1809-1884 (Fig. 18). First described lichen planus in 1869 and attributed its cause to stress. He practiced in London, and published a "System of Human Anatomy," (1842),

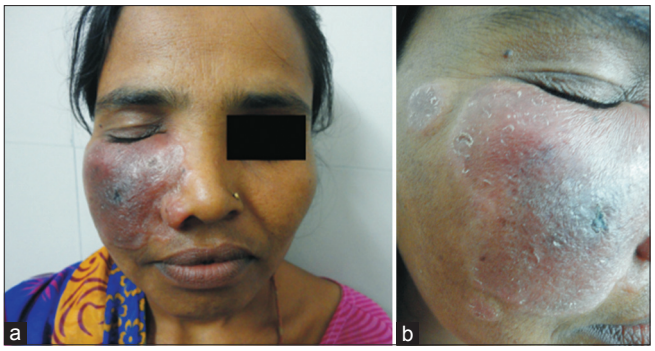

Figure 16: (a, b) Willan's cheek sign.

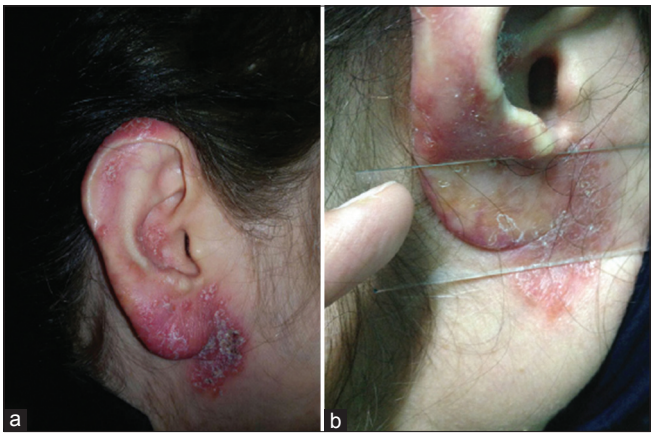

Figure 17: (a, b) Willard's sign.

Figure 18: Sir William James Erasmus Wilson.

which has passed through many editions, "Disease of the Skin" and other works relating to dermatology; "Cleopatra's Needle" and "The Egypt of the Past,". Known as Sir Erasmus, he was of the greatest dermatologists of his time. He is so well known as a dermatologist, occupying the first rank in England, that any contributions from his pen must command attention. He was also known for his philanthropy. Erasmus Wilson was knighted in 1881 [51].

WIMBERGER'S SIGN

Erosion of the upper end of the tibia in carly syphilis (Fig. 19).

Wimberger's sign is the presence of bilateral, symmetrical, and well-defined metaphyseal defects on the medial surface of upper tibia, can result in pseudoparalysis, and is considered pathognomonic of congenital syphilis [52,53].

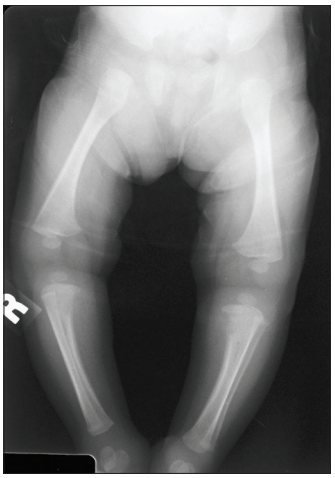

Figure 19: Wimberger's sign.

WINE SWEAT SIGN

Perspiration with the taste of wine [54].

CASPAR BARTHOLIN THE YOUNGER (SECUNDUS)

Danish anatomist and physician, born September 10, 1655, Copenhagen; died June 11, 1738 (Fig. 20). Caspar Bartholin began his medical studies in 1671, and already in 1674, aged 19, he was appointed professor of philosophy by the King, Christian IV. In 1678 he was conferred doctor of medicine by his father, Thomas Bartholin [31].

Figure 20: Caspar Bartholin the Younger (Secundus).

WINTERBOTTOM'S SIGN

Enlargement of posterior cervical lymph nodes in African trypanosomiasis [55,56]. It is seen in early stages of African trypanosomiasis caused by Trypanosoma brucei rhodensiense and Trypanosoma brucei gambiense known Sleeping sickness. Winterbottom's sign is enlargement of lymph nodes in the posterior cervical chain.

THOMAS MASTERMAN WINTERBOTTOM

English physician, philanthropist and abolitionist 1765-1859 (Fig. 21). He studied medicine at the University of Edinburgh and then the University of Glasgow. He was appointed physician to the colony of the Sierra Leone Company in 1792. Wilson went on to become one of the first European trained African medical staff in Africa.

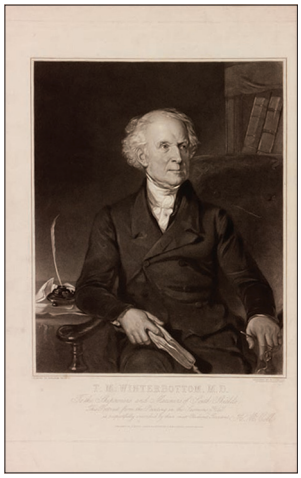

Figure 21: Thomas Masterman Winterbottom.

Winterbottom noted that slave traders used the sign of neck swelling as an indicator of sleepiness, and would avoid those slaves. He had no children, so his considerable estate was left to a number of charities which he had supported during his life. The bulk of this bequest was to found the South Shields Marine College, which he had established in 1837 [57].

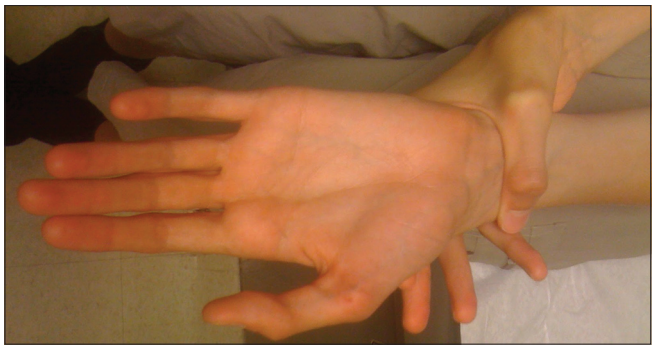

Figure 22: Wrist sign (Walker–Murdoch sign).

WOOL-SORTERS' SIGN

A form of anthrax attacking those who handle wool [58].

WRIST SIGN

Loss of pulse at the wrist, an indication of cholera [59].

WRIST SIGN (WALKER–MURDOCH SIGN)

The distal phalange of the first and fifth fingers of the hand overlaps when wrapped around the opposite wrist seen in patients having Marfan syndrome (Fig. 22) [60].

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