Author’s response to reviews

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Red eyes and fistulous lesion in left lower extremity: a case report.

Running Title: Red eyes and fistulous lesion in left lower extremity

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ABSTRACT

INTRODUCTION:

We consider relevant this case report because in the last few years, very few cases of scar sarcoidosis have been described affecting the eyes or bone together.

CASE PRESENTATION. We describe the case of a 49-year-old Spanish male patient with recurrent bilateral granulomatous uveitis together with a fistulous nodular lesion in the left pretibial region (scar granuloma) on the site of an 8-year-old scar, with bilateral hilar adenopathies and elevation of inflammatory markers and angiotensin-converting enzyme. Biological agents are considered an alternative for the treatment of conventional treatment – resistant sarcoidosis.

CONCLUSION: Sarcoidosis is a disease of unknown cause characterized histologically by noncaseating granulomas than can involve any organ or tissue. Osseous sarcoidosis is relatively rare case. However, many bones sarcoid lesions cases reported in literature are generally asymptomatic. We present a case of histological confirmed sarcoid of the tibia with an unusual radiologic appearance for a long tubular bone involvement and ophthalmologic bilateral involvement and due to worsening symptoms of sarcoidosis.

INTRODUCTION

Scar sarcoidosis of the tibia is a rare disease. It is usually described in old scars (10 years) and is most common in the upper extremities and facial area, together with an exacerbation of sarcoidosis symptoms (Löfgren syndrome) affecting the eye or, in this case, bone. In the last few years, very few cases of scar sarcoidosis have been described affecting the eyes or bone. In the literature, the appropriate treatment consists of steroids with gradual dose increases until the condition is controlled, followed by 15 mg doses of methotrexate for inflammatory control.

We describe the case of a patient with recurrent bilateral granulomatous uveitis together with a fistulous nodular lesion in the left pretibial region (scar granuloma) on the site of an 8-year-old scar, with bilateral hilar adenopathies and elevation of inflammatory markers and angiotensin-converting enzyme (ACE).
CASE PRESENTATION

We describe the case of a patient with recurrent bilateral granulomatous uveitis together with a fistulous nodular lesion in the left pretibial region (scar granuloma) on the site of an 8-year-old scar. A 49-year-old Spanish male referred in June 2010 by ophthalmology with red eyes. The uveitis protocol was implemented. A chest X-ray was ordered, showing mediastinal adenopathy, for which he was referred to Respiratory Medicine. Respiratory function tests were normal and a high-resolution lung CT scan was ordered. As there was no interstitial disease, he was diagnosed with grade I pulmonary sarcoidosis and no systemic treatment was prescribed. A sacroiliac X-ray and MRI showed sclerotic changes which appeared chronic. No bone edema was observed, HLA-B27 was negative and ACE elevated. Physical examination showed that he was haemodynamically stable, afebrile and with good overall status. Musculoskeletal examination found a raised fistulous erythematous lesion with serous-bloody secretion. There was no erythema or joint effusion. On examination of the skin, there were no erythematous bullous lesions on the lower extremities.

Blood results showed elevated acute-phase reactants (ESR, CRP), but no leukocytosis or left shift and kidney and liver function, electrolytes and clotting were normal. Angiotensin-converting enzyme (ACE) was somewhat elevated and urine sediment was normal. The serology tests were negative (hepatitis, HIV, rubella, cytomegalovirus, Epstein-Barr virus, Toxoplasma, Treponema pallidum, Borrelia, Mycoplasma, Chlamydia). To rule out the possibility of tuberculosis, we ordered a Mantoux test (negative) and serial urine cultures with auramine staining (negative). A high resolution CT scan was compatible with grade I sarcoidosis (bilateral hilar and mediastinal adenopathies).

The patient was also under follow-up by Internal Medicine for a possible infection after a lesion resembling osteomyelitis was observed on a CT of the left lower limb (Fig.1). A biopsy was taken which was compatible with foreign body granuloma. Cultures were negative and there were no malignant cells but pseudomonas and corynebacterium were isolated in the fistulous secretion. Antibiotics were prescribed for 6 months, with no improvement, so he was referred to Rheumatology. A second pretibial skin biopsy showed giant-cell granuloma. Ziehl-Neelsen and PAS stains were negative.

At the same time as the lesion on his left leg worsened, his eye symptoms returned, so he was referred by Ophthalmology to be assessed for immunosuppressant treatment as, although he had improved with topical and oral corticosteroid therapy, the symptoms persisted.
Treatment was started with prednisone, gradually increasing the dose from 15 mg to 30mg/day, with very good clinical response. The patient remained afebrile, with reduction of malleolar swelling and progressive disappearance of the fistulous lesion. We immediately started to reduce the corticosteroid regimen, prescribing treatment with methotrexate 15 mg as a measure to avoid corticosteroids.

The patient was subsequently followed-up in the Rheumatology, Trauma and Internal Medicine departments, where he was found to be asymptomatic with no further attacks of uveitis. The lesion did not recur.

DISCUSSION:
Sarcoidosis is a multi-systemic granulomatous disease of unknown aetiology that particularly affects young people. Its most common symptoms are bilateral hilar adenopathies, pulmonary infiltrates and skin and eye lesions. It is characterised by the formation of non-caseating granulomas.\[4-6\]. When bone is affected, it is normally asymptomatic. It is described as lytic and cystic lesions on the fingers and toes (42%), which do not generally require treatment. However, soft tissues can be affected, with formation of fistulas to the skin that require curettage and corticosteroid therapy or chloroquine, which generally works very well with cutaneous sarcoidosis. The incidence of these lesions is 1-13%. and diagnosis is by biopsy showing bone lesions due to sarcoid granulomas.\[3, 7\]

Approximately 38% of all cases of erythema nodosum are associated with sarcoidosis in Löfgren syndrome and occur with skin lesions, such as plaques, nodules and scars.\[8-10\] When the eyes are affected, it is usually bilateral, recurrent or chronic and secondary and requires us to rule out other systemic causes. In 50-70% of the cases of sarcoidosis associated with other sites, there is also eye involvement and the eye condition often becomes chronic and recurring.\[11-13\]

ACE values are elevated in 88% of patients with active sarcoidosis but using these levels to diagnose the disease can be misleading as approximately 10% of results are false positives and 40%, false negatives; however, they are useful for monitoring disease progression.\[6\]

Looking at bibliography we found 4 clinical cases report about: Scar sarcoidosis that is a rare and uncommon but specific cutaneous manifestation of sarcoidosis: one of them developed scar sarcoidosis on his right index finger, 4 years after the tendon of the long digital flexor got accidentally cut by an angle grinder.\[14\]. Another case was in an old scar present on his forehead with a development of a
lögfren syndrome [15]. Finally two following cases were in herpes zoster scars [16] and the last one explained a case of disseminated scars may predict a pulmonary envolment [17]. So to our knowledge this is the first case in literature of scar sarcoidosis on a tibia.

CONCLUSIÓN

Sarcoidosis generally responds well to corticosteroid therapy, but it is not self-limiting and often also requires the use of an immunosuppressant to avoid corticosteroids and to achieve remission without recurrence; when the eyes are involved, it is often associated with other sarcoidosis symptoms and if the disease is not controlled, these symptoms are also not controlled. It is usually treated with methotrexate, cyclosporine, azathioprine or cyclophosphamide. New biological therapies have also been used, with infliximab showing the best response, although the number of studies in this respect is limited. [18-20]
REFERENCES

Figura 1 microscopic description: granulomas epiteloids multiples no necrotic with multinuclear giant cells, without BAAR microorganisms by Zhiel Nilsen and pass techniques.
FIGURE 1: A lesion resembling osteomyelitis was observed on a CT of the left lower limb.