

CASE REPORT

Acute kidney injury as the presenting feature of sarcoidosis

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ABSTRACT

Acute kidney injury is rarely the presenting feature of sarcoidosis. We report the case of a patient whose diagnosis was brought to light by the investigation of impaired kidney function. Concurrent hypercalcaemia was noted and prompted further investigation, which led to the diagnosis of sarcoidosis. This is a rare phenomenon and is an important consideration in the patient with acute kidney injury and hypercalcaemia, without an apparent explanation. Rapid improvement in both kidney function and hypercalcaemia occurred in response to treatment.

Keywords: sarcoidosis; acute kidney injury; hypercalcaemia.

INTRODUCTION

Sarcoidosis is primarily a disease of the lungs and reticuloendothelial system, which are affected in up to 90% of individuals. As extra-pulmonary manifestations may be protean, the diagnosis may be delayed [1], and kidney involvement may be under-recognized. Case reports typically describe symptomatic involvement of other organ systems, and kidney injury is seldom the presenting feature of the illness [2,3]. Aside from the complications of hypercalcaemia, the renal manifestations of sarcoidosis include granulomatous and non-granulomatous tubulointerstitial nephritis, retroperitoneal sarcoidosis with obstructive uropathy, and a wide range of glomerulopathies including membranous nephropathy, IgA nephropathy, crescentic glomerulonephritis, focal segmental glomerulosclerosis and membranoproliferative (mesangiocapillary) glomerulonephritis [4].

CASE REPORT

A 38-year-old male presented with a 2-week history of generalized weakness, intermittent abdominal pain, constipation, reduced appetite and polyuria. He had no past

history of diabetes, hypertension or other comorbidities. He was a non-drinker and non-smoker, with no significant occupational or environmental exposure. There was no history of fever, cough, shortness of breath, chest pain, weight loss, joint pains, oral ulceration, rash, ocular complaints or any other constitutional symptoms. On examination, he was haemodynamically stable. His ocular and dermatological examination was normal. There were two cervical lymph nodes, each approximately one centimetre in diameter, palpable on the left side of the neck. On chest examination, there were fine crackles heard diffusely over both lung fields, suggestive of interstitial lung disease. The rest of systematic examination was unremarkable. Urinalysis revealed a bland sediment without any evidence of microscopic haematuria or proteinuria on dipstick testing.

Laboratory testing revealed haemoglobin to be 14 g/dL, platelets $168 \times 10^9/L$, white blood cells $5.7 \times 10^9/L$ (neutrophils 52%, lymphocytes 40%, monocytes 4%, eosinophils 2%, basophils 2%) and the ESR 48 mm/hour. Serum sodium was 137 mmol/L, potassium 4.5 mmol/L,

urea 19.9 mmol/L, creatinine 318 μ mol/L, total protein 144 g/L and albumin 42g/L. Total bilirubin was 50 μ mol/L, SGOT 15 U/L, SGPT 9 U/L, alkaline phosphatase 241 U/L, calcium 3.55 mmol/L, phosphorus 1.24 mmol/L, vitamin D3 121 nmol/L, PTH 0.8 pg/L, and serum ACE level 269.18 U/L. His antinuclear antigen was negative and viral markers were non-reactive for HIV, hepatitis B and hepatitis C. Thyroid functions and complement levels were normal.

The chest radiograph revealed bilateral hilar prominence suggestive of hilar lymphadenopathy.

Renal ultrasonography revealed normal-sized kidneys and a 4 mm calculus at the left vesicoureteric junction without any evidence of hydronephrosis. The following day, computer tomography was normal, suggesting spontaneous passage of the calculus; biochemical evaluation of the stone could therefore not be done. The 24-hour urinary calcium excretion was elevated at 600 mg/day (upper limit of normal range 300 mg/day), suggestive of the hypercalciuria which may be seen with sarcoidosis, and which may lead to kidney stone formation. The hypercalcaemia improved 3–4 days after treatment with calcitonin and there was improvement in the kidney function after resolution of the hypercalcaemia.

A biopsy of a left-sided cervical lymph node was performed, which revealed non-caseating granulomas suggestive of sarcoidosis (Figure 1).

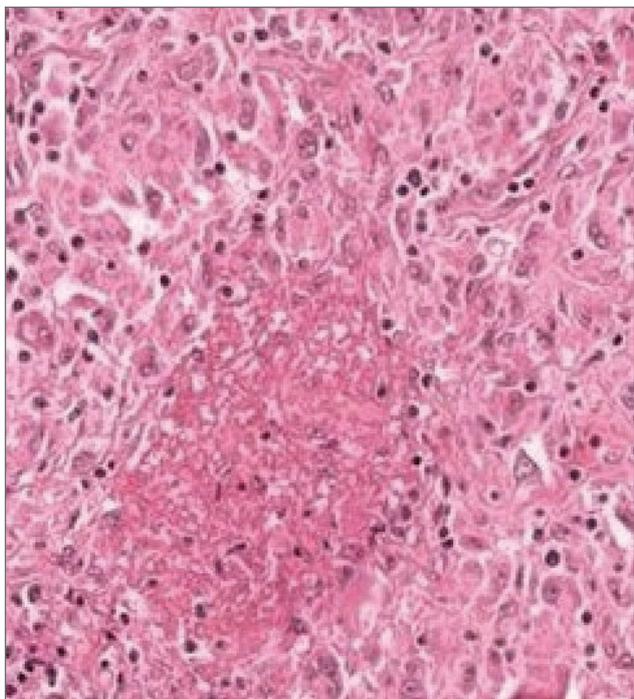


Figure 1. Histology of the left sided cervical lymph node. There is a background of lymphocyte-rich cellular infiltrate. In the centre, there is a collection of epithelioid cells forming a granuloma without evidence of caseating necrosis (haematoxylin and eosin stain, original magnification \times 100).

In view of the improving serum creatinine and the normal urinalysis without an active sediment, the aetiology of the AKI was attributed to hypercalcaemia, and a kidney biopsy was not performed. When the kidney function did not completely normalize after two weeks, even after resolution of the hypercalcaemia, a kidney biopsy was considered but the patient was not willing to provide consent. He was started on oral prednisolone (1 mg/kg/day). The kidney dysfunction completely resolved after one month of treatment.

DISCUSSION

The pathological hallmark of sarcoidosis is the presence of non-caseating granulomata that can affect many different organ systems with predilection for the lungs, lymph nodes, eyes and skin. The inciting event is not fully understood but appears to be driven by a cellular immune response to an unknown antigen and involves complex interactions of genetic and environmental factors [5]. It is a rare disease, with an estimated prevalence of approximately 20 per 100,000 in Whites, with a similar incidence in both males and females [6]. The diagnosis is made by the presence of compatible clinical, laboratory, radiological and histological findings, and the exclusion of other causes of granulomatous disease.

In India, sarcoidosis primarily involves the lungs and lymphatic system [7,8], whereas kidney involvement is less frequent. The incidence of kidney involvement in Western countries ranges from 7% to 22% [9]. Studies from India and other low- and middle-income countries did not report kidney involvement as the presenting feature in their patients [10-13]. Morphologically, involvement of the kidneys in sarcoidosis can occur in three ways: nephrocalcinosis and nephrolithiasis, granulomatous involvement of the tubulointerstitium, or glomerulonephritis. In a large retrospective study, Rizzato et al. reported that renal calculi were the first manifestation of disease in 2.2% of their patients, although none of the patients in that series presented with AKI [1].

The pathophysiological mechanisms responsible for kidney injury in sarcoidosis include a direct effect of hypercalcaemia, hypovolaemia, nephrocalcinosis and tubulointerstitial disease [1]. About 10–20% of patients with sarcoidosis have hypercalcaemia and 10% have kidney stones [14]. Activated mononuclear cells within granulomas can express 1-alpha-hydroxylase, which is resistant to normal negative feedback mechanisms, resulting in unregulated production of 1,25-dihydroxy vitamin D [15]. This leads to hyperabsorption of dietary calcium, hypercalciuria and, if the amount of absorbed calcium surpasses the renal excretion threshold, hypercalcaemia. Both hypercalciuria and hyper-

calcaemia are common in patients with sarcoidosis, occurring in 40–62% and 5–10%, respectively [16]. Hypercalcaemia can cause renal injury through afferent renal arteriolar vasoconstriction, thereby decreasing renal blood flow and leading to AKI [5]. Calcium dysregulation can also cause nephrolithiasis with obstructive uropathy, and tubulointerstitial inflammation associated with calcium deposits. If prolonged, the latter can lead to nephrocalcinosis, which may be the most common cause of progressive renal failure in sarcoidosis [17]. Due to the variety of presentations and the lack of consensus about what constitutes renal sarcoidosis, estimates of renal involvement in sarcoidosis vary considerably, from 0.7% to 48% of cases [6,18]. Granulomatous interstitial nephritis and granulomatous vasculitis are rare manifestations of renal sarcoidosis [19]. In cases where treatment is required, corticosteroids are the mainstay of therapy and higher doses may be required for those with renal involvement.

In conclusion, we describe a case report of a patient who was admitted for investigation of acute kidney injury, which was the presenting feature of underlying sarcoidosis. This rare phenomenon should be a consideration in the patient with AKI and unexplained hypercalcaemia.

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