CASE REPORT

Renal sarcoidosis: a rare case

Maria Menezes,[1] Eunice Patarata[2]

[1]Nephrology Department, Centro Hospitalar de Lisboa Central EPE, Lisboa, Portugal
[2]Internal Medicine Functional Unit 7.2, Centro Hospitalar Lisboa Central, Lisboa, Portugal

Correspondence to
Maria Menezes,
mariamarmenezes@gmail.com

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SUMMARY

Sarcoidosis is a multisystemic granulomatous disease with rare renal involvement. We describe a case of a 45-year-old female patient admitted to the hospital with severe acute kidney injury and uveitis. After clinical investigation, sarcoidosis with renal, hepatic and ocular involvement was diagnosed. Renal biopsy revealed acute granulomatous interstitial nephritis and treatment with systemic corticosteroids was started with marked improvement in renal function.

BACKGROUND

Sarcoidosis is a multisystemic granulomatous disease of unknown aetiology. It is characterised by the presence of non-caseous granulomas (accumulation of activated T cells CD4+ and macrophages) in several organs. The lung is the most affected organ (90%), followed by lymph nodes, skin and eye.[1] The incidence and prevalence are uncertain. Renal involvement is rare, corresponding to 0.7% of cases.[1]

Renal involvement of sarcoidosis may present abnormal calcium metabolism, nephrolithiasis and nephrocalcinosis, as well as acute tubulointerstitial nephritis with or without granulomas.

Other rare findings include glomerular disease (cases of membranous nephropathy, IgA nephropathy), tubular dysfunction (proximal or distal renal tubular acidosis and Fanconi syndrome), obstructive uropathy (due to nephrolithiasis, retroperitoneal fibrosis, retroperitoneal lymphadenopathy, bladder, urethra or ureter obstruction by granulomas) and even granulomatous angiitis.[2]

The classical renal lesion consists of non-caseous granulomatous tubulointerstitial nephritis. However, this seldom leads to significant kidney disease. Hypercalcaemia and hypercalciuria are main cause of kidney injury, and nephrocalcinosis is the major cause of chronic kidney disease in sarcoidosis.[2] However, progression to terminal chronic kidney disease is rare.[2]

This case is utterly interesting because this patient, despite having an altered calcium metabolism did not have nephrocalcinosis and suffered from severe acute kidney injury, making the presentation atypical.

CASE PRESENTATION

We present a case of a 45-year-old female patient, child caretaker, with a medical history of anaemia of unknown aetiology for about 20 years and smoking habits.

The patient was admitted to the emergency department presenting with nausea, vomiting, non-selective anorexia, blurred vision and diplopia, fever and dry non-productive cough in the previous 48 hours. She denied diarrhoea, urinary complaints or any type of drug intake.

At the emergency department, the physical examination revealed a thin and dehydrated patient, temperature of 37.6°C and blood pressure of 131/80 mm Hg.

She was initially observed by an ophthalmologist and diagnosed with anterior bilateral uveitis. Topical ocular corticosteroids and antihistamines were prescribed.

The laboratory investigation revealed the following results: hypochromic microcytic anaemia (haemoglobin 10.7 g/L), acute renal lesion with serum creatinine 7.89 mg/dL and urea 168 mg/dL, hypercalcaemia (serum calcium 10.4 mg/dL/12.4 mg/dL corrected for albumin) and phosphorus of 5.2 mg/dL. Liver enzymes were altered (elevated gamma glutamyl transferase 136 U/L and alkaline phosphatase 296 U/L but normal aspartate aminotransferase 24 U/L and alanine aminotransferase 20 U/L), serum protein electrophoresis showed increased beta 2 and gamma and low albumin 1.9 g/dL. Low fibrinogen of 0.7 g/L and erythrocyte sedimentation rate of 26 mm/h were found. Urinalysis revealed proteinuria (50 mg/L) and no white or red blood cells. Urine culture was negative. Blood gas analysis showed metabolic acidosis (bicarbonate of 15.7 mEq/L and ionised calcium of 1.49 mmol/L).

The remaining evaluation had no changes.

Renal and abdominal ultrasound revealed hepatomegaly (17 cm), steatosis and kidneys in normal topography, regular contours, normal size (right kidney with 12.7 cm and left kidney with 12.4 cm), preserved corticomedullary differentiation without expansive lesions, excretory dilatation, lithiasis nor perirenal collections. Chest X-ray did not reveal pleuroparenchymal lesions.

The patient was admitted to the Internal Medicine ward and the following diagnostic work-up was done to study the acute kidney injury associated with uveitis and liver involvement. Intravenous hydration with saline solution (sodium chloride 0.9%) was started with no improvement in renal function.

INVESTIGATIONS

Since the patient had multiple organ involvement (kidney, liver and eye), systemic conditions had to be ruled out. Also, blood and urine infectious diseases were excluded (HIV, hepatitis A, B, C and

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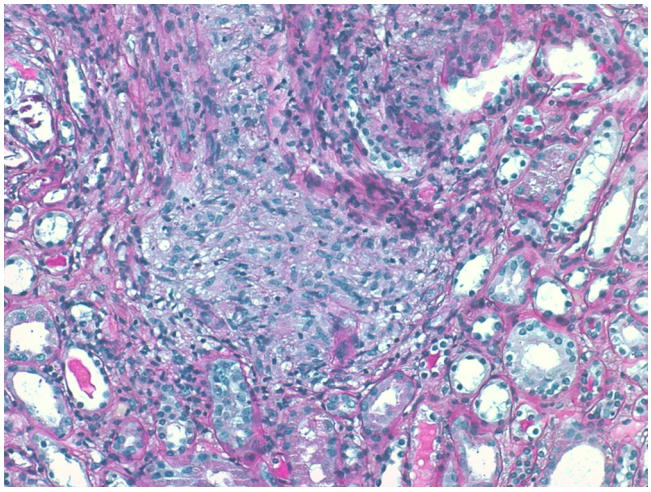

Figure 1 Periodic acid Schiff ×200. Early granuloma formation.

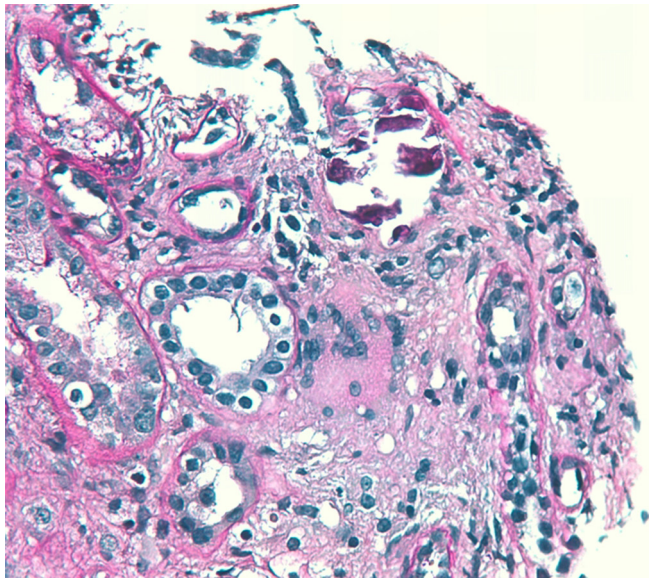

Figure 2 Periodic acid Schiff ×400. Giant multinucleated cell.

delta, syphilis, Epstein Barr virus and tuberculosis), Epstein Barr virus IgM was negative and IgG was positive (750 U/mL). VDRL (venereal disease research laboratory) test and IGRA (interferon gamma release assay) were also negative.

Drug toxicity was excluded by patient information.

Therefore, hepatitis was ruled out as a possible cause of prerenal insufficiency, regarding the clinical chart of vomiting, dehydration, elevated liver enzymes and liver enlargement. Autoimmune and infiltrative disorders were then investigated.

CT scan confirmed liver enlargement, with no other organ involvement.

Antinuclear antibody was weakly positive, but no other autoantibodies or abnormal serum complement levels were detected. There were no other clinical signs or symptoms. Taking these results into consideration, systemic lupus erythematosus or Sjogren syndrome seemed less likely. ANCA (antineutrophil cytoplasmic antibodies), PR3 (proteinase 3) and MPO (myeloperoxidase) were negative and no respiratory involvement was noted so granulomatosis with polyangiitis was also excluded.

We tried to exclude Hyper IgG4 disease, as the initially IgG was high (21.60 g/L), but the IgG subclasses IgG 1, 2, 3 and 4 were within normal range.

As sarcoidosis was suspected, the ACE was measured and found to be high (495 U/L).

Renal biopsy was performed, which revealed an acute interstitial nephritis with non-caseating granulomas, giant cells, lymphocytic infiltration and rare calcium deposits on light microscopy (figures 1–4).

TREATMENT

The probable diagnosis of sarcoidosis with renal, ocular and hepatic involvement was assumed and treatment was started with pulses of intravenous methylprednisolone 1000 mg per day for 3 days, followed by prednisolone 40 mg per day.

OUTCOME AND FOLLOW-UP

The patient showed a sustained improvement of renal function with no need for renal replacement therapy during hospital admission. At discharge (on the 15th day) serum creatinine was 1.76 mg/dL with improvement of all the other abnormal analytical parameters.

She was later submitted to respiratory function tests that showed no changes.

The patient completed 4 weeks of the initial corticosteroid dose. One month after discharge, all the analytical parameters (serum creatinine 1 mg/dL, haemoglobin, calcium, liver enzymes and urinalysis) had normalised. A slow weaning of corticosteroids (to prednisolone 10 mg once a day) was tried and, to date, no recurrence was noted.

DISCUSSION

High serum creatinine, a mild urinary sediment (only with discrete proteinuria), hypercalcaemia, liver involvement, uveitis, an elevated ACE and histologically proven granulomatous acute interstitial nephritis made the diagnosis of sarcoidosis likely.

Nevertheless, other aetiologies of granulomatous interstitial nephritis had to be excluded. In addition to sarcoidosis, the most frequent causes are drugs, infections (such as tuberculosis or syphilis), Wegener's disease and tubulointerstitial nephritis and uveitis (TINU).[3–5] Our patient denied any prescribed or over the counter medication. Tuberculosis, syphilis and granulomatosis with polyangiitis (Wegener's disease) became unlikely with the clinical results.

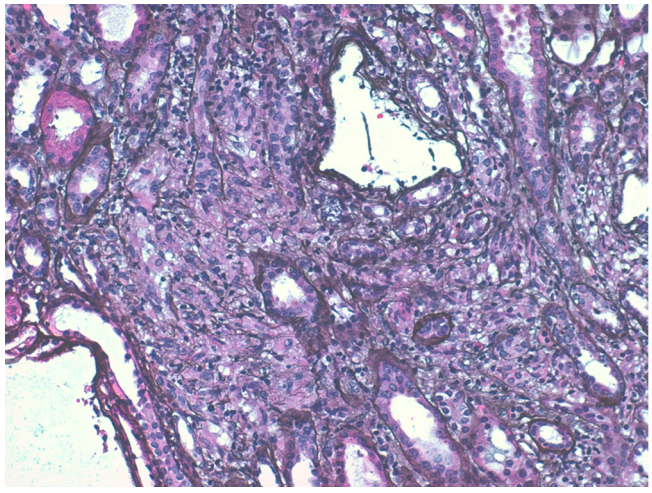

Figure 3 Periodic acid Schiff ×400. Tubulitis and disruption of tubular basement membranes.

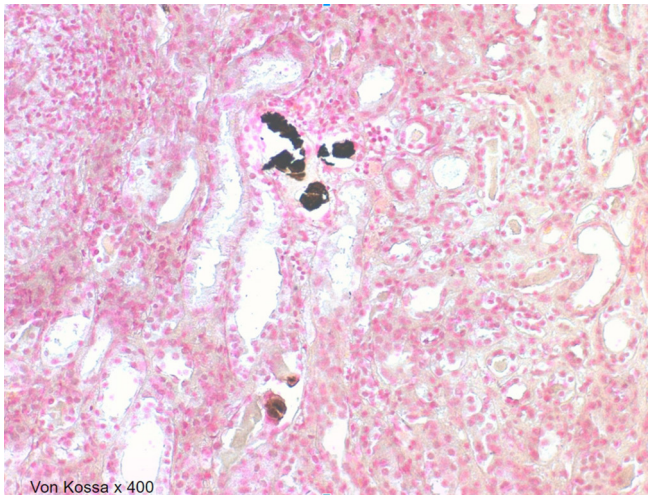

Figure 4 Von Kossa ×200. Tubular calcium deposition.

We cannot safely rule out TINU, as it is common in young women (with a mean age of 15 years), but may occur in adults with TINU.[6] Elevated liver enzymes and erythrocyte sedimentation rate may also be found in this condition. However, this is an exclusion diagnosis. Hepatomegaly, hypercalcaemia and an elevated ACE were more suggestive of sarcoidosis and therefore, this was the presumptive final diagnosis.

This case is particularly interesting for its atypical presentation: acute renal injury (which is rare in the context of acute granulomatous interstitial nephritis) and the absence of lung involvement (as proven by CT scan and blood gas analysis) that is present in about 90% of sarcoidosis cases.[1]

Literature concerning patients with renal sarcoidosis is scarce. One study analysed 47 patients with renal sarcoidosis, of which 66% presented with moderate proteinuria and granulomatous interstitial nephritis.[7] The same pattern was found in our patient. In contrast, in another study of 27 patients, non-granulomatous interstitial nephritis was more common.[8] These two studies[7 8] showed renal function improvement after oral corticosteroids treatment, as observed in our patient and as recommended by others.[9]

Since this disease has high recurrence, we decided to maintain low dose corticosteroids for 2 years in our patient.

We emphasise that all the investigation performed only allowed us to make the sarcoidosis diagnosis more likely and were in no way exhaustive or exclusive. Unfortunately, no single test confirms this hypothesis and it is still a difficult condition to address.

Learning points

- Sarcoidosis is a systemic disease with rare renal involvement.
- The primary renal manifestations are nephrolithiasis, nephrocalcinosis and interstitial nephritis with or without granulomas.
- Interstitial nephritis with non-caseous granulomas is the classic histological finding, but rarely causes significant kidney injury.
- Hypercalcaemia and hypercalciuria are usually responsible for relevant kidney disease.
- Renal biopsy findings are only suggestive. Clinical and complementary examinations are essential for the diagnosis.

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