Sultan Qaboos University Med J, Aug 2017, Vol. 17, Iss. 3, pp. e375–377, Epub. 10 Oct 17
Submitted 16 May 17
Revision Req. 1 Jun 17; Revision Recd. 3 Jun 17
Accepted 15 Jun 17
doi: 10.18295/squmj.2017.17.03.025

INTERESTING MEDICAL IMAGE

Multiple Clustered Dermatofibromas Following Ustekinumab Treatment for *Psoriasis Vulgaris*

*Ricardo Ruiz-Villaverde,[1] Miguel A. Díaz-Martinez,[1] Daniel Sánchez-Cano[2]

أورم ليفية جلدية عنقودية متعددة عقب علاج الصدفية الشائعة بدواء يوستكنيوماب

ريكاردو رويز-فيلافيردي، مقويل أنطونيو دياز-مارتنيز، دانيل سانشيز-كانو

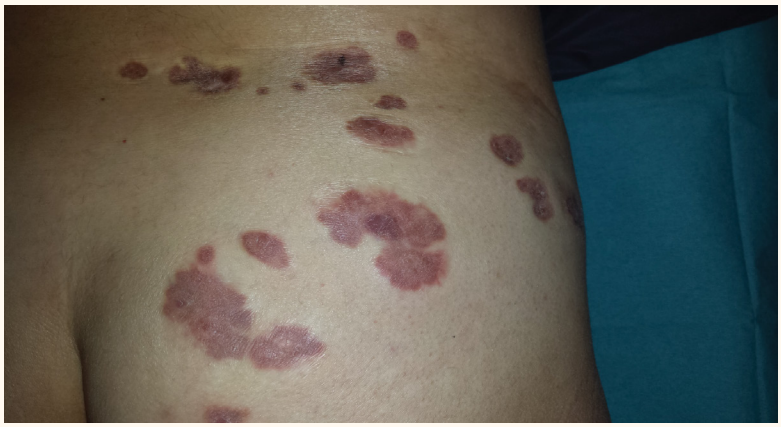

Figure 1: Photograph of multiple clustered purple-brown plaques in the right gluteal region of a 24-year-old man with *psoriasis vulgaris*.

A 24-year-old man with a six-year history of *psoriasis vulgaris* was referred to the dermatological outpatient clinic of the Complejo Hospitalario de Granada, Granada, Spain, in 2016 with multiple brownish cutaneous lesions of different sizes in the right gluteal region. No previous injuries, comorbid conditions or use of concomitant medications were reported. The patient had been undergoing treatment for *psoriasis vulgaris* with 45 mg of ustekinumab every three months over the previous eight months after other methods of treatment had failed, including methotrexate, cyclosporine and narrowband ultraviolet B phototherapy. The ustekinumab treatment had since resulted in good control of the *psoriasis vulgaris* (Psoriasis Area and Severity Index score: 0.8; body surface area: 1; Physician Global Assessment score: 1). However, the gluteal lesions had begun to appear one month after ustekinumab treatment was initiated.

A physical examination revealed a total of 17 hyperpigmented nodules and plaques grouped within the right gluteal area ranging from 0.3–2.4 cm in size [Figure 1]. A polarised dermoscopy using the DermLite III Dermascope (3Gen LLC, San Juan Capistrano, California, USA) revealed a peripheral delicate pigment network and white scar-like patch [Figure 2]. A histological examination of a punch biopsy of one of the lesions showed acanthosis and hyperpigmentation of the basal keratinocytes on the epidermis with fibroblastic proliferation without *atypia* on the reticular dermis [Figure 3A]. An immunohistochemical study indicated positivity to vimentin and factor XIIIa and negativity to S100 and cluster of differentiation (CD)34 [Figures 3B and C]. These findings excluded a diagnosis of dermatofibrosarcoma *protuberans* and confirmed a diagnosis of multiple dermatofibromas.

Routine laboratory investigations, including a complete blood count and general biochemistry, HIV, hepatitis B, hepatitis C, autoimmune and thyroid tests, were within normal limits. Serological tests were negative for rheumatoid factor and antinuclear antibodies. A purified protein derivative test and

[1]*Department of Dermatology, Complejo Hospitalario de Granada, Jaén, Granada, Spain;* [2]*Department of Internal Medicine, Hospital Santa Ana, Motril, Granada, Spain*

**Corresponding Author e-mail: ismenios@hotmail.com*

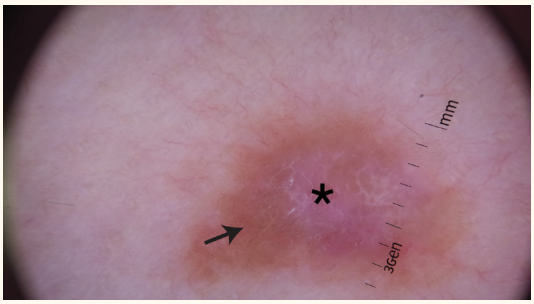

Figure 2: Dermoscopy image at x10 magnification showing a peripheral delicate pigment network (arrow) and white scar-like patch (asterisk).

radiography of the thorax also indicated no anomalies. With the patient's consent, the decision was made to continue ustekinumab treatment. As the patient refused any surgical or medical treatment, the lesions persisted.

Comment

Multiple dermatofibromas are defined as the appearance of at least 15 dermatofibromas in less than a year or 5–8 dermatofibromas within four months.[1] Dupré *et al*. first used the term 'clustered' in 1984 to refer to the grouping of these lesions in a segmental distribution.[2] To date, very few cases of multiple clustered dermatofibromas have been reported in the literature.[3] The individual lesions of multiple dermatofibromas are not clinically, histologically or phenotypically different from that of a solitary dermatofibroma.[3]

Multiple clustered dermatofibromas have not been found to be associated with any underlying malignancies, immunosupression, previous trauma or other comorbidities.[4] Viseux *et al*. reported a kidney transplant patient who had developed multiple clustered dermatofibromas over the pathway of thrombosed superficial veins.[5] Although a congenital case has been reported, the age of onset for most patients with multiple clustered dermatofibromas is between the first and third decade of life.[6,7] No reports of metastasis or malignancy have been described so far, even with follow-up periods of up to 20 years.[7]

In the present case, with regards to the role of ustekinumab, causation cannot be proven; however, a similar case has been described with the biological drug efalizumab.[8] Moreover, the development of multiple eruptive dermatofibromas in immunomodulated situations could be explained by the inhibition of downregulatory T cells.[8–10] Systemic *lupus* erythematosus is the most common underlying disease associated with multiple eruptive dermatofibromas.[9] However, it is important to note that the degree of immunosuppression does not seem to correlate with the number of dermatofibromas.[11]

Histologically, the differential diagnosis for multiple clustered dermatofibromas includes dermatofibrosarcomas *protuberans*, dermatomyofibromas, leiomyomas and, in paediatric cases, plaque-like myofibroblastic tumours. Immunostaining with CD34 may be helpful in confirming the diagnosis.[12] Clinically, the lesions may mimic atypical fibroxanthomas, nodular *fasciitis* and dermatofibrosis *lenticularis disseminata*.[13] From a therapeutic point of view, a conservative approach is advisable. Techniques used with varying success include cryotherapy, intralesional steroids, surgery and phototherapy.[13,14]

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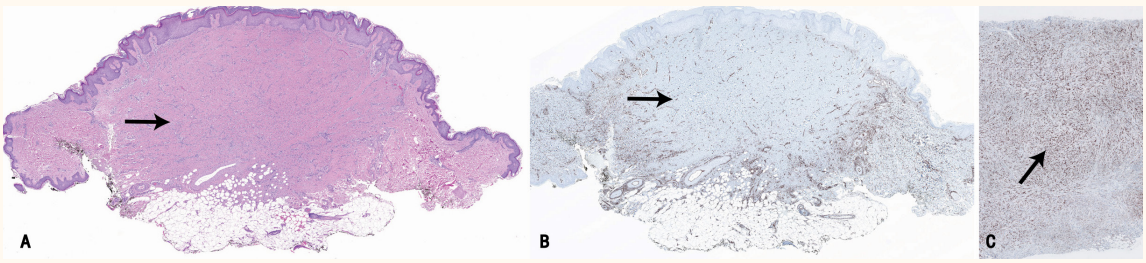

Figure 3: A: Haematoxylin and eosin stain of a punch biopsy at x2 magnification showing a proliferation of spindle cells (arrow) in the dermis and subcutaneous tissue. **B:** Immunohistochemistry stain at x4 magnification showing cells negative for cluster of differentiation (CD)34 (arrow). **C:** Immunohistochemistry stain at x10 magnification showing cells positive for factor XIII (arrow).

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