Solitary Glomus Tumor Presenting as a Telangiectatic Macule☆

Mácula telangiectásica como forma de presentación de un tumor glómico solitario

Dear Editor:

Glomus tumors of the skin are neoplasms derived from dermal glomus cells. These are modified smooth muscle cells and form part of the glomus body, a neuromyoarterial structure that serves to regulate blood flow to the skin.[1] These tumors are usually classified according to the predominant cell type or vessels. Thus, tumors are denoted glomus tumors when there is high cellularity, the most frequent variety; glomangiomas when a vascular pattern predominates; and glomangiomyoma if abundant smooth muscle is present.[2,3] Generally, solid glomus tumors are painful acquired nodules, whereas glomangiomas usually present as multiple lesions and are congenital or onset occurs at a young age. Not infrequently, they may be hereditary, and so are considered as a different entity. They are denoted glomuvenous malformations and a relation to a mutation on chromosome 1p21-22 has been found,[4] in a gene that encodes glomulin.[5] We report the case of a solitary glomus tumor with a distinctive clinical presentation, in form of a telangiectatic macule.

A 60-year-old woman with no medical history of interest was assessed for a painful lesion on the internal face of the left thigh. The lesion had been present for 2 years and had appeared spontaneously, with no apparent relationship with prior trauma. The patient reported pain on touch and pressure, but not spontaneously or with changes in temperature. She did not report any similar lesions in family members. Examination showed a macule with telangiectatic appearance, measuring 1.5 cm in diameter, which was painful to palpation, and no other indications of dermal or epidermal involvement (Fig. 1). Dermatoscopy showed a small blue-grey poorly delimited structure immersed in an extensive fine network with a reticular configuration (Fig. 2). The lesion was resected, and histopathological study showed a solid, well-delimited nodule, measuring 6 mm, located in the hypodermis, formed of monomorphic, rounded cells with oval nuclei, without atypia, that surrounded dilated vessels with thin walls. The cells expressed actin in smooth muscle and endothelial markers in vessels. In the papillary dermis, vessels were observed with dilated lumens, but without glomus cells nearby (Fig. 3). The diagnosis was of a solitary glomus tumor.

Solitary glomus tumor, given its origin in the glomus body, can appear anywhere on the skin, but it is much more frequent at sites where these structures are more numerous, that is, fingers and particularly the subungual region. They have also been reported ectopically in internal organs, where normally these structures do not appear. Solitary glomus tumors are thus divided into digital and extradigital.[1,3]

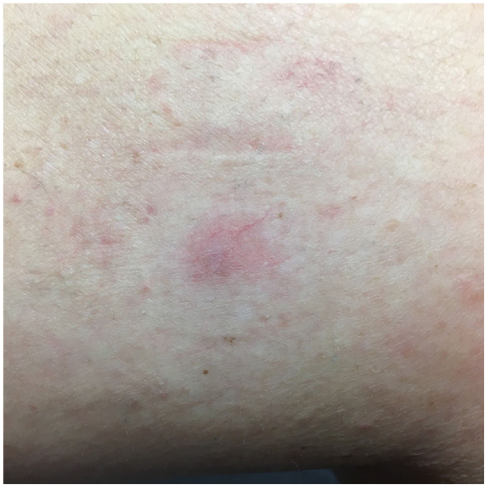

Figure 1 Erythematous-pink macule surrounded by a pale halo.

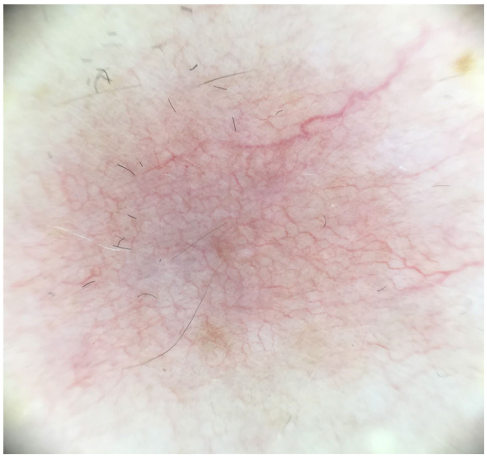

Figure 2 Dermatoscopy showing a fine telangiectatic network and poorly-defined blue-grey area.

The characteristic symptomatic triad of these tumors is spontaneous pain, painful hypersensitivity to touch or pressure, and pain triggered by cold; these symptoms therefore enable rapid diagnostic suspicion in the event of pain in the fingers or subungual region.[1,3] However, extradigital solitary glomus tumors do not usually present with the full range of symptoms, particularly pain triggered by cold,[1,3] and so diagnosis at these sites is usually delayed 6 or 7 years, with multiple visits to the clinic and even psychological repercussion.[1,3] Extradigital solitary glomus tumors usually present as erythematoviolaceous or bluish macules or papules, subcutaneous nodules, or even without clinical findings. In our patient, we could not palpate the nodule, although this was in principle accessible, because of the intense pain with the merest of brushes of the area with the telangiectatic macule. Imaging studies, such as magnetic resonance imaging[1] and high-frequency ultrasonography,[6] can help with diagnosis prior to histopathology. In ultrasound imaging, solitary glomus tumors appear as a well-delimited,

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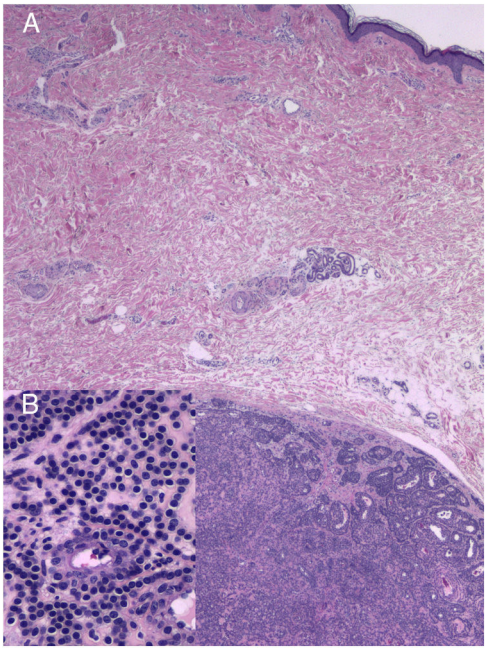

Figure 3 Vascular dilatations in the dermis and a well-delimited, highly vascularized, nodule located in the hypodermis. (A) HE ×40. This lesion is formed by glomus cells with no malignant features, surrounded by blood vessels. (B) HE ×400.

hypoechoic oval or rounded lesion in the dermis, occasionally known as the *stalk sign* (presence of a hypoechoic vascularized prolongation that connects the lesion to adjacent tissues).[6,7] In addition to these findings in B mode, Doppler mode provides additional signs: lesions generally well vascularized, with prominent vessels within, but without forming true *vascular lakes*, and predominantly arterial flows in pulsed Doppler studies, without clearly visualizing an arteriovenous shunt.[7]

This form of presentation as a telangiectatic macule is exceptional and is not clearly reflected in the literature of solid solitary glomus tumors. Schiefer et al.[1] mentioned a small, painful, telangiectatic lesion that served as a guide to detect a solitary glomus tumor measuring 6 mm on the subcutaneous cell tissue. There is also a rare clinical-pathological variant of glomangioma with a certain resemblance. In 1998, Requena et al.[8] reported a plaque-like telangiectatic glomangioma as a new entity based on the telangiectatic appearance and its acquired nature. In 2013, Farias et al.[9] reported another case of plaque-like telangiectatic plaque glomangioma. Apart from the clinical appearance of telangiectatic macula, they also have other features in common with those of our patient's lesion: they are solitary, acquired, painful lesions that occur in women. In 2007, Monteagudo et al.[10] published another case of solitary glomangioma as a telangiectatic plaque in a 41-year-old women. The lesion was very similar but for the fact that it was congenital and asymptomatic. Unlike our case, these 3 lesions were larger and, histopathologically, they were glomangiomas.

We are unsure of the etiopathogenesis of these telangiectasias. We do not know whether they are induced by the tumor or are a reactive phenomenon, but in all cases, we believe that this is not a coincidence. Differential diagnosis could be considered with those processes that can present a telangiectatic appearance, such as mastocytosis; elastotic hemangioma; post-traumatic or drug-induced telangiectasias; angioma serpiginosum; collagen vasculopathy; generalized essential telangiectasia; acquired capillary malformation (Fegeler syndrome); those processes considered as reactive cutaneous angiomatoses, such as reactive angioendotheliomatosis, diffuse dermal angiomatosis, acroangiodermatitis, intravascular reactive histiocytosis, glomeruloid reactive angioendotheliomatosis, and angipericytomatosis[11]; as well as Kaposi sarcoma. However, the clinical presentation of a single painful lesion and the histopathology enable diagnosis to be established beyond doubt.

We describe an unusual presentation for solitary glomus tumor, with the appearance of a telangiectatic macule. It would be important to take into account such a presentation when assessing local and unexplained pain in extradigital regions so as not to delay diagnosis and to avoid the associated physical and psychological discomfort.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Methotrexate-Induced Mucositis as a Sign of Bone Marrow Toxicity: A Retrospective Study of Clinical and Epidemiological Characteristics☆

La mucositis por metotrexato como marcador de toxicidad medular. Estudio retrospectivo de las características clínicas y epidemiológicas

To the Editor:

Methotrexate (MTX) is an antimetabolite that inhibits folic acid synthesis. It is widely used in dermatology, rheumatology, and oncology.[1] Although MTX has a good safety profile, serious adverse effects such as pneumonitis, hepatic fibrosis, and bone marrow aplasia can occur.[1–3] Previous studies have suggested that MTX-induced mucositis may be a sign of bone marrow toxicity.[2,3] The aim of this study was to analyze clinical, laboratory, and epidemiological characteristics of patients with MTX-induced mucositis.

We performed a retrospective study of patients with a diagnosis of MTX-induced mucositis or mouth ulcers evaluated by the dermatology department at our hospital between January 2013 and July 2018. The patients' medical records were reviewed to collect epidemiological, clinical, and pictorial information. Five patients (1 man and 4 women) with a median age of 72 years (range, 50–90 years) were included. The epidemiological and clinical characteristics are summarized in Table 1. The median MTX dose was 15 mg/wk (range, 10–35 mg/wk). The route of administration was subcutaneous in 3/5 patients and oral in 2/5 patients. Two of the patients were taking MTX for psoriasis and 3 were taking it for rheumatoid arthritis. All the patients had erosions and necrotic crusts in the oral cavity (Fig. 1A–D). Additional conditions included pancytopenia or bicytopenia in 4/4 patients, fever in 2/5, and skin ulcers in 2/5 (one had ulcerated psoriatic plaques and the other had an ulcerated basal cell carcinoma on the leg (Fig. 2A and B). Median peripheral blood leukocyte count was 2475×10^6 (range, $330–4200 \times 10^6$). Additional laboratory values (median [range]) were hemoglobin 73.5 g/L (range, 53–92 g/L), mean corpuscular volume 98.5 fL (range, 93–105 fL), and platelets $92\,500 \times 10^6$ (range, $37\,000–128\,000 \times 10^6$). Serum creatinine levels were elevated in 2/4 patients (median, 2.42 mg/dL [range, 0.44–5 mg/dL]). Only 1 patient had impaired liver function reflected by elevated gamma-glutamyl transferase (156 mg/dL [reference value < 40 mg/dL]) and prothrombin time (international normalized ratio, 1.4). Bone marrow aspiration was performed in 3/5 patients and showed marked hypocellularity, which is consistent with MTX toxicity. The most common trigger was use of a nonsteroidal anti-inflammatory drug (NSAID) (2/5), followed by an administration error (1/5), infection (1/5), and a lack of folic acid intake (1/5). Plasma MTX levels were normal (<0.3 mol/L) in 3/3 patients. Treatment included MTX withdrawal in 5/5 patients, intravenous folic acid in 4/5, and granulocyte colony stimulating factor in 1/5. All the patients achieved complete recovery and just 1 was restarted on MTX.

The most common serious adverse effect of MTX is bone marrow toxicity, which has been observed in 2.5% to 10% of patients and is potentially fatal.[4] Mucocutaneous ulceration is a characteristic finding in patients with acute MTX toxicity.[3,5] MTX inhibits cells with a fast turnover and therefore hematopoietic and skin cells are more likely to be affected by its antiproliferative action.[6] MTX is mainly eliminated by glomerular filtration, and just a small fraction is metabolized in the liver. Decreased glomerular filtration rate due to dehydration, infection, and use of drugs such as NSAIDs can therefore lead to MTX accumulation and subsequent toxicity.[3,7] In our study, 3/4 patients had impaired kidney function and 3/5 were taking NSAIDs. These associations are consistent with previous reports describing dosing errors, kidney failure, drug-drug interactions (NSAIDs, antibiotics, or salicylates), and MTX reintroduction or dose increments as the main causes of MTX toxicity.[2,3,5,7]

All the patients in our study with blood test results (4/4) had pancytopenia or bicytopenia, and 2 required empirical antibiotic therapy due to febrile neutropenia. These findings highlight the complex management of MTX-induced toxicity, the potential complications, and the need for a high index of clinical suspicion in patients who develop mucocutaneous ulcers while on MTX, particularly if they have risk factors for decreased glomerular filtration rate.[2,3] Elevated mean corpuscular volume (present in 2 of our

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