Acute Renal Failure as a Manifestation of Sarcoidosis

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Sarcoidosis is a common disease of unknown etiology, characterized by non-caseating pithelioid granuloma formation and derangements of the normal tissue architecture. Although pulmonary involvement with hilar lymphadenopathy is the most common finding, sarcoidosis can involve many organs and systems. Renal disease is rare and may occur in the absence of pulmonary disease, resulting in diagnostic difficulties [1]. We describe a woman with acute renal failure associated with sarcoidosis.

Patient Description

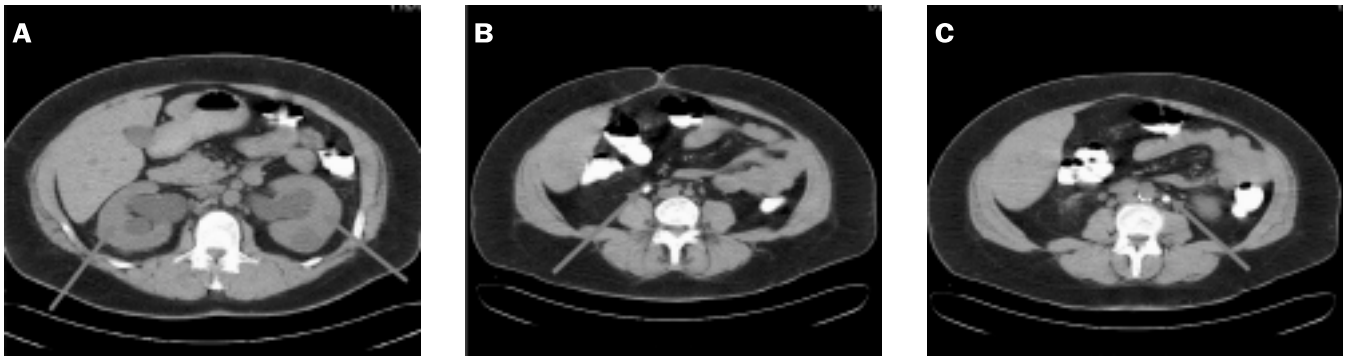
A 43 year old women was admitted for evaluation of acute renal failure (urea 70 mg/dl, creatinine 1.7 mg/dl) that was discovered incidentally in routine blood analysis. Her previous medical history was remarkable for pulmonary sarcoidosis dating 9 years earlier. She was successfully treated with steroids for one year. Chest X-ray, pulmonary function test and routine blood analysis were stable for 8 years. Her physical examination was normal. Laboratory results included hypercalcemia of 12.5 mg/dl and an elevated erythrocyte sedimentation rate of 40 mm/hour. The parathyroid hormone level was 15 pg/ml (normal 10–70 pg/ml). Urine sediment was normal and no proteinuria was present. Twenty-four hour urinary collection did not reveal hypercalciuria. Abdominal ultrasound demonstrated bilateral hydronephrosis. Spiral computed tomography of the abdomen showed evidence of bilateral ureterolithiasis with complete obstruction of both ureters, and bilateral hydronephrosis with no changes in renal parenchyma or enlargement of lymph nodes [Figure]. Treatment with fluids, furosemide and corticosteroids (prednisone 1 mg/kg) was begun, resulting in a decrease in creatinine and calcium level. Extracorporeal shockwave lithotripsy was then performed. Two weeks after this procedure, renal function returned to normal limits and repeated ultrasound did not show hydronephrosis or uretherocalcinosis. Involvement of other systems was excluded by pulmonary function test, total body Gallium scan, cardiac echo and ophthalmologic evaluation. Angiotensin-converting enzyme level increased to 168 U/L (normal 55–120 U/L).

The patient continued to take prednisone 20 mg daily for 3 months, after which the dose of corticosteroids was tapered. Four months after cessation of treatment laboratory analysis revealed normal renal function and calcium plasma level.

Comment

Renal involvement in sarcoidosis may be a part of the systemic disease or an isolated manifestation. The incidence of renal disease ranges from 7 to 27%, but less than 1% of patients with sarcoidosis develop renal insufficiency [1]. Renal involvement may manifest as hypercalcemic nephropathy, granulomatous interstitial nephritis, renal tubular dysfunction, glomerulonephritis or renal amyloidosis [2].

The most common causes of renal involvement in patients with sarcoidosis is abnormality of calcium metabolism secondary to increased synthesis of calcitriol (1,25-dihydrohy-vitamin D3) by the macrophages of the granulomatous lesions. The consequent increased calcium absorption from the gastrointestinal tract results in the hypercalciuria that is detected in more than 50% of patients. Polyuria and reduced capacity to concentrate the urine are its main manifestation. Hypercalcemia is less common and usually depends on the coexistent deterioration of renal function when the capacity of the kidney to excrete calcium is compromised. Nephrolithiasis occurs in about 10% of patients; another 10% may develop nephrocalcinosis. Hypercalcemia, hypercalciuria and nephrocalsinosis may be asymptomatic [2]. In contrast, nephrolithiasis usually presents as renal colic, pyuria or hematuria. Renal stones may be



Spinal CT of abdomen demonstrating **[A]** bilateral hydronephrosis, **[B]** right ureteral stone, **[C]** left ureteral stone.

the first presentation of sarcoidosis and this diagnosis should be considered when patients present with nephrolithiasis of unknown origin [3].

Several entities in differential diagnosis of acute obstructive renal failure associated with nephrolithiasis in patents with sarcoidosis were ruled out. These include obstruction caused by intrarenal granulomatous infiltrates, extensive retroperitoneal lymphadenopathy and fibrosis [1].

The circulating level of parathyroid hormone should be determined because of the increased prevalence of parathyroid adenomas in patients with sarcoidosis [1]. The treatment for hypercalcemia and hypercalciuria associated with sarcoidosis entails corticosteroids. Restriction of calcium intake and increased fluid intake are important measures in the treatment. The use of extracorporeal shockwave lithotripsy in combination with corticosteroids appears to be the treatment of choice for renal stones secondary to abnormalities of calcium metabolism in sarcoidosis [4].

In conclusion, we have described a rare case of acute renal insufficiency associated with hypercalcemia and bilateral nephrolithiasis as an isolated presentation of sarcoidosis. This disease must be included in the differential diagnosis of renal insufficiency even in the absence of multiorgan manifestations. Renal involvement in sarcoidosis responds well to corticosteroids and this treatment can prevent further renal insufficiency.

References

1. Carmichael P, O'Donnell JP The protean face of renal sarcoid. *J Nephrol* 2003;16:721–7.
2. Erten N, Saka B, Artinesen B, et al Extrapulmonary sarcoidosis with renal failure. *Eur J Intern Med* 2003;14:262–4.
3. Rizzato G, Colombo P. Nephrolithiasis as a presenting feature of chronic sarcoidosis: prospective study. *Sarcoidosis Vasc Diffuse Lung Dis* 1996;13:167–72.
4. Sharma OP, Alfaro C. Hypercalciuremia and renal stones in a sarcoidosis patient treated by extracorporeal shockwave lithotripsy. *Sarcoidosis* 1986;3:7–9.

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Research Projects

Characterization of the molecular basis of a salt-wasting syndrome (pseudohypoaldosteronism) that results from unresponsiveness to aldosterone

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Background: Pseudohypoaldosteronism type I (PHA) is a hereditary salt-wasting disease of unresponsiveness to steroid hormone aldosterone. We previously reported for the first time that PHA includes two distinct forms: renal and multi-system PHA, and that the multi-system form is caused by mutations in the epithelial sodium channel (ENaC) alpha, beta and gamma subunits. ENaC transports sodium ions across epithelial cells lining the distal colon, distal renal tubule, respiratory airways, and exocrine glands. By osmosis-driven flow of fluid, ENaC also regulates blood volume and pressure.

Objectives: In this project our aims included identification of the mutations responsible for multi-system PHA in patients from different ethic groups and analysis of the phenotype genotype relationship.

Methods: To search for mutations we determined the complete coding sequences of all ENaC subunits in individuals representing different ethnic groups [*J Clin Endocrinol Metab* 2002;87:3344]. All the patients suffered from severe salt wasting and required prolonged hospitalizations.

Results: Our analyses revealed six novel single nucleotide homozygous and compound heterozygous mutations in alpha and beta subunits. All except one of the mutations led to inactivation of the affected subunit by either a base insertion or deletion causing frame shift error, or nonsense mutation. A single missense mutation was associated with a milder form of multi-system PHA that shows absence of severe pulmonary symptoms.

Conclusions: Elucidation of the molecular basis PHA has revealed "natural" gene knockout cases in humans, establishing that ENaC is an absolutely essential component in the action of aldosterone in regulating fluid and electrolyte homeostasis.

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