Acute Granulomatous Interstitial Nephritis – A Rare Case of Sarcoidosis

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ABSTRACT

Sarcoidosis is a systemic granulomatous disease of unknown etiology with a wide range of clinical presentations. Authors describe the case of a 72-year-old man with severe acute renal injury secondary to granulomatous interstitial nephritis. Despite the suggestive renal biopsy, only the exclusion of other granulomatous diseases enabled the definitive diagnosis of renal sarcoidosis. The patient underwent hemodialysis and therapy with prednisolone 1mg/kg/day. His serum creatinine returned to baseline over the following months, with no evidence of residual injury. Sarcoid interstitial nephritis is usually silent, and there are very few reported cases associated with severe acute renal failure.

Keywords: acute interstitial nephritis; sarcoidosis

1. INTRODUCTION

Sarcoidosis is a systemic granulomatous disease of unknown etiology, which affects predominantly young males and it was first described by three doctors, Besnier-Boeck-Shauman(1). It is characterized by the increased activity of the macrophages and CD4+ T helper cells and the formation of granulomas in affected organs(2). Despite the progress observed over the last two decades regarding the understanding of the disease’s pathogenesis, the causative agent is not yet identified.

The diagnosis is based on clinical findings and imaging analysis and is supported, wherever possible, by histological evidence of non-caseating granulomas on biopsy of an affected organ. The clinical course of sarcoidosis is quite variable and can progress to spontaneous resolution or evolve in a chronic and progressive form. Over 90% of patients present pulmonary involvement. Intrathoracic manifestations are the most common and clinically significant(3). Symptoms are usually nonspecific and depend directly on the affected organs. About 20-50% of the patients are asymptomatic, and the diagnosis results from incidental findings on the chest radiography. The most frequent extrapulmonary involvement affects the skin, the eyes, and liver, and the most severe cases result from cardiac and nervous system involvement(3).

Sarcoidosis can also be the cause of nephropathy through: a) calcium metabolism changes, and b) granulomatous infiltration of the renal parenchyma. Of these, the calcium metabolism changes are the most common. Epithelioid cells, which form granulomas, have the capacity to produce calcitriol, which consequently may lead to hypercalciuria.
On physical examination, he had a fishy breath suggestive of uremic fetor, normal blood pressure, no fever, no adenopathy, no skin lesions, and lower limbs presented pitting edema. It was also evident a hearing loss, not apparent in the first assessment in the previous week. A prompt otorhinolaryngology evaluation was requested and revealed bilateral sensorineural hypoacusis.

On admission, his serum creatinine was 17.54 mg/dL, and BUN was 113 mg/dL, corresponding to a rapid decline in renal function, considering that a week before presented only 1.05 mg/dL and 21.3 mg/dL, respectively. Other blood tests indicated anemia (hemoglobin 8.4 g/dL), a mild elevation of inflammatory parameters (erythrocyte sedimentation rate 59 mm/h, C-reactive protein 2.47 nmol/L), and a slightly elevated angiotensin converting enzyme (62 U/L, normal range: 8-52 U/L). Urine analysis showed 2+ proteinuria, microscopic examination revealed no erythrocytes and 75 leukocytes per high-power field. There was no elevation of serum and urinary calcium. Anti-nuclear antibody (ANA), myeloperoxidase anti-neutrophil cytoplasmic antibody (ANCA), proteinase-3 ANCA, anti-glomerular basement membrane antibody (anti-GBM), serum cryoglobulins, anti-streptolysin O (ASLO), C3 and C4, were within normal ranges. Hepatitis panel and HIV serology were negative. A renal ultrasound revealed normal kidneys in size, good parenchymal thickness and no signs of hydronephrosis.

The patient began hemodialysis and treatment with prednisolone 1 mg/kg/day. Three days later underwent kidney biopsy. Renal histology was conclusive, the glomeruli were normal, but there was a diffuse interstitial inflammation with extensive non-caseating granuloma infiltrates. The diagnosis of severe acute interstitial nephritis, secondary to sarcoidosis with renal involvement, was established.

During admission, the patient also performed: body CT scan presenting multiple enlarged mediastinal, hilar and abdominal lymph nodes, without significant pulmonary findings; immunophenotypic study of lymphocytes in the bronchoalveolar lavage (BAL), which revealed a high CD4/CD8 ratio (4.2); tuberculin test with anergic response and interferon gamma release assay (IGRA) was negative; electrocardiogram showing right bundle branch block pattern. Head MRI, echocardiogram, eye fundoscopy, and chest radiograph were normal.

Haemodialysis was required for about a month. There was a progressive improvement of the renal function (Fig. 1), with the resolution of the initial symptoms.
including hearing improvement. The patient was discharged 42 days after admission, maintaining corticosteroid therapy. His serum creatinine returned to baseline (1.12mg/dL) over the following four months, with no evidence of residual injury.

**Figure 1. Evolution of serum creatinine of the patient.** The graph represents the serum creatinine evolution (continuous lines) at the first observation (baseline) and then from admission (day 1) to the date of discharge (day 42). Haemodialysis (bar) was initiated on the first day of admission and ceased on day 34.

### 3. DISCUSSION

**Diagnosis**

The diagnosis of sarcoidosis is challenging, and it is often established several months after the initial symptoms of the disease. In this patient, the first manifestations of sarcoidosis may have been the skin findings presented two years earlier. The cutaneous changes are relatively frequent in sarcoidosis (about 25%), may have different presentations, and normally appear in the early stage of this pathology. In this particular case, renal involvement was the most severe manifestation of the disease, precipitating the diagnosis of sarcoidosis. Although rare, the granulomatous interstitial nephritis secondary to sarcoidosis may present itself as a rapidly progressive renal failure. Renal biopsy is essential to confirm sarcoidosis, namely through the evidence of non-caseating granulomas. However, only the exclusion of disorders of calcium metabolism, as well as other granulomatous diseases, enabled the definitive diagnosis of renal sarcoidosis.

The presence of non-necrotizing granulomatous lymphadenitis in lymph node biopsy carried out previously, the evidence of high CD4/CD8 ratio in the BAL and the elevation of serum angiotensin converting enzyme reinforce the diagnosis.

**Extrarenal systemic involvement**

Most cases of renal sarcoidosis present a concomitant multi-systemic involvement. The additional study highlighted the diffuse lymphatic involvement of the disease, as well as the bilateral sensorineural hypoacusis, secondary to vestibulocochlear nerve damage. These findings are described in the literature and can be attributed to sarcoidosis. Especially acute hearing loss, which improved with therapy. On the other hand, the lack of pulmonary lesions is atypical, since they are present in up to 90% of all cases.

**Treatment and follow-up**

Corticosteroids are the first-line treatment regarding renal sarcoidosis. The most common initial therapy is prednisolone 1mg/kg/day. Corticosteroids are generally effective in sarcoid interstitial nephritis, leading to normalization of renal function, especially
in the absence of interstitial fibrosis. Despite the excellent response to the treatment, most patients have residual renal damage, and there may be relapses after treatment discontinuation\(^{8,10}\). Treatment duration should be individualized, and it is essential to maintain a close monitoring of these patients, particularly in the first two years after the diagnosis.

4. CONCLUSION

We present a patient with a predominant extrapulmonary form of sarcoidosis, who remained undiagnosed until developing a severe acute renal injury. Despite the severity of renal dysfunction, timely diagnosis of sarcoid interstitial nephritis and early treatment with corticosteroids allowed a complete recovery.

REFERENCES