48-Year Old Male With Subcutaneous Inflammation and Eosinophilia

Manuel Vives Soto,[a] Ginés Sánchez Nievas,[b] and Luis Iñiguez de Onzoño[c]

[a]Servicio de Medicina Interna, Clínica Recoletas, Albacete, Spain
[b]Servicio de Reumatología, Hospital General Universitario, Albacete, Spain
[c]Servicio de Anatomía Patológica, Hospital General Universitario, Albacete, Spain

Clinical Case

A 48-year old male without any history of interest presented progressive pain with an inflammatory rhythm and arthritis of the wrists and ankles lasting 20 days, without morning stiffness of fever. He denied presenting aphtous ulcers, skin erythema, photosensitivity, Raynaud's phenomenon, or any other symptom. He hadn't traveled overseas nor had he come in contact with animals or potentially toxic substances. Treatment with ibuprofen and omeprazole was started and after 10 days the patient returned to the outpatient clinic with inflammation and a diffuse burning sensation in both lower extremities up to the inguinal region, as well as in his hands, wrists, and forearms. Upon physical examination he did not present a fever and had hard edema, with the totality of the lower extremities and the upper extremities from the elbow distally, being warm to the touch and with diffuse erythema, having a scleroderma-like aspect and with a reduced elasticity (Figure 1). There were no other skin lesions, or other signs of neither arthritis nor palpable adenopathy and the rest of the examination was considered normal. Laboratory analysis showed eosinophilia (1210/μL) and a C reactive protein (CRP) of 10 mg/L, with an erythrosedimentation rate (ESR) of 16 mm in the first hour; the rest of the blood and biochemical parameters were within normal limits. The thyroid hormone levels, immunoglobulins, serum proteins, antistreptolysins, and rheumatoid factor (RF) were normal. Antinuclear antibodies (AAN), anticentromeric antibodies, and antineutrophil cytoplasm antibodies (ANCA) determinations were negative. Urine tests, electrocardiogram, and chest x-rays were all normal.

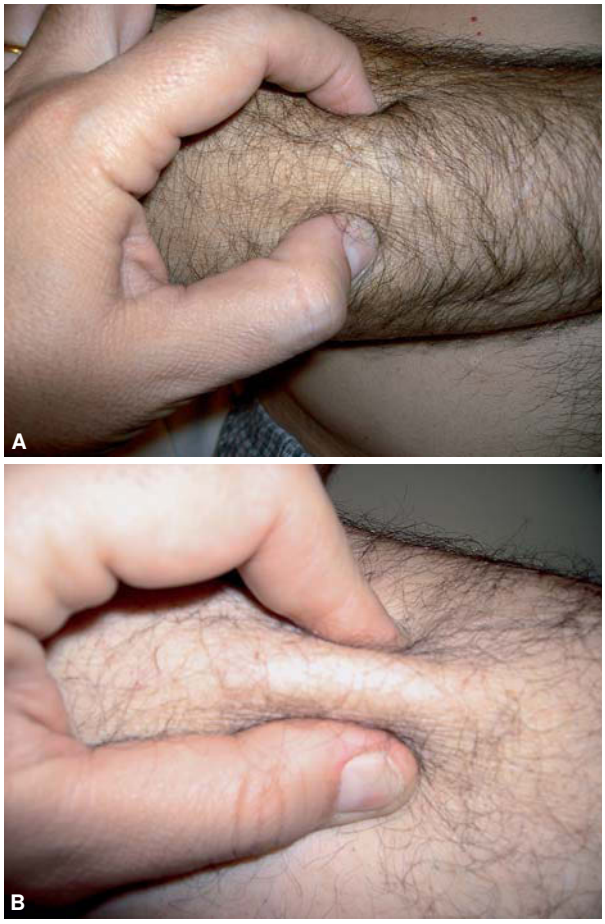

Figure 1. *The patient presented with a thickening and loss of elasticity of subcutaneous fat (A) as can be observed in contrast with a healthy person (B).*

Evolution

A skin, hypodermis, muscle fascia, and superficial muscle (thigh) biopsy was carried out (Figure 2). Edema, fibrosis, and inflammation (lymphocytes, plasma cells, and eosinophils) were evident in it, thickening the muscle fascia and extending to the perimysium and the hypodermis

Correspondence: Dr. M. Vives Soto.
Servicio de Medicina Interna. Clínica Recoletas.
Pl. del Madroño, 11. 02006 Albacete. España.
E-mail: mvivess@medynet.com

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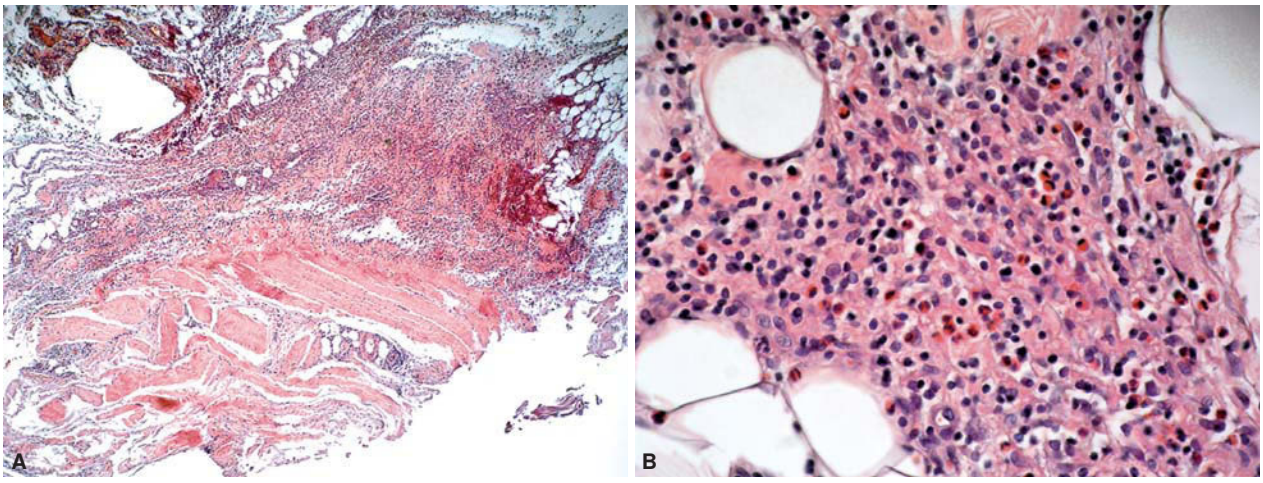

Figure 2. *Hematoxylin-eosyn stain of a biopsy section that shows the fascial thickening, with fibrosis and a dense polymorphous inflammatory infiltrate that extends directly to the hypodermal septae and toward the perimysium (A). At a higher magnification the infiltrate is evidently lymphoplasmocytic with numerous eosinophils (B).*

septae, mainly the deeper ones. On the superficial septae and the profound part of the dermis, alterations were less evident and only the occasional eosinophil was found. Treatment with prednisone 60 mg/day and cimetidine 400 mg bid was started and progressively improved the course of the lesions. Once the diagnosis was confirmed, treatment with hidroxycloroquine was initiated.

Commentary

This is a characteristic case of eosinophilic fascitis, with very expressive pathological images that are difficult to see in the daily practice due to the low prevalence of the disease and because the eosinophilic infiltrate disappears when tissue biopsy is delayed. Eosinophilic fascitis is characterized by chronic inflammation and fibrosis of the muscle fascia that extends in a limited manner to the septae of the hypodermis, the epimysium, and the perimysium.[1] It is clinically manifested by subcutaneous inflammation, stiffness, and distal pain, with predominance on forearms and the posterior legs; the skin initially can be edematous, progressing to an elastic thickening and ultimately scleroderma-like fibrosis.[2] It can be associated to other skin lesions, mainly morphea (25%-30%). In 40% of cases there is joint pain with predominance over elbows, shoulders, and knees, and associated to carpal tunnel syndrome in 20% of cases. The most frequent alterations in the laboratory analysis are eosinophilia (90%), polyclonal hypergammaglobulinemia (75%), and an elevation of the ESR (50%-70%). It can be associated to AAN (15%), RF (10%), or antithyroidal antibodies, and only occasionally are muscle enzymes found elevated.[2] Only 10% of the cases are associated with a blood disorder (aplastic anemia, leukemia, lymphoma), which is generally evident and no specific search for neoplasia is recommended. There is a continuous spectrum between eosinophilic fascitis, which is a form limited to the fascia and hypodermis, and the myalgia-eosinophilia syndrome (MES), which is associated to the ingestion of contaminated L-tryptophan or the toxic-oil syndrome (TOS), in which multi-organ affection can be found. It is probable that the majority of the cases are associated with the ingestion or exposure to environmental agents such as L-tryptophan or trycloroethylene, niacin, lysine, or 5-OH-tryptophan, though most of them have not been identified.[3] To get to the diagnosis a deep biopsy is essential, one that includes skin, hypodermis, fascia, and superficial muscle; it must be carried out during the early stages because late lesions only show fibrosis with a scarce inflammatory infiltrate, predominantly in the fascia.[1]

Due to its rarity[4,5] there are no established guidelines and only small case-series and accumulated experience with the MES and TOS orient treatment. The most commonly employed treatment consists in the administration of oral prednisone (40-60 mg/day) for a month, with a slow reduction over the following months. Some authors recommend associating cimetidine (400 mg bid) from the beginning because some cases have remitted only with this treatment and it is accepted that hydroxycloroquine (200-400 mg/day) is useful and allows for a faster reduction in the steroid dosage.[6] In refractory cases, treatment with methotrexate or azathyoprine can be tried. Approximately 25% of the patients have a spontaneous remission, 50% experience complete recovery or improvement with prednisone, alone or associated with hydroxycloroquine, and another 25% have a chronic fibrosis and symmetrical illness with skin sclerosis in spite of treatment.[2]

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