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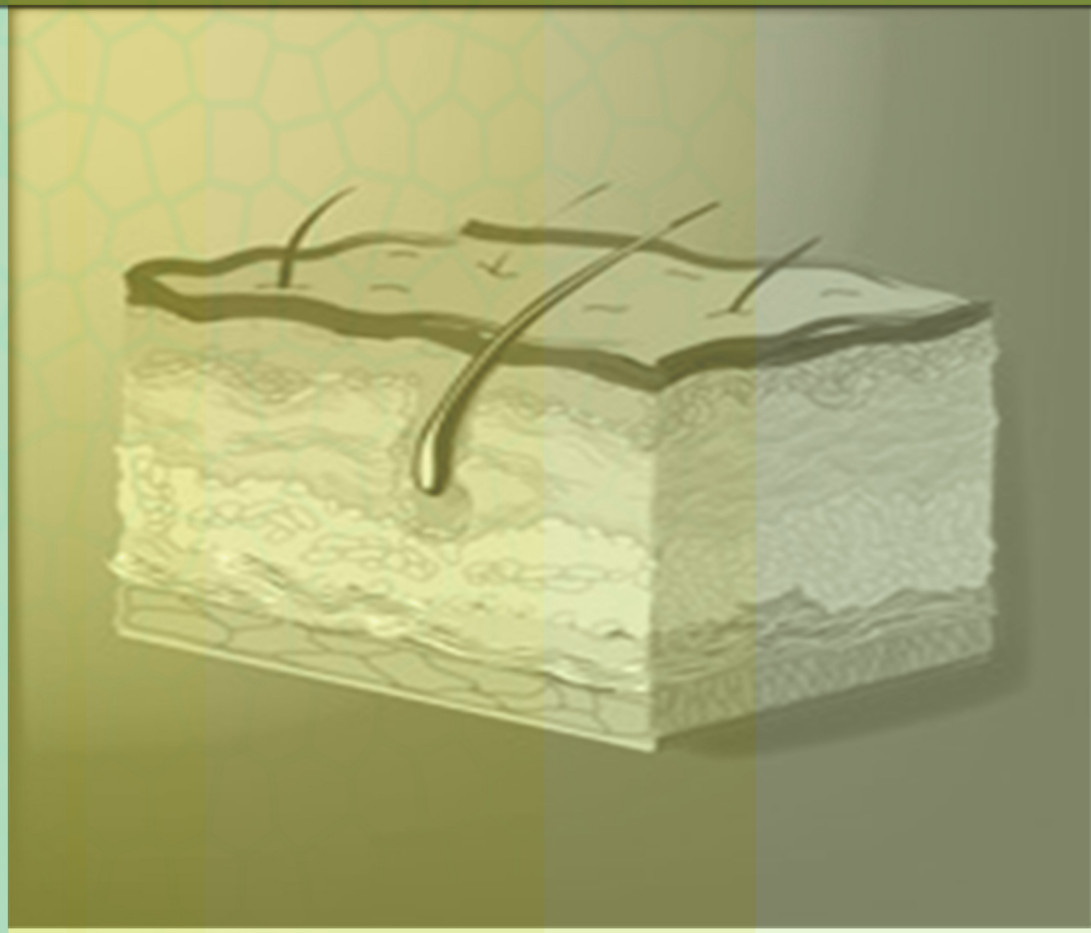

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Letter to the Editor

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Multiple Cysts Localized to the Vulva: A Case Report

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KEYWORDS: Genital cysts; Vulvarcysts; Vulvar benign tumors.

Epidermal, or inclusion cysts, are the commonest type of epithelial cysts of the skin. These are keratin-containing cysts lined with stratified squamous epithelium. Multiple vulvar cysts are rarely reported.[1,2]

A 61-year-old woman presented to the dermatology outpatient clinic for lesions on the vulva of about 25-years duration. On physical examination the patient exhibited multiple yellow cystic papules and nodules measuring less than 1 cm each on the labia majora (Figure 1). Histopathological examination revealed a keratinous cyst lined by stratified squamous lining consistent with epidermal cysts. The patient was referred to surgeon for excision.

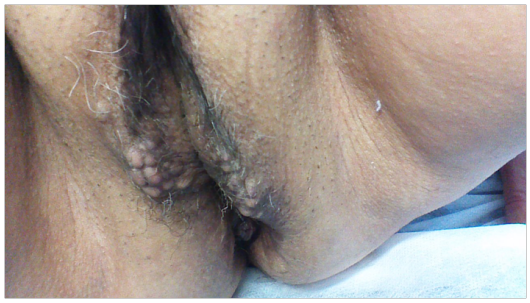

Figure 1: Multiple yellowish cystic papules or nodules on the labia majora measuring less than 1 cm.

DISCUSSION

Epidermal, or inclusion cysts, are the commonest type of epithelial cysts of the skin. These are keratin-containing cysts lined with stratified squamous epithelium. Multiple vulvar cysts are rarely reported.[1,2]

Epidermal cysts, mistakenly called sebaceous cysts, are formed as result of invagination of keratinized squamous epithelium and common sites of presentation are face, trunk, neck, extremities or scalp but genital cysts are less common. Clinical presentation of genital cysts can be single or multiple. When they are multiple demonstrate characteristic yellow-white papules, typically measure 2-5 mm.[3] Vulvar epidermoid cysts have been reported to be localized on the clitoral region (sometimes after female genital mutilation), labia majora and rarely on labium minus.[4,5] The differential diagnosis for papular/tumour genital lesions include cystic lesions (mucous cyst, cysts of the canal of Nuck, Bartholin´s cyst, Skene´s duct cyst), molluscum contagiosum, lichen nitidus, steatocystoma multiplex, milia, and calcinosis cutis. Other benign solid tumors, mesenchymal tumors, or malignant tumors of the vulva though rare, should be considered.[3,4] Steatocystoma multiplex is an autosomal dominant disorder characterized by multiple dermal cysts that are lined by epithelium containing hair follicles and sebaceous glands.[6] Cases of sporadic steatocystoma multiplex and multiple primary milia confined to the vulva have been recently described.[7,8] Idiopathic calcinosis, defined as the deposition of

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insoluble calcium salts under epidermis, has been rarely reported on the vulva.[9]

Multiple epidermal cysts are not symptomatic but sometimes excision is required for cosmetic reasons or recurrent infection and can have a detrimental effect on quality of life of patients. Laser therapy could be an effective alternative to the surgical treatment.[2,10]

CONCLUSIONS

It is important consider benign vulvar cysts in the differential diagnosis of vulvar complaints. Although most of pathological lesions that affect the vulva are benign, it is important to rule out a carcinoma or premalignant lesions. Vulvar cysts can adversely affect the quality of life of women.

CONSENT

The patient has provided written permission for publication of the case details.

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Mini Review

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Aquagenic Pruritus: First Manifestation of Polycythemia Vera

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ABSTRACT

Aquagenic Pruritus (AP) can be a first symptom of systemic disease; especially strong correlation with myeloproliferative disorders was described. In Polycythemia Vera (PV) patients its prevalence varies from 31% to 69%. In almost half of the cases AP precedes the diagnosis of PV and has significant influence on sufferers' quality of life. Due to the lack of the insight in pathogenesis of AP the treatment is still largely experiential. However, the new JAK1/2 inhibitors showed promising results in management of AP among PV patients.

KEYWORDS: Aquagenic pruritus; Polycythemia vera; JAK inhibitors.

Aquagenic pruritus (AP) is a skin condition characterized by the development of intense itching without observable skin lesions and evoked by contact with water at any temperature. Its prevalence varies from 31% to 69% in Polycythemia vera (PV) patients.[1,2,3] It has significant influence on sufferers' quality of life and can exert a psychological effect to the extent of abandoning bathing or developing phobia to bathing. Although, AP as an important clinical feature of PV was described for the first time more than 3 decades ago, its pathophysiology, frequency and management have not been fully established.[1,4]

PV-associated pruritus is characterized by patients as a generalized itching, tingling, burning or pricking skin sensation appearing mainly after contact with water, especially during warm bath or shower, but it could also be triggered by sudden change in temperature, sitting next to a fire-place or just sweating after exercises. AP tends to occur on extensor surfaces of the limbs, inter-scapular area, chest and abdominal wall with varying severity–from occasional, mild symptoms to severe, prolonged itching.[5]

PV is one of the most common myeloproliferative neoplasms characterized by indolent course and usually recognized incidentally by the discovery of high hemoglobin or hematocrit concentration. Whereas the onset of AP precedes diagnosis of PV in almost half of the cases,[5] a small number of patients presenting with AP provokes the physicians to consider a hematologic condition as an underlying cause. There is an easy opportunity for improvement in the process of establishing a final diagnosis among patients with AP, because a complete blood count conducted as a routine can be highly informative and may prevent the occurrence of fatal complications of PV, including venous or arterial thrombosis. Of note, AP may also occur simultaneously or just follow the diagnosis of PV.[6]

One of our patients–55-years old Caucasian male was admitted to our department with history of a non-resolving pruritus of 2-years duration, distributed on the lower limbs and trunk. Itch appeared mainly few minutes after bathing or showering in hot water and lasts for about one hour. Moreover, pruritus occurred sometimes spontaneously. The intensity of itching sensation after contact with water during the last three days before admission was assessed by patient as 5 points using Visual Analogue Scale (VAS) (range, 0 [no itching] to 10 [the worst itching imaginable]). The exacerbation of the symptoms occurred mainly in summer months. In medical history of the last months a fatigue and redness of cheeks were also reported. In the

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treatment of pruritus antihistamines (levocetirizine dihydrochloride), high potency corticosteroids (clobetasol propionate 0.05 % ointment) and emollients were used. Patient was investigated few times by general practitioner and dermatologist, nevertheless prescribed medications did not bring him any relief of itch. In conducted laboratory tests, high hemoglobin (25 g/dL), red blood cell ($6.3x10^6$ µL) and hematocrit (62%) levels were found; consequently the diagnosis of PV was suspected. Hematologic evaluation revealed JAK2V617F gene mutation and typical bone marrow changes confirmed the diagnosis of PV. Initially, the repeated phlebotomy and simultaneously given hydroxyurea of 500 mg daily dose were managed. The reduction of pruritus was achieved. After three months of hematologic treatment, the patient reassessed itching severity after contact with water as 3 points in VAS scale. The sustenance of improvement remains unknown.

Differential diagnosis of AP should rule out presence of other subtypes of AP, including idiopathic or AP of the elderly. One third of patients with idiopathic AP have family history of AP with tendency toward AP appears to be hereditary, whereas in AP of the elderly itching sensation affects mostly female patients above 60-years old with clinical features of dry skin.[7] It has also been linked to several conditions such as juvenile xanthogranuloma,[8] myelodysplastic syndrome,[9] T-cell non-Hodgkin's lymphoma,[10] hepatitis C infection,[11] drugs like bupropion[12] or hormonal replacement therapy[13] and idiopathic hypereosinophilic syndrome.[14]

The pathophysiology of PV-associated pruritus remains still poorly understood. Early studies have shown increased acetylcholinesterase activity in the nerve fibers surrounding eccrine sweat glands[15] and higher histamine levels.[16] However, others did not confirm these correlations.[3] Previous reports have revealed significantly elevated number of cutaneous mononuclear cells and eosinophils after water challenge, and manifestation of mast cell degranulation.[17] Moreover, Tefferiet al[18] proved that patients demonstrating homozygosity for the JAK2V617F mutation had a significantly higher incidence of pruritus (69% *vs.* 38%, p=0.04) in comparison with heterozygous patients, while Siegel et al[5] and Pieri et al[19] revealed the presence of the JAK2 mutation in the mast cells and basophils of the skin of patients with PV, respectively.

Management of PV-associated AP is unceasingly challenging. The lack of insight in the mechanism of cutaneous induction of AP is partly responsible for the inadequacy of current symptomatic treatment. Similarly to described case, patients often are taking various medications; generally with modest success. Improvement or even resolution of pruritus may be achieved after correction of hematological parameters of PV in some of the patients, while in others there may be no noticeable difference.[7] The most effective drug in control of AP used in PV sufferers is Interferon alfa (IFN-α). Previous data consisting of 16 prospective studies and three case reports involving 279 patients established that IFN-α reduced significantly itching sensation in 81% patients.[20] Other "popular" hematological options include busulphan, hydroxyurea and danazol, which were able to improve pruritus in 88%, 45% and 75%, respectively.[7] Of note, the populations of above mentioned groups were small–four patients in each. Phlebotomy is another frequently therapy used, but it shows mixed results with predominance of poor outcome in terms of PV-associated pruritus. Photochemotherapy (PUVA) was evaluated as good treatment modality and has been found superior to UVB-phototherapy in the terms of controlling of PV-associated pruritus.[21] The analysis of the efficacy of Selective Serotonin Reuptake Inhibitors (SSRI) in the group of 10 patients with AP confirmed that 80% of them had a near total or total resolution of pruritic sensations.[22] Antihistamines demonstrate mixed efficacy results and should not be so readily recommended.[7] Promising early results in the treatment of AP in population of PV sufferers were found with new JAK1/2 inhibitors. In the studies on ruxolitinib–JAK2/JAK1-inhibitor, the Response Rates (RR) for AP were up to 92%[23] and the selective JAK2 inhibitor (TG101348) trial showed a clinically significant reduction in pruritus with RR of 75% (50% with complete resolution).[24] Administration of an inhibitor of the mammalian target of rapamycin (mTOR) to patients with post-PV or essential thrombocytopenia myelofibrosis resulted in complete resolution of AP in all the five patients affected.[25]

In conclusion, pruritus associated with PV remains still underestimated clinical feature, despite AP is a common symptom resulting in significant morbidity. Pathogenesis of PV-related pruritus remains to be elucidated, although recent data about ongoing clinical trials with JAK2/JAK1 and mTOR inhibitors present favorable prospect with regard to the mechanisms and effective treatment strategies for aquagenic pruritus in polycythemia vera.

CONFLICTS OF INTEREST: None.

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Case Report

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Acquired Melanocytic Nevus: An Unusual Case Presentation

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ABSTRACT

Acquired Melanocytic Nevi (AMV) are common benign pigmented skin lesions. There are three types which include junctional nevus, compound nevus and Intradermal Melanocytic Nevus (IMN). IMN are characterized clinically by dome-shaped, soft, fleshy papules and are seen commonly in adults. Herein we reported a case with an unusual large IMN. A 35 years old otherwise healthy male presented with history of asymptomatic skin lesion on his scalp of several years duration that started to get bigger within the previous few months prior presenting to us. Skin examination revealed solitary firm skin colored nodule measuring 1.5×1.5 cm on his scalp. Exccesional skin biopsy revealed sharply-defined intradermal tumor composed of nests and fascicles of nevus cells. The tumor cells in superficial dermis are composed of epithelioid cells arranged singly and in clusters with heavy pigmentation in the superficial part. The deeper portion of the tumor is composed of bland looking spindle cells. No atypia or mitosis has been seen. Nerve corpuscles resembling Meissner corpuscles have also been seen in the deeper portions of the tumor. Histochemical analysis showed positivity for S100 and HMB-45. On the basis of the above clinicopathological findings, the diagnosis of intradermal melanocytic nevus was made and the patient was reassured.

KEYWORDS: Intradermal melanocytic nevus; Common melanocytic vevus; Acquired melanocytic nevus.

INTRODUCTION

Acquired Melanocytic Nevi (AMV) are benign proliferations of melanocytic cells (also known as nevus cells) that are characterized histopathologically by presence of nests of nevus cells in the dermoepidermal junction (junctional nevus), or in the papillary dermis (compound nevus) or deep in the dermis and subcutaneous tissues (Intradermal Melanocytic Nevus (IMN)).[1-3]

The AMV in general increase in size and number with increase of age, and peak in the 3rd decade of life. They then start to regress over time, so by 7th decade they usually disappear. IMN are characterized clinically by dome-shaped, soft, 'fleshy' papules and are frequently found on the head and neck. Their sizes range from a few millimeters to ≥1 cm in diameter. The dermoscopic features of an intradermal nevus consist of focal globules or globular-like structures. In addition, there may be pale to whitish structureless areas and fine linear or comma vessels.[3-5]

CASE REPORT

A 35-year old otherwise healthy male presented with history of asymptomatic slowly progressing skin lesion on his scalp of several years duration that suddenly got bigger within

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the previous months prior presenting to us. Past medical history and systematic review were unremarkable. Skin examination revealed solitary firm skin colored nodule measuring 1.5×1.5 cm on his scalp (Figure 1). Differential diagnosis of cylindroma, neurolimmoma, neuroma, neurofibroma, and schwanoma has been made. Exccesional skin biopsy revealed sharply-defined intradermal tumor composed of nests and fascicles of nevus cells. The tumor cells in superficial dermis are composed of epithelioid cells arranged singly and in clusters with heavy pigmentation in the superficial dermis. The deeper portion of the tumor is composed of bland looking spindle cells. No atypia or mitosis has been seen. Nerve corpuscles resembling Meissner corpuscles have also been seen in the deeper portions of the tumor (Figure 2). Histochemical analysis showed positivity for S100 and HMB-45. On the basis of the above clinicopathological findings, the diagnosis of intradermal melanocytic nevus was made and the patient was reassured.

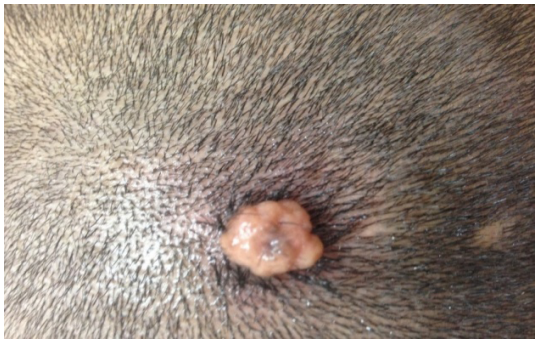

Figure 1: Skin colored firm exophytic nodule with smooth surface on the scalp measuring 2.5×2.5 cm.

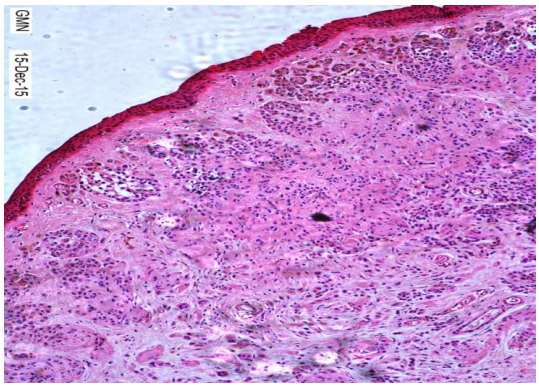

Figure 2: Skin biopsy showing intradermal tumor composed of nests of nevus cells. The tumor cells in superficial dermis are composed of epithelioid cells arranged singly and in clusters with heavy pigmentation in the superficial dermis. The deeper portion of the tumor is composed of bland looking spindle cells.

DISCUSSION

Nevocytes are cells that have epithelioid cell topography. Deep in the dermis, these cells show a diminished content of cytoplasm, giving a picture that resemble lymphocytes and are arranged in linear cords. More deeper, there will be a further transition to cells that assume a spindled configuration, similar to fibroblasts or Schwann cells. This process, which has been seen in the histopathology of our case, is known as normal maturation of the benign melanocytic nevi. After the third decade of life, nevus maturation continues leading to destruction and replacement of nevus cells by fibrous or fatty tissue.[2] Our case showed positivity of cells for S100 and HMB-45 which indicate melanocytic origin of these cells.

Neurotized Melanocytic Nevi (NMN), previously known as Masson nevus, is one of the main histological differential diagnoses in our case. In NMN, all cellular components of the tumor are spindle shaped rather than epithelioid-like or lymphocyte-like in the superficial parts of the tumor.[2] Our case is unusual in its large size 1.5×1.5 cm in diameter.

The gold standard technique for removal of IMN, which is excision followed by histological examination, may result in a scar formation that is an undesired cosmetic outcome, a feature that did not happen in our case.[6]

CONSENT STATEMENT

Consent has been taken from the patient for purpose of using patient's photographs for publication in print or on the internet.

CONFLICTS OF INTEREST

The authors have no conflicts of interest that are directly relevant to the content of this clinico-pathological case. No sources of funding were used to assist in preparation of this manuscript.

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Research

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Quality of Life is More Affected in Psoriasis than Vitiligo: A Study of 40 Moroccan Patients

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KEY MESSAGE: Quality of Life (QoL) impairment among Moroccan psoriasis patients was higher than vitiligo. Dermatology Life Quality Index (DLQI) high scores in psoriasis were significantly associated with female sex, uncovered areas involvement, disease extent areas and low socioeconomic level but not with PASI scores.

ABSTRACT

Background: Quality of life (QoL) assessment is becoming crucial in clinical trials, particularly with psoriasis.
Objectives: The aim of this study was to evaluate QoL by the Moroccan version of the DLQI (Dermatology Life Quality Index) among psoriatic patients compared to vitiligo.
Methods: This is a prospective study of patients aged 18 or older, who consulted at the dermatology clinic for psoriasis or vitiligo, between June 2012 and October 2012. The DLQI has been used in its Moroccan version validated and published. A high score indicates an impaired QoL.
Results: Forty-Psoriatic subjects (12 Male (M), 28 Female (F)) and 28 consultants for vitiligo (5 Male (M), 23 Female (F)) completed the DLQI. The mean duration of psoriasis was 13±13 years. The main clinical type of psoriasis was plaque-type psoriasis in 19 cases (47%) followed by guttate psoriasis in 11 cases (27%). The mean Body Surface Area (BSA) was 19%. Uncovered areas were affected in psoriasis as follows: face 9 cases (22.5%), hand 11 cases (27.5%) and both 3 cases (7%). The mean PASI was 6.3±7. The total mean score of DLQI was 11.15±6.2 for psoriasis and 7.9±4.6 in vitiligo (p=0.017). DLQI high scores in psoriasis were significantly associated with female sex, uncovered areas involvement, disease extent areas (BSA) and low socioeconomic level.
Conclusion: This study showed that psoriasis was associated with a great effect on QoL in outpatient subjects. QoL impairment in psoriasis was greater than in vitiligo.

KEYWORDS: Psoriasis; Quality of Life (QoL); DLQI; Vitiligo.

INTRODUCTION

Health-Related Quality of Life (HRQoL) assessment has become an important endpoint in clinical management decision-making of skin disease,[1] particularly in psoriasis.[2]

QoL impairment in psoriasis is not limited to physical discomfort. A number of studies showed that the disease has a particularly negative effect on self-perception of body image leading to low self-esteem, stigma, and a feeling of shame in the patient because of the psoriasis lesions. These are all factors affecting quality of life, as well as having a chronic disease with treatment side effects.[3,4] Therefore, it is important to consider psoriasis as a serious disease and resist the tendency to underestimate its impact on the overall patient well-being.[2]

Several quality of life scales were used in this dermatosis known for its negative impact on the patient's health related life quality. The Dermatology Life Quality Index (DLQI) is

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one of the useful questionnaires in assessing quality of life especially in psoriasis.[5] Developed by Finlay and Khan,[6] the DLQI has been used internationally for more than 15 years and translated into more than 80 languages.[7,8] It's reliable, validated in its Moroccan version and easy to administer.[9]

This study aims at estimating health related QoL in psoriatic population which is compared to the level of disability caused by vitiligo. It is also our purpose to detect patients at risk of experiencing a poor quality of life and to identify variables that may predict this impairment.

METHODS

A prospective study was conducted at the Dermatology and Venerology Department at Ibn Rushd University Hospital from June to October 2012. Subjects were selected among patients referred to the outpatient department for psoriasis or vitiligo. Patients requiring hospitalization were excluded. All participants (≥18 years) were interviewed and examined by the dermatologist, who carried out a Body Surface Area (BSA) and Psoriasis Area and Severity Index (PASI) assessment in psoriasis. A questionnaire collecting socio-demographic data such as: age, gender, skin color, marital status and education level, lesions topography and visible areas involvement (face, hands and feet) were completed by the same dermatologist.

The validated Moroccan version Dermatology Life Quality Index (DLQI) questionnaire was implemented to determine the impact of QoL on all study subjects.[9] It includes 10 questions (Q) grouped into 6 items : Q1-2 symptoms and feelings, Q3-4 daily activities, Q5-6 leisure, Q7 work/ school, Q8-9 personal relationships and Q10 treatment over the previous week. Each item includes four possible answers: much, a lot, a little, not at all or not relevant, scored from 0 to 3, giving a total DLQI ranging from 0 (no impairment of QoL) to 30 (maximum impairment of QoL). Higher scores represented a greater impact on quality of life. Results from 0-1 show no effect of the disease on the patient's QoL, scores 2-5 show a small effect, scores 6-10 mean a moderate effect, scores 11-20 correspond to a great effect and scores 21-30 show a very important effect of the disease on the patient's QoL.[10] As required by Finlay and Khan, a specific authorization for its use was obtained by the authors.

Documentation and analysis of the data were carried out using SPSS version 16. This analysis was used to calculate descriptive statistics of the study's variables including the DLQI score, the mean and standard deviation for quantitative variables and proportions for qualitative variables.

The bi-variant analysis based on Student's test consisted of the comparison of two medium variances analysis for comparison of multiple means and Pearson correlation coefficient for the two quantitative variables comparison. A value $p<0.05$ for two-tailed test was pre-fixed as a cutoff point.

RESULTS

During the study period, 68-patients were enrolled. Psoriasis patients group included 40 consultants (28 females and 12 males, mean age 44 years, ranged from 18 to 81 years). The other group was represented by 28 patients with vitiligo (23 females and 5 males, mean age 39 years, ranged from 16 to 62 years). Demographic characteristics of the patients are summarized in Table 1. The mean duration of psoriasis was 13±13 years. The main clinical type of psoriasis was plaque psoriasis in 19 cases (47%) followed by guttate psoriasis in 11 cases (27%). Psoriasis was associated with comorbidity in 16 cases. The mean BSA was 19±2% (1 to 80%). Visible areas were affected in psoriasis as follows: face 9 cases (22.5%), hand 11 cases (27.5%) and both (face and hands) 3 cases (7%). Pruritus was noted in 34 patients. The mean PASI was 6.3±7 (range 1-38.8). In vitiligo, the main clinical type was localized vitiligo 15 cases (53.6%), followed by focal 1 case (3.6%), acrofacial 6 cases (21.4%), segmental 4 cases (14.3%) and generalized vitiligo 2 cases (7.1%). Visible areas affected were: the face in 9 cases (32%), hands in 2 cases (7%) and simultaneously face and hands in 13 cases (46%). The mean BSA in vitiligo was 29% ±28 (1 to 95%).

	Psoriasis	Vitiligo
Nb (%) Nb	(%)	
Gender		
Male	12(30)	5(18)
Female	28(70)	23 (82)
Marital status		
Married	25(62.5)	11(39)
Widower	5(12.5)	0
Single	10(25)	13(47)
Divorced	0	4(14)
Socioeconomic level		
low	10(25)	8(29)
average	24(60)	17(60)
high	6(15)	3(11)
Educational level		
illiterate	10(25)	6(21)
primary	8(20)	10(36)
secondary	16(40)	8(29)
university	6(15)	4(14)

Table 1: Sociodemographic data.

Filling the DLQI required 1-3 minutes. The total mean DLQI score was 11.15±6.2 (range 1-25) in psoriasis, which is statistically significantly higher than 7.9±4.6 (range 0-18) in vitiligo (p=0.017). Based on the result interpretation of the DLQI scale, no impairment in QoL was found in 2 cases (5%) of psoriasis and in 2 cases (7%) of vitiligo, a small impairment of QoL was found in 4 cases (10%) and in 10 cases (35.7%), moderate impairment of QoL was found in 16 cases (40%) and in 10 cases (35.7%), large impairment of QoL was found in 15 cases

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(37.5%) and in 6 cases (21.4%) respectively, a very large impairment of QoL in 3 cases (7.5%) of psoriasis (Figure 1).

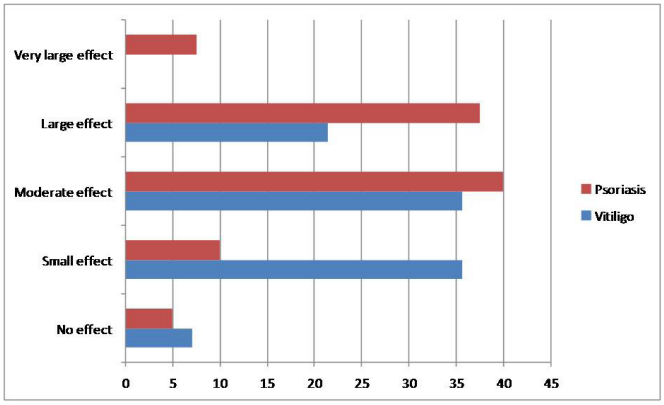

Figure 1: DLQI scores in 40 psoriasis and 28 vitiligo patients.

The highest DLQI scores in psoriasis were obtained with the symptoms and feelings as well as daily activities (Figure 2). On the other hand, vitiligo did not influence activities such as going to school or work compared with psoriasis. In psoriasis, the total DLQI score was significantly associated with female sex (p=0.013), visible areas involvement (p=0.041), disease extension (BSA) (p=0.006) and the low socioeconomic status (p=0.032).

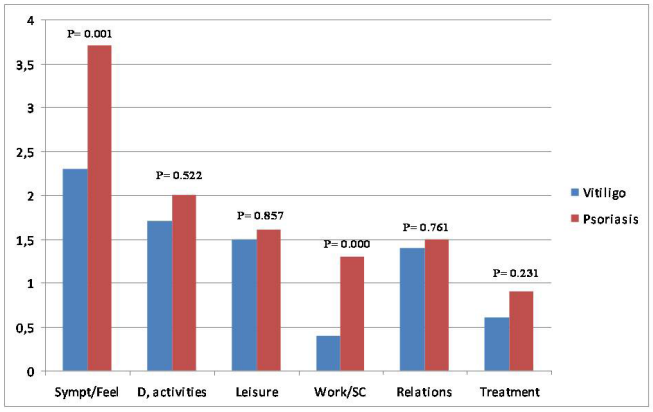

Figure 2: Items of DLQI in 40 psoriasis and 28 vitiligo patients. Symp/feel: symptoms and feelings; D activities: dialing activities.

DISCUSSION

This study demonstrates a great disease-related effect of psoriasis on QoL. The mean DLQI score was 11.1 which is significantly higher than in vitiligo (DLQI 7.9). The same results were given by different studies showing more apparent disability in psoriasis compared to vitiligo (Table 2).[11-15] These data can be explained by the fact that vitiligo has no impact on activities such as going to school or work, as pigment loss does not cause physical disability. On the contrary, besides suffering from physical discomfort, impaired emotional functioning and a negative body self-image, psoriatic patients suffer from limitations in daily activities, social contacts and work.[3] Indeed, the DLQI's questions focus on physical limitations and few items address the frequent psychological impact of skin diseases. This implies that the DLQI is better at assessing the impact of severe (inflammatory) diseases than that of diseases with a relatively mild impact or with few physical symptoms but high psychological impact such as vitiligo.[16] Besides, the DLQI lack of items assessing stress, financial cost, and addictive behavior.

Study	Psoriasis DLQI	Vitiligo DLQI	*p*
Karelson (2013)	13.1	4.7	*P*<0.0001
Ghajarzadeh (2012)	12.8	8.4	*P*<0.001
Radtke (2009)	8.6	7.0	-
Ongenae (2005)	6.26	4.95	*P*=0.01
Tejeda (2011)	15.5	13	-
Our study	**11.1**	**7.9**	**0.017**

Table 2: DLQI in studies comparing psoriasis and vitiligo.

The mean DLQI score in psoriasis in the present study (11.1) seems to be higher than the original one reported by Finlay et al,[6] as well as other studies.[11,17-21] This difference may be due to the characteristics of our patients (mean body surface area was 19% and 50% with visible areas involvement). Although having the same grade of impaired QoL, one study suggests that psoriatic patients belonging to different countries respond differently to DLQI because of language and culture diversity.[22] This point may interfere with the comparison between our results and those reported in the literature.

In other studies, the quality of life related to health in psoriatic patients was more impaired than in ours.[4,9,13,15,22] A possible inclusion of hospitalized psoriatic patients in these studies could increase the mean score of DLQI. Psoriasis has a highly significant impact on patients' QoL on the scale of symptoms, feelings and daily activities. This profile is in agreement with previous studies in which psoriasis was compared with vitiligo.[11,12,14] Predictive clinical factors for low QoL in psoriasis were: female gender, visible areas involvement, disease extension (BSA) and low socioeconomic level.

The impact of visible areas involvement and of disease extension on the QoL has been previously suggested in the literature.[22] However, we didn't find any correlation between the DLQI and the PASI as was previously described by various studies.[9,12,24-28] It has been suggested that unlike the PASI score, where each area of the body is weightest proportionally to the surface area covered, the DLQI is more heavily influenced by areas of the body that are visible. Therefore, the DLQI may provide information regarding outcomes beyond that described by the PASI score.[25] The DLQI and PASI measure different aspects of psoriasis and are useful tools to assess the severity of psoriasis and its treatment.[29,30] In addition, the small size of our sample did not reveal any other correlations.

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CONCLUSION

The impact of psoriasis on a patient's health-related quality of life is profound and has been well documented in the scientific literature. In this study, psoriasis had a great effect on QoL in outpatient psoriatic subjects using the DLQI in its Moroccan version. These patients were more disabled and showed more severe impairment in QoL compared to those with vitiligo. Psoriasis has a greater impact on QoL when the disease affects female gender, visible areas, and more extended lesions in patients with low socioeconomic level. We found, however, no correlation between QoL impairment and severity of psoriasis (PASI). A quality of life assessment in these patients is desirable to specify the most affected dimensions and set up an adequate treatment to improve quality of life and reduce the risk of psychological damage.

CONFLICTS OF INTERESTS: None.

CONSENT STATEMENT

The patients have provided written permission for publication of the case details.

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Case Report

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Natural Honey In The Management of Thermal Burn of The Foot In a Type 2 Diabetic Patient: A Case Report

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CASE REPORT

We report the case of a 58-year old male with type 2 diabetes who was admitted to Um-Gwailinah Health Center with a second degree burn involving his big hallux, 4th and 5th toe and the bases of 2nd, 3rd, 4th and 5th toe of the right foot. The patient had sustained the second degree burn after exposing his right foot to hot charcoal during winter time in the desert. The patient reported loss of sensation in his feet which he described as being numb. He was diagnosed with type 2 diabetes thirty years ago and was suffering from hypertension, hypercholesterolemia and obesity. The patient divulged that he is a chronic heavy smoker with 40 cigarettes per day (i.e., 40 packs/year).

He was managed by oral hypoglycemic agents including Metformin 500 mg three times daily, Gliclazide 120 mg once daily and 100 mg enteric coated aspirin. His biochemical profile revealed HbA1c of 8.8% denoting uncontrolled glycaemia, according to the International Diabetes Federation (2013). His lipid profile was normal except for a high LDL-C level, which showed a value of 3.5 mmol/L. His liver function tests were normal but had chronic kidney disease; however his Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) were normal. Vital signs examination revealed a temperature of 36.8 °C, a heart rate of 76 beats per minute, which was regular in rate and rhythm, a respiratory rate of 14 per minute and a blood pressure (BP) reading of 130/83 mmHg with a Body Mass Index (BMI) of 31 kg/m^2. An initial assessment was made by the consultant family physician who has a special interest in diabetic foot conditions.

NEUROLOGICAL ASSESSMENT

The patient presented with a painless foot condition, sensory neuropathy was suspected. This was further proven by neurological assessment of light pressure utilizing a Semmes-Wienstein 10 g monofilament, which was applied to the head of the big hallux and the bases of the first, third and fifth metatarsals which revealed loss of sensation. This was further consolidated by the use of the 128 Hz tuning fork applied to the big hallux showing loss of sensation. Finally, vibration sense was measured using the Biothesiometer which was applied to the big hallux and showed a recording of 65 volts, denoting diabetic peripheral neuropathy. The Biothesiometer was used as it provides a quick and reliable assessment of vibration threshold, which gives an objective measure of the degree and progress of diabetic peripheral neuropathy. Upon palpation, pedal pulses were manually palpable but weakly felt (dorsalis pedis and tibialis posterior), and this was further consolidated by Doppler examination using a hand-held Doppler (Huntleigh Super Dopplex 2; Huntleigh Health Care, UK). This revealed weak triphasic foot pulses (abnormal sounding) suggesting presence of peripheral vascular disease. The Ankle Brachial Index (ABI; systolic ankle to brachial BP ratio) was also measured using the hand-held Doppler and a BP cuff (Reister Big Ben Round, Germany). The ABI was measured by dividing the systolic ankle pressure at the malleolar level divided by the higher of the two brachial

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pressures, which gave us a reading of 0.8 (confirming the diagnosis of lower-extremity PAD). The wound was cleaned with normal saline and Natural Honey was applied directly on the burnt areas and covered with Adaptic (systagenix wound management) which is a Non-Adhering Silicone Dressing – flexible, open-mesh primary wound contact layer comprised of cellulose acetate coated with a soft tack silicone. The soft tack silicone assists dressing application, prevents adherence of the secondary dressing to the wound and is a traumatic to the wound and surrounding skin. The open mesh structure allows free passage of exudate in to an absorbent secondary dressing. The Adaptic layer was covered with secondary cotton gauze and the foot was offloaded using felt pad. Natural honey used in this case was a homogenous, thick, white honey mixed with royal jelly and produced by Russian bees (i.e., *Apis mellifera*) native to the PrimorskyKrai region of Russia. Prior to use with patients, the honey was sent to the microbiology laboratory of the Ministry of Health in Qatar. After rigorous testing it was found to be sterile and free from *Clostridium difficile* spores. Afterwards the honey was kept in sterile jars for subsequent use. Natural honey dressing was done on a daily basis. The initial ulcer (Figure 1) measured 7.5 cm × 3.1 cm, while those on the digits measured an average 0.3 cm × 1.1 cm. The periwound area of the ulcer was composed of dry callus which was debrided using a sharp surgical blade. One week later the main ulcer reduced in size by about 50% measuring 3.6 cm × 0.6 cm (see Figure 2). Three weeks later the ulcer reduced further to 2.5 cm × 0.3 cm (Figure 3) and at four weeks the ulcer had completely healed (Figure 4).

DISCUSSION

Health professionals in the medical field are embracing ionic silver impregnated products to treat a variety of acute and chronic wounds mainly due to a very extensive global marketing campaign especially in wound conferences worldwide. A recent study,[1,2] Cochrane reviews[2,3] have concluded that there is insufficient evidence to show that silver dressings improve healing rates. Furthermore, silver ions released by silver-containing dressings were found to be cytotoxic to keratinocytes and fibroblasts, and to impair epithelialization in animal wound models.[4,5] While silver-based products are used extensively in the market, randomized controlled trials supporting its efficacy are lacking. Natural honey is re-emerging as a viable and cost effective alternative to expensive wound dressings and technologies in the market mainly due to the collective properties it contains including an osmotic gradient which inhibits microbial growth, and an ability to release Tumor necrosis factor-α (TNF-α)[6,7]; an ability to release hydrogen peroxide at 1:1000 dilution thereby inhibiting microbial growth and stimulating angiogenesis without causing damage to health granulation tissue, increased lymphocytic and phagocytic activity[8]; IL-1 beta, and IL-6. Natural honey deodorizes wounds,[9-11] provides moisture and initiates tissue repair.

Natural honey antimicrobial efficacy has been long documented through research conducted on *Leptospermum scoparium* (manuka) honey,[12] which has shown antibacterial activity against *Escherichia coli* (*E. coli*), *Salmonella Typhi*, *Enterobacteraerogenes*, and *Staphylococcus aureus* (*S. aureus*).[12,13] Furthermore, honey is effective against Vancomycin resistant Enterococci (VRE), methicillin-resistant *S. aureus* (MRSA), haemolytic streptococci.[14,15] However, *Pseudomonas aeruginosa* (*P. aeruginosa*) and Enterococcus species are less susceptible to the antibacterial activity of honey.[16]

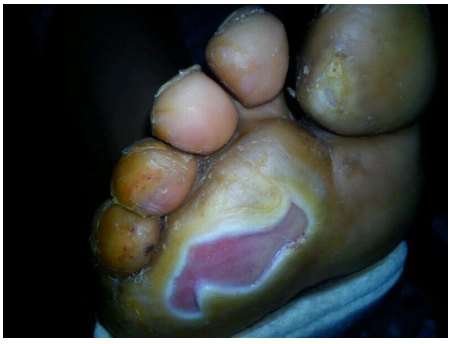

Figure 1: Initial ulcer size 7.5 cm × 3.1 cm.

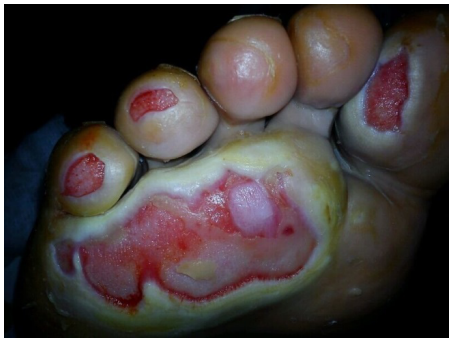

Figure 2: Reduction of ulcer size by 50% by 1 week.

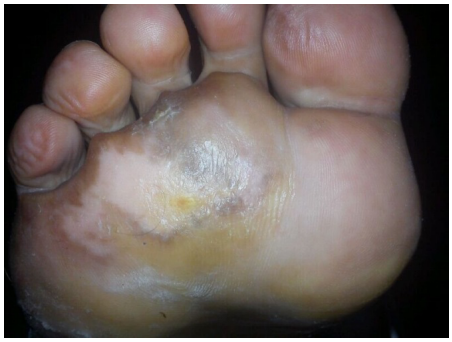

Figure 3: Reduction of size by 80%.

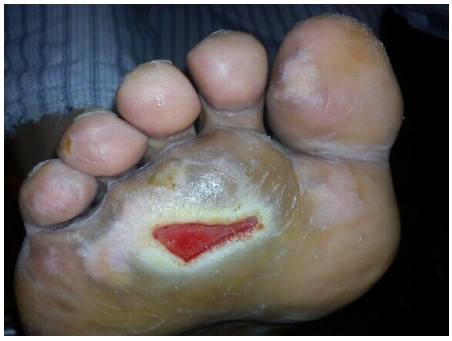

Figure 4: Complete healing four weeks later.

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Al-Waili et al[17] found that honey concentration ranging from 30% to 50% inhibits the growth of several yeasts including *Candida albicans*. This is further supported by Irish et al[18] who reported anti-fungal efficacy of various honeys against clinical isolates of *Candida glabrata*, *Candida albicans*, and *Candida dubliniensis*. Khosraviet al[19] on the other hand has demonstrated anti-fungal activity against *Candida parapsilosis*, *Candida tropicalis*, *Candida kefyr*, and *Candida dubliniensis*.

Natural honey has antiviral activities including those against Rubella virus,[20] had been used topically to treat recurrent herpes simplex lesions[21] and shown antiviral activities against varicella zoster in *in vitro* studies.[22]

A recent systematic review[23] assessing published Clinical Controlled Trials (CCTs) and Randomized Controlled Trials (RCTs) using two electronic databases; ISI Web of Science and Pub Med studied the efficacy of honey compared to other dressing materials among patients with diabetes. Four RCTs and two CCTs met the inclusion criteria for the effect of honey on chronic ulcers. The authors concluded that natural honey was far superior to advanced wound products in terms of wound healing stimulating capacity, for which two out of four RCTs report a statistically significant reduction in wound size, and two CCTs support the positive effect of honey on wound healing. A statistically significantly improvement was noted in favor of natural honey for the wound size.

This case clearly demonstrates lack of education on behalf of the patient which signifies failure of the health system to prevent such cases. Hence footwear and foot care education must be specific, targeting activities both inside and outside the house. The high-risk nature of this case (peripheral neuropathy) prompted us to schedule the patient for a regular monthly follow up. Although important health education per se is not enough to prevent or reduce recurrence of re-ulceration. A combination of optimal glycaemic control, psychological support, anti-platelet therapy, lipid lowering therapy, optimal blood pressure control, family support, protective therapeutic footwear, regular screening, nutritional support, smoking cessation and an integrated health system will help to minimize the risk of ulceration and re-ulceration, especially among high-risk patients.

The management of this case at primary care level demonstrated feasibility and cost-effectiveness of managing diabetic foot complications at primary care level provided that the attending physician is competent and trained to handle such cases. The cost of the entire course of treatment using honey is US $40. In comparison, using other products or dressings that contain silver or alginate cost between US $40 and US $588 per product unit. It has been estimated that in the United States the cost of treating a single DFU costs US $8000, US $17000 if it was infected and US $45000 if it required amputation.[24-25]

The success of honey application to many wounds especially burns is partly due to the fact that Natural Honey has a significant amount of antioxidants which mops up free radicals thereby reducing inflammation and as a result prevent partial-thickness burns from turning into full-thickness burns requiring plastic surgery.[26,27] Other properties which makes Natural Honey an optimal dressing is its cost effectiveness especially in developing countries where diabetes has reached epidemic proportions, its ability to provide moisture to the wound bed to help cells proliferate and migrate without causing maceration to the wound edges, and the ability to be removed without causing damage to the newly formed granulation tissues. Natural Honey also contains antioxidants, flavonoids, propolis, beeswax, nectar, all of these properties lead to minimization of scarring and stimulation of angiogenesis.[27] Furthermore, a recently published meta-analysis demonstrated that available evidence indicates markedly greater efficacy of Honey compared with alternative dressing treatment for superficial or partial thickness burns.[28-33]

CONCLUSION

This case report provides further evidence for the efficacy of Natural Honey in the treatment of second degree burns at primary care level.

CONSENT

The patient has provided written permission for the publication of the case details.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Case Report

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Phakomatosis Pigmentovascularis: Case Report of Type IIa

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ABSTRACT

Phakomatosis Pigmentovascularis (PPV) is a rare sporadic developmental disorder characterized by coexistence of a cutaneous vascular malformation and pigmentary nevi. There are different classifications of PPV. When systemic involvement is there, a designation 'b' is used, whereas if no systemic involvement, a designation 'a' is used. Herein, we reported a 12 years old girl presented with a symptomatic persistent progressive skin lesions since birth. Systemic review and past medical history were all unremarkable. Skin examination revealed mixture of diffuse non-scaly, bleachable erythematous patches, greenish patches, and hypopigmented patches over her trunk. Ophthalmologist and neurologist consulations did not reveal any abnormalities. Based on the above clinical findings, the patient was diagnosed to have port-wine stains, Mongolian spots, and nevus anemicus. Constellation of these clinical findings without presence of extracutaneous manifestations made the diagnosis of PPV type IIa.

KEYWORDS: Phakomatosis; Pigmentovascularis.

INTRODUCTION

Phakomatosis Pigmentovascularis (PPV) is a rare sporadic developmental disorder characterized by coexistence of a cutaneus vascular malformation and pigmentary nevi. Traditionally, there are 4 types of PPV. However, later on a fifth type has been described.[1] Happle proposed a new classification of PPV composed of 4 types.[1] When there is systemic involvement, a designation 'b' is used, whereas if no systemic involvement, a designation 'a' is used. Systemic involvement is present in 50% of patients with PPV.The most common form of PPV is type II.[1-4]

CASE REPORT

A 12-year-old girl presented with a symptomatic persistent skin lesions, since birth. The lesions were increasing in size in the first few years of life but later on became stable. She did not recieve any treatment for the skin lesions. Systemic review and past medical history were all unremarkable. There was no similar case in the family and her parents are not consanguinous. Skin examination revealed mixture of non-scaly, bleachable erythematous patches, greenish patches, and hypopigmented patches over her trunk only (Figure 1). Ophthalmologist and neurologist evaluations did not reveal any abnormalities. Based on the above clinical findings, a diagnosis of port-wine stains, mongolian spots and nevus anemicus were made. Constellations of these clinical findings without presence of extracutaneous manifestations made the final diagnosis of PPV type IIa. Patient was reassured and put under periodic follow up.

DISCUSSION

The Greek word '*phakos'* means birth mark or spot. Phakomatosis is a term mainly applied to genetically determined disease characterized by the presence of oculoneurocuta-

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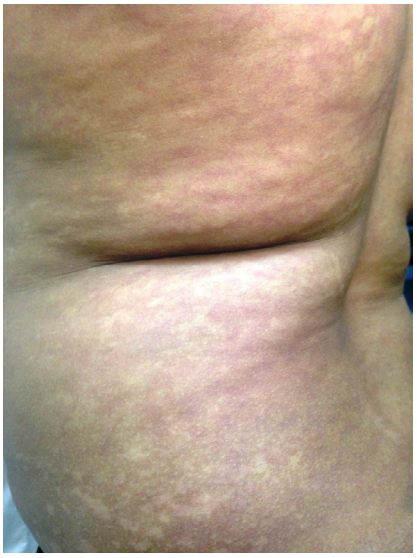

Figure 1: Mixture of diffuse non-scaly, bleachable erythematous patches, greenish patches, and hypopigmented patches over the trunk of the patient.

neous findings.[4] PPV was first described by Ota and Hasegawa in 1947. In 1985, PPV was classified into 4 types (traditional classification). Recently a fifth type has been described. Table 1 shows these 5 types of PPV. A subtype 'a' was used if there is only cutaneous involvement and subtype 'b' if there are cutaneous and extra cutaneous manifestations. Table 2 shows the systemic associations with PPV.[1]

Happle proposed a new simplified classificationof PPV.[3] Table 3 shows this new classification. In this classification, the distinction between cases that do or do not show extracutaneous anomalies is eliminated and the existence of type I. PPV is rejected on the argument that epidermal nevus never originates from pigmentary cells.[1]

The dermal melanocytosis includes Mongolian spots, nevus of Ota or nevus of Ito.[1] The pathogenesis is not completely understood. PPV may reflect twin spotting phenomenon (didymosis) as a result of hypothetic allelic mutation presented as paired melanocytic and achromic macules or nevus vascularis mixtus.[1-4]

The importance of periodic follow-up with ophthalmologist and neurologist should be emphasized, since systemic alterations can be evident with time, changing the classification and prognosis.[5,6]

The cutaneous lesions of PPV are persistent. Pulsed dye laser for nevus flammeus and Q-switched ND-Yag laser for intradermal melanocytosis have been used with good outcome.[7]

CONFLICTS OF INTEREST

The authors have no conflicts of interest that are directly relevant to the content of this case report. No sources of funding were used to assist in preparation of this manuscript.

CONSENT STATEMENT

Informed consent has been taken from the patient for purpose of using patient's photographs for publication in print or on the internet.

Type	Vascular nevus	Pigmented nevus
I	Nevus flammeus	Epidermal nevus
II	Nevus flammeus	Dermal melanocytosis ± nevus anemicus
III	Nevus flammeus	Nevus spilus ± nevus anemicus
IV	Nevus flammeus	Dermal melanocytosis + nevus spilus ± nevus anemicus
V	Cutis marmorata telangiectatica congenita	Dermal melanocytosis
Unclassified		Other associations not includedpreviously

Table 1: Classification of phakomatosis pigmentovascularis.

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Cutaneous lesions	Vascular abnormalities	Neurologic abnormalities	Ocular alterations	Miscellaneous
• Nevus anemicus • Cafe´-au-lait spots • Generalized vitiligo • Triangular congenital alopecia	• Sturge-Weber • Klippel-Trénaunay	• Seizures • Cortical atrophy • Arnold-Chiarri type I • Bilateral deafness • Idiopathic facial paralysis • Hydrocephalia • Diabetes insipidus • Plexiform neurofibroma • Delay in psychomotor development • Electroencephalogram alterations	• Melanosis oculi • Iris mammilations • Iris hamartomas • Glaucoma • Prominent vessels in sclera • Chronic edema in the cornea • Pigmentary alterations in retina • Pigmentary cataract	• Discrepancy in the length of extremities • Scoliosis • Spinal dysraphism • Hemihypertrophy • Syndactilia • Macrocephalia • Renal agenesia • Renal angiomatosis • Hepatosplenomegaly • Pyogenic granuloma • Cavernous hemangioma • Umbilical hernia • Hypoplasia of leg veins • IgA deficit • Hyper-IgE syndrome • Ezcemas • Premature eruption of the teeth

Table 2: Systemic associations with PPV.

Type	Correspondence with traditional classification	Vascular nevus	Pigmented nevus
Cesioflammea	II	Nevus flammeus	Blue spots
Spilorosea	III	Nevus flammeus	Nevus spilus
Cesiomarmorata	V	Cutis marmorata telangiectatica congenita	Blue spot
Unclassifiable	IV	Nevus flammeus	Blue spot + nevus spilus

Table 3: New classification of PPV proposed by Happle (type I does not exist).[3]

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Research

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Clinical and Ultrastructural Skin Alterations in the Ehlers-Danlos Syndrome, Hypermobility Type

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ABSTRACT

Ehlers-Danlos Syndrome (EDS) represents a cluster of specific genetic connective tissue disorders. It is clinically evoked when skin appears velvety and hyperextensible, in combination with joint laxity and connective tissue fragility. The hypermobile variant (EDSH) is among the most common presentations. It presents as an autosomal dominant pathology. The genetic mutation presently remains undisclosed in most cases. However, ultrastructural alterations are often distinguishable. Ehlers-Danlos Syndrome Hypermobile (EDSH) is mostly observed in women in whom additional signs to joint laxity are present. Hyperextensibility and/or velvety presentation of skin is one of the two major diagnostic signs in EDSH. Atrophic scars and delayed wound healing are commonly present. These features have to be considered in particular by plastic surgeons. The ultrastructural skin changes show various numbers of flower-like collagen fibres as well as other abnormalities in the connective tissue components.

KEYWORDS: Collagen; Elastic fibre; Ultrastructure; Tenascin; Decorin.

INTRODUCTION

Ehlers-Danlos Syndrome (EDS) encompasses an heterogenous cluster of connective tissue disorders, currently classified into six principal types.[1,2] They are characterized by variable combinations of increased skin distensibility and elasticity, joint laxity and connective tissue fragility. The Ehlers-Danlos Syndrome Hypermobile (EDSH) type is probably the most frequent entity. It is perceived as an autosomal dominant disease, although women are more frequently affected than men.[3-5] This condition remains difficult to diagnose due to variable clinical expressions, the largely undisclosed genetic origin, and the possible correction in joint laxity during aging and various degenerative disorders. Somewhat EDSH is clinically identified by joint laxity, and moderate skin hyperextensibility. It is frequently observed in association with delayed wound healing and atrophic scar development**.** Curative surgery and more often corrective esthetic surgery are concerned by these skin complications in EDSH women.

Collagen and elastic fibres are major extracellular matrix fibrous structures of the dermis. Other molecular components contribute to the overall mechanical properties of the skin. The main non-collagenous molecules of the dermis are the proteoglycans corresponding to a core protein and a covalent carbohydrate. Two major proteoglycans are found in the extracelllar matrix of the dermis. Versican is a large proteoglycan which belongs to the lectican family prone to bind hyaluronic acid. In contrast decorin is a small leucine-rich proteoglycan representing about 30-40% of the total proteoglycans of the skin. Decorin plays a key role in fibrogenesis and functional organization of the skin connective tissue. Tenascin X (TNX) is a minor component of connective tissue and appears to regulate the assembly of collagen.

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EDSH AND WOMEN

EDSH is disclosed more frequently in women than in men.[3-5] Indeed, a study showed that the sex ratio reached 43 women (84%) for 8 men (16%).[4] In our experience from 156 Caucasian patients, we shared a similar gender distribution with 131 (84%) women, aged 10-65 year-old, and 25 (16%) men, aged 9-67 year-old. Only 8/25 (36%) men, aged 9-26 year-old, compared to 102/131 (77,8%) women, aged 10-58 year-old, had a Beighton score above 5/9. The 15/25 men, aged 32-67 year-old, and 29/131 women, aged 42-65 year-old, had a lower Beighton score under 5/9, and they presented with complications of joint laxity including chronic joint pains, joint dislocations, sprains, (sub)luxations, tendinitis, hyperextensibility and/or velvety skin and positive familial history.

The gender difference in EDSH prevalence is in part related to distinct articular pain perception[6,7] and in musculature which are influenced by sex hormones.[4] The presence of estrogen receptors in ligaments,[8] as well in tenocytes[9] and muscles[10] suggests that estrogens play a role in the metabolism of these structures. Hormone replacement therapy in menopausal women improves skin and tendon elasticity and muscle performances.[11-13] These observations suggest a role of estrogens on the skeletal muscular system and explain that joint laxity is more notified in women.

DIAGNOSTIC CRITERIA

The EDSH diagnosis[1,2] is rooted on the presence of one or two major criteria including hyperextensible and/or velvety skin, and generalized joint laxity. This latter aspect is assessed according to the Beighton score reaching 5/9 or more defining joint hypermobility. The global score is calculated by adding each single joint mobility obtained by passive dorsiflexion of the little fingers beyond 90°, passive apposition of the thumbs to the flexor aspect of the forearm, hyperextension of the elbows and knees beyond 10°, and flexion of the trunk with the knees extended, and the hands flat on the floor. Skin hyperextensibility is assessed by pulling up the skin on the volar aspect of the forearm until resistance is felt. Skin must return to its original position without transient redundant folds. More precise information is obtained by objective measurements of the mechanical properties of skin.[14,15]

The minor diagnostic criteria for EDSH are recurring joint dislocations, chronic joint/ limb pain and positive family history. A minor criterion is just suggestive of the diagnosis.

In the Caucasian population the overall prevalence of EDS is assessed in the range from 1/5,000 to 1/1,000,000 births. Clearly, such estimation differs according to the EDS type. The rates are commonly higher for Blacks. Some EDS patients are identified by molecular biology particularly when the EDS types are characterized by a single defined and specific genetic mutation. Mutations in collagen I, III and V have been identified, but non-fibrous connective tissue components including TNX and decorin are also involved in various EDS types. However, some EDS clinical types are associated with a few distinct molecular alterations. Furthermore, a set of EDS types share similar gene mutations. Still other clinical variants have not been identified by molecular means. Therefore, such molecular methods are not fully satisfactory for routine identification of each EDS case.

In EDS classic type, most of the mutations are disclosed in *COL5 A1* and *COL5 A2* genes with some exceptions related to COL1 and TNX mutations. Hypermobile EDS, and its related condition called the family benign joint hypermobility syndrome, appear commonly as an underdiagnosed EDS hypermobile type. Sporadic mutations, including *COL5 A1* and *TNX-B* haploinsufficiency, were reported in a few cases of hypermobile EDS, but mutations remain undisclosed in most cases. The EDS vascular type is caused by type III procollagen gene (*COL3 A1*). Distinct other EDS types represent scarities.

CLINICAL MANIFESTATIONS

Beyond the classical diagnostic criteria, EDSH presents several other clinical manifestations including gyneco-obstetric, neurologic, cardio-pulmonary and gastrointestinal features.[16-21]

In EDSH, skin hyperextensibility is variable, and usually discrete compared with the EDS classic type.[15] Measurements of the skin mechanical properties provide an objective evaluation of the cutaneous hyperlaxity.[14,15,22] Other cutaneous signs are possibly observed, including delayed wound healing, and atrophic enlarged scars (Figure 1), but not molluscoid pseudotumors associated with papyraceous scars as seen in the EDS classic type, striae rubrae and other aspects of striae distensae. Such presentations of dermal atrophy possibly induce subcutaneous fat herniations, and easy bruising. Among our 131 EDSH women, 88(67.2%) exhibited scars, corresponding to 65 (49.6%) enlarged atrophic scars, 21(16.0%) had normal scars and 2(1.5%) showed hypertrophic ones. Nevertheless, delayed wound healing status was disclosed in only 19(14.5%) women. Delayed wound healing and atrophic enlarged scars are clues for EDSH, particularly in esthetic surgery. Indeed, in EDSH patients, less robust tissues, with increased blood vessel fragility and delayed wound healing commonly lead to complications set in some surgical interventions.[23,24]

DERMAL ULTRASTRUCTURAL ABNORMALITIES

The EDSH diagnosis appears frequently missed following the casual clinical presentation. In fact, joint laxity commonly decreases with age and/or following some degenerative processes. In addition, and each single joint is not considered in the Beighton score. Tenascin-X deficiency is present in some EDSH,[24,25] but the genetic mutations remain undisclosed in the majority of the EDSH cases.

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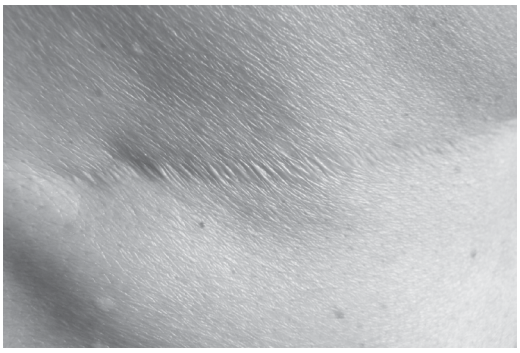

Figure 1: Atrophic scar in EDSH.

Skin ultrastructural abnormalities still represent an important aid for the EDSH diagnosis.[19,21,26-32] Each ultrastructural dermal changes, although individually unspecific appeared relevant and contributed to the diagnosis. Ultrastructural examinations revealed collagen and elastic fiber changes that were more obvious in the reticular dermis. The collagen scaffolding was altered showing bundles with uneven fibril sizes. Some fibril outlines were discretely serrated, and others showed flower-like transversal sections. Some fibrils appeared whirled and the interfibrillar spaces were unevenly enlarged (Figure 2). Elastic fibers exhibited irregular contours. The combination of such aspects was absent in skin samples from normal individuals. In short, ultrastructural changes were not only focused on flower-like collagen fibrils, but rather on the erratic orientation of the collagen fibrils, and their irregular interfibrillar spacing,[29,31] as well as on abnormal elastic fibers, granulo-filamentous deposits and large stellate hyaluronic acid-like globules.[30-31] Some of these non-fibrillar deposits combined with thinned collagen fibrils were possibly related to alterations of tenascin-X.[24,25]

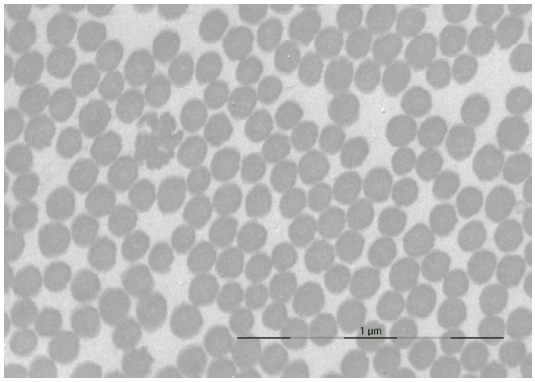

Figure 2: Flower-like collagen fibres and uneven interfibre spacing.

SPONTANEOUS CERVICAL ARTERY DISSECTION

The dermal ultrastructure of EDSH shows some similarities with the aspect present in some cases of the condition called Spontaneous Cervical Artery Dissection (SCAD).[30-34] The clinical criteria are, however, distinct. These two conditions have been reported in the same family.

CONCLUSION

The EDSH is a multisystemic disorder with multiple implications in the quality of life (QoL). It is mostly diagnosed in women. Some minor cutaneous signs, such as hyperextensibility, velvety skin, striae distentae and atrophic scars should evoke the EDSH diagnosis. A skin punch biopsy with ultrastructural examination is currently helpful to confirm the diagnosis and for adequate management. Currative and plastic surgeons should be aware of this pathology for limiting postsurgical complications and unaesthetic scars. Peculiar surgical approaches are recommended for EDSH patients.[35,36]

The fibrous collagen structure and its environment are uncovered by electron microscopy. In spite of the relatively unspecific ultrastructural criteria of EDS, the global architecture and the ultrastructure of the dermis are of diagnostic relevance, and they occasionally suggest a specific EDS type.[37] The defects in collagen fibril formation are likely multiple suggesting variable penetrance. Abundant granulofilamentous deposits are found in subjects with mutations in the gene coding for tenascin-X.

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CONFLICTS OF INTEREST: None.

CONSENT STATEMENT

All participants agreed to publish the manuscript, entitled "*Clinical and ultrastructural skin alterations in the Ehlers-Danlos syndrome, hypermobility type*" in Dermatology - Open Journal, and provided the written informed consent.

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DERMATOLOGY

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Case Report

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Photodynamic Therapy for the Treatment of Skin Cancer in Patients with Idiopathic Thrombocytopenia: A Case Report

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ABSTRACT

Idiopathic Thrombocytopenia (IT) is an autoimmune disease in which the patients present a reduction of blood platelets, increasing the risk of bleeding and its complications. Especially, elderly patients those with neoplasia associated to idiopathic thrombocytopenia are more likely to severe risks of bleeding. Here were report a case of an eighty-year-old man with diagnosis of idiopathic thrombocytopenia and confirmed biopsy of nodular basal cell carcinoma (nBCC) located on the nose. The use of the standard treatment surgery was not carried in this case due to risks generated by autoimmune disease. Photodynamic Therapy (PDT) was indicated as an adjuvant therapy associated to shaving and electrocoagulation providing elimination of recent cancer cells. This PDT is an alternative for the treatment of modular basal cell carcinoma no greater than 2 cm of diameter and small depth. The patient was treated with shaving, electrocoagulation and topical PDT using 20% methyl aminolevulinate (MAL) and fluency of 150 J/cm^2 with 630 nm light. This adjuvant treatment of nodular BCC is minimally invasive and can be indicated to patients with surgical risks, and that is the importance for this report. The success of this case is an important precedent for thousands of patients' with similar conditions.

KEYWORDS: Idiopathic thrombocytopenia (IT); Nodular basal cell carcinoma (nBCC); Photodynamic therapy (PDT); Adjuvant therapy; Surgical risks.

BACKGROUND

Non-Melanoma Skin Cancers (NMSC) are the most prevalent cancer worldwide and the Basal Cell Carcinoma (BCC) is the most common and with high frequency.[1,2] The NMSC are located in the many anatomic sites with high frequency in head and neck (80% of cases). It is estimated that 50% of all BCCs can recur within 10 years.[3] The surgery is the gold standard for the treatment of BCC.[4] The type of surgery and the functional capacity of patients identify the risk of this treatment.[5,6]

Idiopathic Thrombocytopenia (IT) is an autoimmune disease and characterized by low platelets levels in blood. Hemostatic changes during and after surgical procedure may cause serious risk to the patient. Thrombocytopenia is one of the main hemostatic disturbances observed in postoperatively procedure in the case of IT. The electrocoagulation to a patient with IT is an option to stop the bleeding in case if there is necessity of tissue removal. The mortality related to IT in adult patients can be up to 7.5% and the morbidity is directly related to serious bleeding complications. Bleeding may occur in aged patients and in those cases with neoplasias complications much more frequently.[7]

Topical treatments of NMSC including photodynamic therapy (PDT) have been approved due to clinical efficacy[8] and minimized risks and cost. In this technique, a light source with an appropriate wavelength activates a photo sensitizer (such as protoporphyrin IX, chlorins and curcumin) and produces reactive oxygen species (ROS), which are cytotoxic to tumor

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cells and microorganisms. In general, the geometrical factors as size and depth are important factors in PDT outcome results. Normally, shallow and small lesions are ideal for topical PDT. The PDT presents no risks to the patients and may be indicated alone or in association with other techniques.[9]

A common procedure in PDT is the shaving, which removes superficial cancer cells as well as death skin promoting the augment of the photo sensitizer absorption in deeper layers of the skin. The association of a deep penetration and adequate distribution of the light kills deeper tumor cells and increases the chances of cure, reducing tumor recurrence. Although shaving is a common procedure, it may cause bleeding in patients with IT. As a procedure, shave followed by electrocoagulation is an acceptable combination specially in the case of bleeding risk. In this case, we demonstrated the effectiveness of PDT as a co-adjuvant treatment of nodular BCC in patients with idiopathic thrombocytopenia.

CASE STUDY

An eighty-year-old man with four years of nodular BCC diagnosis (18 mm width and 22 mm length) in the ala of nose, refused to undergo the surgery due to his IT condition.

The shaving was realized in the lesion followed by the electrocoagulation. After two weeks, the lesion was curetted previously by PDT. The 20% methyl aminolevulinate (MAL) cream (PDT Pharma, São Paulo, Brazil) was applied and after three hours of occlusion the illumination was performed for 20 minutes using the device LINCE® (MM Optics, São Carlos-SP, Brazil) operating at 630 nm with a superficial intensity of 125 mW/cm^2. After seven days, the second PDT session was performed using the same protocol, and with only a gentle curettage, without bleeding, just before the MAL cream application.

In Figure 1 is shown the lesion before the treatment (Figure 1A); the lesion two weeks after shaving followed by electrocoagulation (Figure 1B); the lesion seven days after the first PDT session (Figure 1C); the lesion 30 days after the second PDT session (Figure 1D).

The clinical and histopathological evaluation was carried out thirty days after the second PDT procedure. The aesthetical and clinical results were satisfactory. A papule measuring 3×2 mm was observed 30 days after second PDT session (Figure 1D) and histopathology indicated fibrosis with the BCC cure.

DISCUSSION AND CONCLUSION

Surgical procedures are not recommended for patients with IT. Minor surgeries may be undertaken in people with IT as tooth extractions and biopsy diagnosis of smaller tumors with great care and concern. There are bleeding risks in those patients during or following the surgery.[10]

Baas et al have shown that PDT may be combined with other techniques such as surgery with great success. Nevertheless, the PDT alone with adequate lesion penetration can also promote excellent outcome. In case of nodular lesion shaving is necessary. The shaving is a technique widely used before PDT removing the cancer cell above the skin surface as well as removing cells layer for cream penetration. The electrocoagulation was performed to assist in blood coagulation promoting the wound healing. The PDT in the shaved lesion, also promotes a favorable environment for wound healing due its efficiency in microbial inactivation.[13,14] The low levels of ROS generated after PDT stimulates the cellular activities involved in healing process as well.[15]

We have observed that the light in wavelength of 630 nm penetrates quite well in a large volume of tissue assuring a wide area of action after the tumor was shaved. The MAL is a compound predominantly used for NMSC treatment, actinic keratosis and cancerization field.[11,12] The margins involved with cell cancer may vary from 4% to 18% of lesion size and the

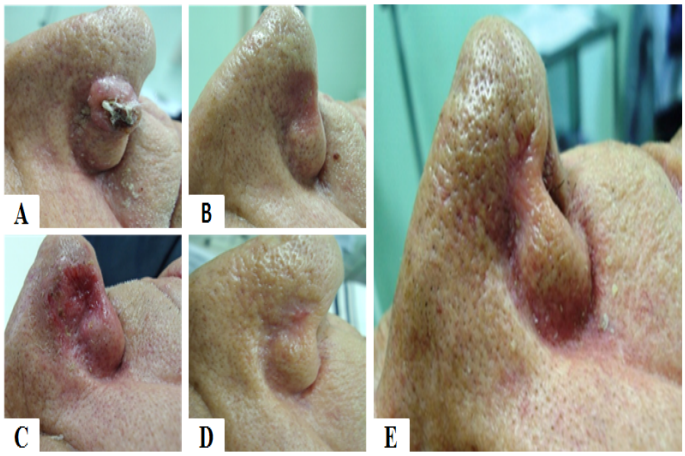

Figure 1: Clinical results of a case report using PDT as adjuvant therapy: Before the treatments (A); two weeks after shaving and electro coagulation (B); a week after the PDT first session (C); 30 days after second PDT session (D).

procedure employed cover this margin. The use of associated techniques may enhance the action field of nodular BCC. Therefore, preventing future recurrences of the lesion that would lead to new treatments and risk to patient.

The anatomical localization of lesion is a relevant factor in PDT indication. The nasal ala presents well-known difficulties in surgical reconstructions. The use of PDT promoted the reconstruction of tissue by healing process after cancer cells elimination, retesting inadequate aesthetic results (Figure 1D).

The number of localized skin cancer cases for patients with natural difficulties for surgical procedure is quite large. In this case, moderate shaving procedure followed by PDT is quite well recommended. In the case of bleeding risks the combined used of shaving with electrocoagulation followed by PDT is a way to assured treatment much beyond removed by the shaving alone.

In summary, PDT is a noninvasive technique with small risks to patients with IT that may be used in association to others therapies expanding its indications. In addition, photodynamic inactivation provides good cosmetic outcomes in difficult anatomical region of surgical reconstruction and improves patient's quality of life. PDT is always provides evidences for an excellent technique as coadjutant in cases where surgery is quite risks.

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CONSENT

The patient has provided written permission for publication of the case details.

CONFLICTS OF INTEREST: None.

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