



Sociedad Española  
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# Reumatología Clínica

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## Letters to the Editor

### Miescher Syndrome: An Uncommon Cause of Recurrent Swelling of the Lips<sup>☆</sup>



#### Síndrome de Miescher: una causa poco frecuente de tumefacción labial

To the Editor,

Cheilitis granulomatosa or Miescher syndrome (MS) is an uncommon disorder of unknown etiology and pathogenesis, characterized by recurrent swelling of the lips. It is included in the spectrum of orofacial granulomatosis, the paradigm of which is Melkersson–Rosenthal syndrome, in the cases in which it is accompanied by involvement of the facial nerve together with fissured tongue.<sup>1</sup>

We report the case of a 45-year-old woman with a history of hypertension who had been treated for several years with atenolol. She presented complaining of recurrent episodes of labial edema accompanied by burning pain. The patient explained that she felt generally unwell, in the absence of fever or chills. She did not have constitutional symptoms, diarrhea or abdominal pain, and denied exposure to toxic agents and was unable to provide epidemiological data of interest. She had not begun to take any new drugs.

Physical examination revealed the presence of lip swelling, in the absence of ulcers or other associated lesions. It also found that her facial nerve and tongue morphology were absolutely normal. The results of cardiopulmonary evaluation were also normal. A biopsy of the upper lip showed the presence of granulomatous dermatitis with a mixed component of predominantly superficial and deep perivascular infiltrate. In the biopsy, the findings with stains for acid–alcohol-resistant bacilli and fungi were negative.

We performed the intradermal Mantoux test and the result was negative. The findings were the same for the syphilis test (Venereal Disease Research Laboratory [VDRL]) and for serological tests for hepatitis B and C viruses, and for human immunodeficiency virus. The systemic study was accompanied by analyses to determine angiotensin-converting enzyme, antinuclear antibodies, nucleolar antibodies, total extractable nuclear antibodies, antineutrophil cytoplasmic antibodies, immunoglobulins and erythrocyte sedimentation rate, in which all of the results were normal or negative. A chest radiograph showed a normal mediastinal silhouette, and the absence of lymphadenopathy.

The response to glucocorticoids was very favorable, and resulted in the disappearance of swelling and episodes of labial edema.

However, 6 weeks later, the patient came back with similar clinical signs, that coincided with the decrease in steroid dose. Treatment was begun with dapsone, followed by an improvement in the symptoms.

Miescher syndrome appears to be an incomplete form of Melkersson–Rosenthal syndrome in 28% of the patients.<sup>2</sup> In general, MS is an uncommon disease with special predilection for the second or third decades of life, although cases have been reported at any age.<sup>3</sup> It characteristically affects the upper lip and has a lesser effect on the lower lip, although there have been anecdotal reports of the involvement of other regions of the oral cavity. The most frequent presentation is acute and symptomatic swelling of the lips that lasts for hours or days. The confirmation of the diagnosis is the discovery of non-necrotizing granulomas and perivascular lymphocyte infiltration in the biopsy of the affected region.<sup>4</sup> Other diseases with a granulomatous etiology, such as sarcoidosis, tuberculosis and inflammatory bowel disease, should be taken into account in the differential diagnosis and must be ruled out.<sup>5</sup>

There is no ideal treatment for this disease. A number of therapeutic strategies have been proposed, including intralesional or systemic glucocorticoids, as well as other options such as oral tetracyclines, thalidomide, dapsone or biological therapy (anti-tumor necrosis factor  $\alpha$ ), with differing results.<sup>6</sup>

Although it is rare, MS should be taken into account in the differential diagnosis of recurrent edema of the lips. A histological study is essential for the definitive diagnosis of the disease. Treatment with corticosteroids is highly effective. However, as occurs with other immune-mediated diseases, treatment of the underlying disease should be included. Despite the few cases in which the use of dapsone is reported, this drug at a dose of 50 mg a day, may prove to be a useful alternative in MS, as is illustrated by the experience we report here.

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## Hemarthrosis and Scurvy<sup>☆</sup>



### Hemarthrosis por escorbuto

To the Editor,

Hemarthrosis refers to the presence of intraarticular blood and its usual presentation is acute monoarthritis, generally of the knee. The differential diagnosis of spontaneous hemarthrosis includes coagulation disorders, pigmented villonodular synovitis, vasculitis, rheumatoid arthritis and calcium pyrophosphate or hydroxyapatite crystal deposition diseases, among other causes.<sup>1</sup>

On the other hand, scurvy is a disease provoked by deficiency of vitamin C or ascorbic acid, a water-soluble vitamin involved in collagen synthesis through the hydroxylation of lysine and proline in precollagen.<sup>2</sup> The diagnosis of scurvy is clinical and it is necessary to consider an extensive differential diagnosis with a number of diseases, especially vasculitides, as cutaneous purpura is one of its most characteristic clinical manifestations.<sup>3</sup>

We report the case of a 42-year-old man with a history of paranoid schizophrenia, who came to the emergency department with pain and progressive swelling of his left knee that had begun 2

weeks earlier. He had experienced no previous injury. Physical examination revealed gingivitis, purpuric cutaneous lesions and arthritis in his left knee.

He underwent arthrocentesis had yielded a blood-stained fluid (940,000  $\mu$ L red blood cells, 24,550  $\mu$ L nucleated cells—11% lymphocytes and 89% neutrophils—and 56 g/L proteins). A plain radiograph of the knee was normal and magnetic resonance imaging (MRI) revealed marked joint effusion and substantial intra-articular circumferential edematous infiltration, which was reported to be compatible with hemarthrosis, with no other pathologic findings (Fig. 1). On the other hand, a biopsy of the purpuric skin lesions showed extravasation of blood and siderophages, with no inflammatory infiltrate.

Antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), cultures of joint fluid, serological tests for hepatitis B or C virus and human immunodeficiency virus, as well as coagulation tests, routine analyses, and determination of acute-phase reactants were negative or normal. The medical history referred to a restrictive diet, in which the patient ate only milk and yogurt, as well as previous episodes of gingival bleeding.

The serum vitamin C levels were  $<0.10$  mg/dL (normal values: 0.4–2 mg/dL).

After the diagnosis of scurvy, treatment was begun with vitamin C supplements and a supervised diet. The outcome was positive, with a rapid improvement of the skin lesions and resolution of the hemarthrosis.

At present, scurvy is a rare finding in developed countries,<sup>4</sup> but rheumatologists should consider this possibility in the case of spontaneous hemarthrosis, especially if it is accompanied by other hemorrhagic manifestations or eating disorders, taking into account that the definitive diagnosis is usually confirmed *a posteriori*, as vitamin C levels are not routinely determined.

In short, scurvy is a very rare deficiency disease in western countries, although it can be observed in some psychiatric patients and alcoholics with eating disorders. With this case, we would like to remind professionals of this condition as the cause of rheumatic disease and, although not very frequent, it must be taken into account in the differential diagnosis of hemarthrosis. The key to the diagnosis is still in the physical examination and the medical history, although the usual ancillary tests are exclusively a help to rule out other processes.

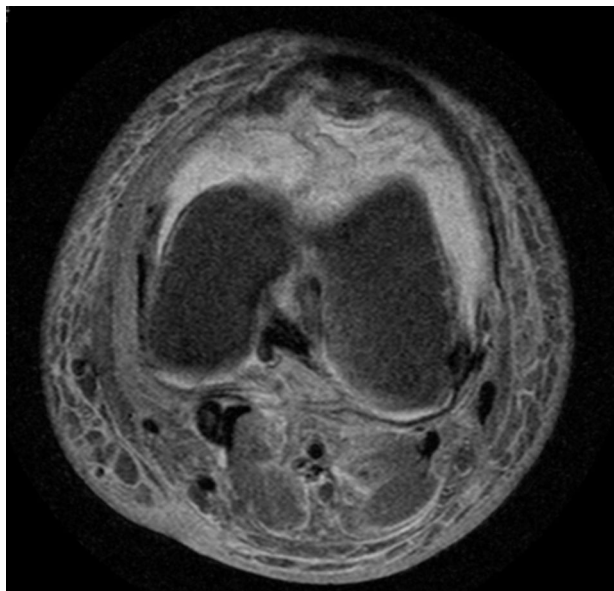


Fig. 1. Coronal T2-weighted magnetic resonance image of the left knee of the patient. A hyperintense signal can be observed in the anterior region in different phases compatible with hemarthrosis.

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