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Hypercalcemia Revealing Isolated Renal Sarcoidosis

Abstract:

Renal involvement in sarcoidosis is rare and is most often a consequence of calcium metabolism disorders or interstitial granulomatous involvement, while glomerular involvement remains exceptional. We report the case of a 56-year-old patient admitted for unexplained renal failure, associated with hypercalcemia, leukocyturia, and minimal proteinuria. A renal biopsy revealed granulomatous interstitial nephritis without caseous necrosis, along with focal areas of mild tubular necrosis. No involvement of other organs was observed. The patient was treated with corticosteroid therapy and symptomatic management of hypercalcemia, leading to a favorable outcome.

Keywords: Isolated Renal sarcoidosis; Granulomatous interstitial nephritis; Hypercalcemia

Introduction:

Sarcoidosis is a multisystem granulomatous disease of unknown etiology, characterized by tissue infiltration with non-caseating tuberculoid granulomas containing multinucleated giant cells. Renal involvement remains rare, with renal failure reported in only 1–3% of patients [1-2]. We present the case of a patient with renal failure and hypercalcemia, revealing isolated renal sarcoidosis.

Case report:

A 56-year-old patient with a history of surgery two years prior for intestinal obstruction, was admitted to the nephrology department for an etiological workup of severe kidney failure, incidentally discovered.

The patient's medical history dates back one month prior to admission, marked by the insidious onset of astehnia, which prompted a consultation in general medicine. A routine workup was performed, revealing incidentally discovered kidney failure without major hydro electrolytic disturbances. A renal ultrasound ruled out obstructive etiology.

Upon admission, the patient was hemodynamically and respiratory stable, with preserved urine output and no signs of fluid overload. The remainder of the physical examination was unremarkable.

Blood tests revealed renal failure (Urea: 1.16 g/L, Creatinine: 67 mg/L) alongside with hypercalcemia (125 mg/L), hyperphosphatemia (57 mg/L) and mild proteinuria (0.3 g/day).

The ultrasound revealed two kidneys of normal size with preserved corticomedullary differentiation and no signs of excretory tract dilation.

Urine cytobacteriological analysis was sterile, showing leukocyturia but no hematuria. Plasma protein electrophoresis showed polyclonal gammaglobulinemia.

Given the unexplained acute kidney injury, a renal biopsy was performed, revealing moderate tubulointerstitial inflammation with nodular and diffuse epithelioid and multinucleated giant cell granulomas affecting the entire cortical surface, along with focal areas of mild tubular necrosis

(Figure 1). Direct immunofluorescence for C3, IgA, IgM, IgG, and kappa/lambda light chains was negative.

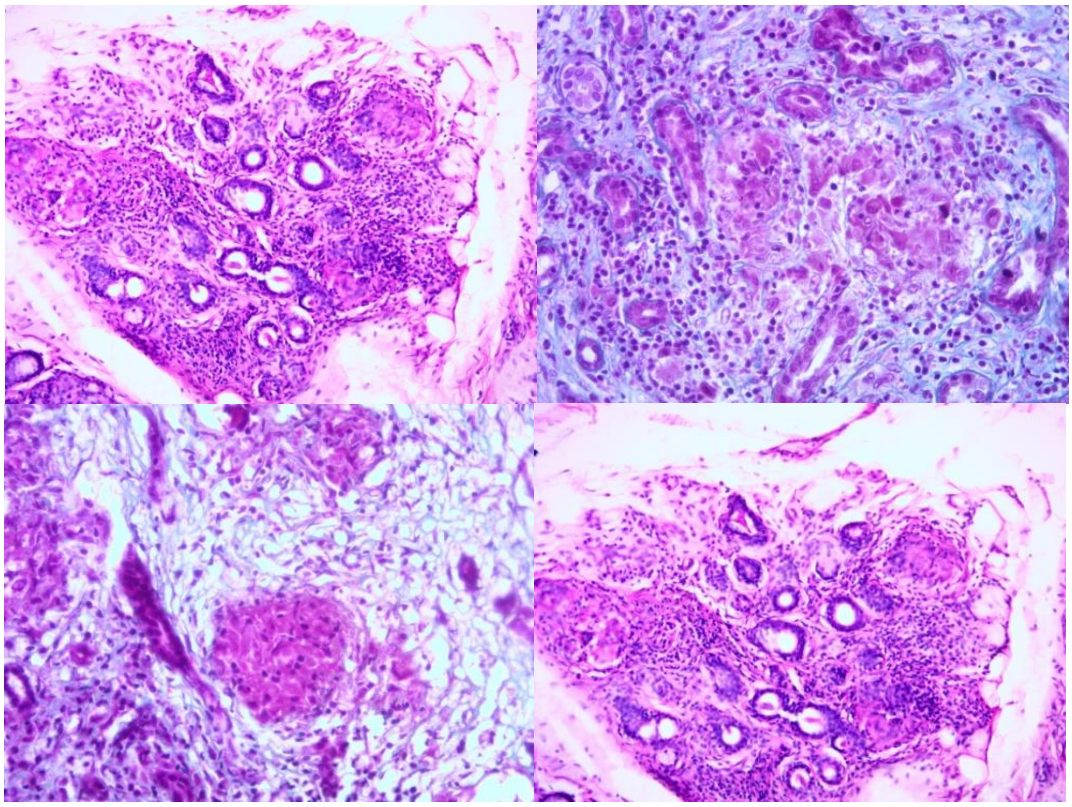

Figure1 : Renal biopsy fragment stained with standard techniques, showing granulomatous interstitial nephritis without caseous necrosis, along with focal areas of mild tubular necrosis.

An extension workup was initiated to search for other organ involvement. A thoraco-abdominal CT scan was normal, as were ophthalmologic and ENT examinations. Dermatologic and lymph node assessments were unremarkable. Serum Mycobacterium Tuberculosis GeneXpert was negative. Angiotensin-converting enzyme (ACE) levels were at the upper limit of normal. Immunological tests, including antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA), anti-extractable nuclear antigen (anti-ENA), anti-neutrophil cytoplasmic antibodies (ANCA), and complement levels, were within normal ranges.

The patient received three consecutive daily pulses of methylprednisolone (500 mg), followed by oral corticosteroid therapy at an initial daily dose of 1 mg/kg. Additional treatment for hypercalcemia included hydration and bisphosphonates, with no need for renal replacement therapy.

The patient's condition improved progressively, with a follow-up creatinine level of 30 mg/L at two months.

Discussion:

Renal involvement is an uncommon manifestation of sarcoidosis, with its prevalence varying across studies depending on the diagnostic methods used [3-4]. While it is typically reported in fewer than 10% of cases, autopsy studies have detected granulomas in renal parenchyma in up to 25% of sarcoidosis patients [5-6].

The increased production of calcitriol, resulting from macrophage activation within sarcoid granulomas, leads to hypercalcemia in approximately 10% of cases and hypercalciuria in 30–45% of cases. These calcium metabolism disturbances can cause nephrocalcinosis or calcium nephrolithiasis [7].

Renal involvement generally occurs in patients with multiorgan sarcoidosis. However, in our case, the patient presented with isolated renal sarcoidosis. In the study by Mahevas et al. [8], renal involvement revealed sarcoidosis in most cases, whereas in 19% of cases, it developed later in the disease course.

Granulomatous tubulointerstitial nephritis is the most specific renal lesion in sarcoidosis. Renal injury may remain isolated for several years, as observed in our patient, but it more commonly occurs in the setting of florid multifocal sarcoidosis. Proteinuria is usually absent or minimal, while leukocyturia is often present and may be accompanied by hematuria [9].

Renal biopsy is essential for diagnosing granulomatous interstitial nephropathy, as it reveals interstitial lymphoid and macrophage infiltrates without glomerular or vascular lesions. Non-caseous epithelioid granulomas are highly specific but are identified in only 40% of cases. Tubular abnormalities secondary to interstitial lesions are observed in 50% of cases [10].

Glomerular involvement in sarcoidosis is rare but can coexist with granulomatous interstitial nephropathy. The most frequently reported glomerular pathology is membranous glomerulonephritis [11].

The mainstay of treatment for renal sarcoidosis is corticosteroid therapy, initiated at a dose of 1 mg/kg/day [12]. Early corticosteroid initiation is crucial to prevent fibrosis. While there is no standardized treatment duration, most experts recommend prolonged therapy (at least 18 months) to reduce the risk of renal relapse.

For patients with hypercalcemia and hypercalciuria, dietary calcium restriction, avoidance of hypercalcemic medications, and limited sun exposure are advised. Alternative therapeutic options include chloroquine and hydroxychloroquine, which may help correct calcitriol levels. Additionally, ketoconazole (a steroidogenesis inhibitor) at a dose of 800 mg/day has been proposed as a treatment for hypercalciuria, as it reduces calcitriol synthesis [13].

Conclusion:

Our case highlights the importance of systematically assessing renal function and calcium metabolism in patients with sarcoidosis, both at initial evaluation and during follow-up. It also underscores the need to consider performing a renal biopsy in cases of renal injury with hypercalcemia in order to to ensure the diagnosis of isolated renal sarcoidosis is not overlooked.

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Conflict of Interest Statement: The authors declare that they have no conflicts of interest.