Sarcoidosis: Revisión de la literatura en el contexto de una presentación atípica

Sarcoidosis – Review of the literature in the context of an atypical presentation

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ABSTRACT

We present the case of a 63-year-old woman who was referred to an internal medicine clinic due to an orbital mass accompanied by fatigue. After a thorough investigation, including exclusion of infectious and malignant aetiologies, the diagnosis of sarcoidosis was established. However, despite a meticulous evaluation and initiation of immunosuppressive treatment, we observed disease progression, with extension of the orbital mass and persistent fatigue, as well as multi-organ involvement.

Thus, this is a case of sarcoidosis with an atypical manifestation and progression, rarely described in the literature. We intend this case to serve as a model of the challenges posed by this disease, explaining the diagnostic hypotheses we have considered and the rationale for their exclusion.

Keyword: Granulomatous disease, multisystem disease, ocular sarcoidosis, atypical manifestation, chronic sarcoidosis.

RESUMEN

Presentamos el caso de una mujer de 63 años que fue remitida a una consulta de medicina interna debido a una masa orbitaria acompañada de fatiga. Tras una exhaustiva investigación, que incluyó la exclusión de etiologías infecciosas y malignas, se estableció el diagnóstico de sarcoidosis. Sin embargo, a pesar de haber realizado una evaluación minuciosa y haber iniciado tratamiento inmunosupresor, hemos observado progresión de la enfermedad, con extensión de la masa orbitaria y fatiga persistente, además de una afectación multiorgánica.

Así, se trata de un caso de sarcoidosis con una manifestación y progresión atípicas, con rara descripción en la literatura. Pretendemos que este caso sirva como modelo de los desafíos que plantea esta enfermedad, explicando las hipótesis diagnósticas que hemos considerado y los fundamentos de su exclusión.

Palabras clave: Enfermedad granulomatosa, enfermedad multisistémica, sarcoidosis ocular, manifestación atípica, sarcoidosis crónica.

INTRODUCTION

Sarcoidosis is a multisystemic inflammatory disease characterized by the formation of granulomas[1,2], with a higher prevalence observed in women[3]. The most commonly affected organs are the lungs and intrathoracic lymph nodes[4,5], although extrapulmonary manifestations are described in 15% to 20% of cases[6]. Ocular sarcoidosis is the second most prevalent extrapulmonary complication, although non-uveitis manifestations are rare[5]. Favourable treatment responses are commonly observed.[5]

Given the heterogeneity of this disease, the diagnosis of sarcoidosis can be challenging and must include: i) compatible clinical presentation, ii) histological presence of non-necrotising granulomatous inflammation in at least one organ, and iii) exclusion of alternative causes of granulomatous disease.[1,5]

CASE PRESENTATION

A 63-year-old black woman presented to an internal medicine consultation due to the onset of eyelid oedema and proptosis of the left eye seven months ago. The patient referred burning, discomfort and dryness in the left eye, accompanied by fatigue. She denied any respiratory symptoms, diplopia, decreased visual acuity, skin lesions, arthralgias, and B symptoms. The patient worked as a housemaid and had a medical history of obesity, hypertension and a daily alcohol intake of 10 grams. She denied the use of tobacco or drugs. Physical examination only revealed restricted eye movements in the extreme left gaze, without diplopia, and limited opening of the palpebral fissure.

Analytically the hemogram was normal, and there was an elevation in alkaline phosphatase (138 UI/L), gamma-glutamyl transferase (69 UI/L), angiotensin-converting enzyme (ACE) (95 U/L), and a slight increase in C-reactive protein (1.16 mg/dL). The patient tested negative for HIV, Venereal Disease Research Laboratory (VRDL), hepatitis B, hepatitis C and Interferon-Gamma Release Assay (IGRA). Thyroid function was normal and anti-thyroid antibodies were negatives. Antinuclear antibodies (ANA) were positive (titre 1:320) with a AC-5 pattern according to International Consensus on ANA Patterns. Thus, we analysed the presence of antibodies including anti-dsDNA, anti-SSA/Ro, anti-SSB and anti-Sm, all of which yielded negative results. Evaluation of immunoglobulins (IgG, IgG4, IgA) and complement components (C3 and C4) revealed values within normal ranges. Antineutrophil cytoplasmic antibodies (ANCA), proteinase-3 (PR3), myeloperoxidase (MPO) and *Borrelia burgdorferi* antibodies IgG and IgM were negative.

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Figura 1

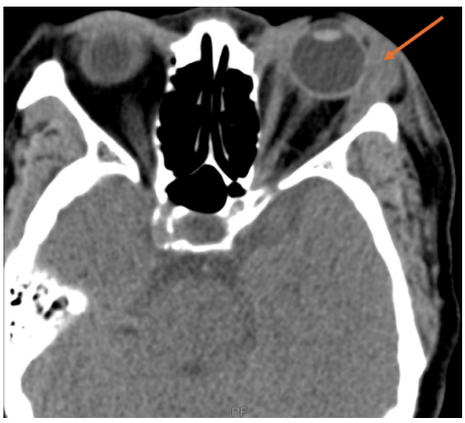
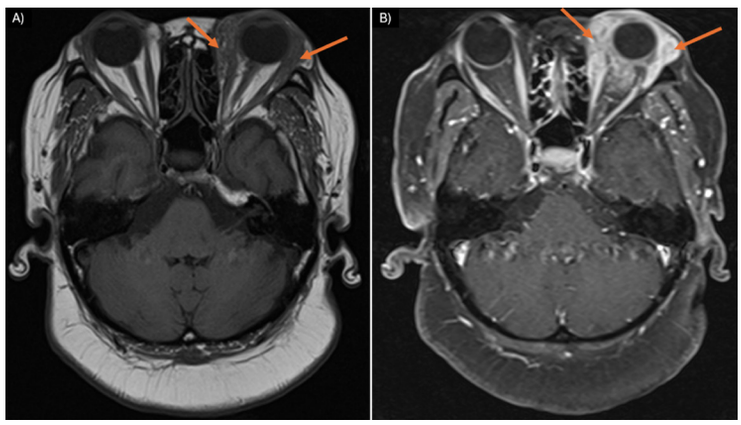


Figura 2



Seric and urinary calcium, ionogram, transaminases, renal function and sedimentary velocity were within normal ranges.

The computerized tomography (CT) scan of the orbits revealed a mass in the left lacrimal gland extending into the pre-septal and extra-conical regions in the upper-external angle (Figure 1). The biopsy of the left lacrimal gland indicated non-caseous necrotising granulomatous inflammation. The thoracic-abdominal-pelvic CT (TAP-CT) scan showed mediastinal adenopathy.

According to these findings, the principal diagnosis hypothesis was sarcoidosis, and the patient initiated prednisolone 40mg. To further characterized the orbital lesion's extent and evaluated the response to therapy, a magnetic resonance imaging (MRI) of the orbits and face was later performed. The MRI revealed an extra-conical lesion in the upper quadrants of the left orbit with ill-defined borders, involving and enlarging the ipsilateral lacrimal gland, and extending into the intra-conical compartment in the upper region (Figure 2).

Given the continued advancement of the lesion despite immunosuppressive therapy, a biopsy of the salivary gland in the lower lip was realised, revealing no alterations. Despite this, sarcoidosis remained the primary hypothesis, prompting the initiation of methotrexate.

After one year into treatment, the patient's clinical symptoms persisted. A new MRI of the orbits and face was carried out, indicating new progression of the lesion with denser infiltration in the pre-septal regions of the upper and inner quadrants. There was also a slight heterogeneous increase in the lacrimal gland volume. A follow-up TAP CT scan was also performed, revealing mediastinal, hepatosplenic, and abdominal lymph node involvement.

Given the continued progression of the disease, it was decided in multidisciplinary reunion to do a mediastinal lymph node biopsy and a bronchoalveolar lavage, which confirmed a diagnosis consistent with sarcoidosis. These findings prompted the initiation of adalimumab.

Currently, the patient continues to be monitored in the internal medicine, showing clinical and analytical improvement.

DISCUSSION

In this case, we began with a differential diagnosis between malignancy, infectious aetiologies (HIV, hepatitis B and hepatitis C), and thyroid disease. Then, with the biopsy showing non-caseating necrotising granulomas, we considered investigating granulomatous diseases.[7]

Mycobacterium tuberculosis is the most common cause of infectious granulomatous lung disease[2,7]. The overlap between sarcoidosis and tuberculosis, along with the risk of initiating corticosteroids erroneously, underscores the necessity of definitively excluding tuberculosis before establishing a diagnosis of sarcoidosis[4,8]. Consequently, an IGRA and a bronchoalveolar lavage were performed, yielding negative results, which allowed us to exclude this hypothesis. Syphilis, another granulomatous infectious disease, was similarly excluded with a negative VDRL test.

Among non-infectious granulomatous diseases, lymphoma assumes particular significance due to the potential for diagnostic confusion with sarcoidosis, compounded by the possibility of coexistence[8]. Exclusion of lymphoma was supported by the absence of typical constitutional symptoms, alongside elevated ACE levels. Further, biopsy of mediastinal lymph nodes realized later contributed to ruling out lymphoma.

We also ruled out small-vessel vasculitis, Systemic Lupus Erythematosus, Sjogren's syndrome, and drug-induced sarcoidosis-like reactions (DISRs).[8]

Later, observing clinical and analytical progression despite corticosteroid therapy, we considered IgG4-related disease[9]. However, the absence of marked lymphocyte and plasmacyte infiltration in the biopsy, along with the absence of elevated serum IgG4 and total IgG[9], allowed us to exclude this hypothesis.

With due consideration of all these findings, alongside mediastinal lymph node biopsy and a bronchoalveolar lavage consistent with sarcoidosis[10], the sarcoidosis diagnosis was established in a patient exhibiting a suboptimal response to corticosteroid therapy.

Corticosteroids are the first line of treatment, being reserved for cases with organ dysfunction[4]. In refractory cases, it is reasonable to consider alternative medications such as methotrexate and TNF-alpha antagonists[5], as we did in our case. Our patient exhibited a chronic sarcoidosis course, compounded by extrathoracic manifestations, and with risk factors for disease progression (black race, age over forty, and elevated ACE levels)[10]. Consequently, follow-up of this patient is imperative not only for symptoms management, but also for monitoring therapeutic response and disease progression, aiming to mitigate organ dysfunction onset and subsequent mortality.[4]

CONFLICTS OF INTEREST
The authors declare that there were no conflicts of interest in carrying out the present work.

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ETHICAL ASPECTS
All participants submitted a consent form to be included in this study.

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