

Case Report

Granulomatous interstitial nephritis causing renal failure, a rare presentation of childhood sarcoidosis

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Abstract

Sarcoidosis is a multisystem granulomatous disorder of unknown cause seen in young adults. Clinically significant renal involvement is rare especially in a young child. We report a case of 6 year old boy with advanced renal failure secondary to granulomatous interstitial nephritis without any evidence of pulmonary sarcoidosis which is distinctly unusual.

Keywords:Renal failure, Childhood sarcoidosis, Nephritis

1. Introduction

Sarcoidosis is a multisystem disorder of young adults in which lungs are involved in more than 90% patients¹. It occasionally involves kidney most commonly due to disorders of calcium homeostasis or by invasive granulomatous infiltration. Granulomatous interstitial nephritis (GIN) is most often a silent disease which does not cause renal failure². We report a case of 6 year old boy with advanced renal failure secondary to granulomatous interstitial nephritis without any evidence of pulmonary sarcoidosis. This is a rare presentation of an uncommon disease.

2. Case Report

A 6-year-old boy presented with incidentally detected increased creatinine. There was history of unexplained fever off and on for the last 2 years. There was no history of joint pains, rash, breathlessness and chest pain, red or sore eyes. During his past episodes of fever, he had been evaluated for tuberculosis, systemic onset juvenile rheumatoid arthritis, systemic lupus erythematosus, and immune-deficiency by relevant investigations which were normal. His renal functions when checked last 1 year prior to admission were normal. At the time of current admission to our hospital, he weighed 23.8kg (75th - 95th percentile) and was 114 cm (50th percentile) in height. His blood pressure was 124/84 mmHg (more than 95th percentile) and clinical examination was unremarkable with no evidence of lymphadenopathy, arthritis or joint deformities. His complete blood count was normal except for increased ESR of 80 mm/hr. Biochemistry showed a BUN of

22.8 mg/dL, creatinine of 2.89 mg/dL corresponding to the GFR of 22 ml/min/m², serum bicarbonate 17.8 mmol/L, serum calcium 9.7 mg/dL, serum phosphorus 5.26 mg/dL, and serum alkaline phosphatase 326 IU/L. Urine analysis revealed 3+ albumin with normal microscopy. Urine culture for tuberculosis and fungus was negative.

On USG, he had normal sized kidneys without loss of corticomedullary differentiation; multiple enlarged mesenteric, periportal, peripancreatic lymphnodes maximum measuring 2.0 x 1.5cm. His chest radiograph and PPD test was negative. The anti-nuclear antibody test; antibodies to double-stranded DNA and anti-neutrophil cytoplasmic autoantibodies (ANCA) were not detected. The serum levels of complement (C3) and immunoglobulins (IgG, IgA, IgM) were normal. Renal biopsy showed extensive tubule interstitial infiltration by lymphocytes and multinucleated giant cells without caseous necrosis. A total 27 out of 41 glomeruli were sclerosed while remaining showed increased cellularity (**Fig 1 and 2**). Immune staining showed C₃ +++ and IgG + in mesangium, but staining for acid fast bacilli was negative. EM was suggestive of chronic proliferative glomerulonephritis and No EDDs. After a diagnosis of granulomatous interstitial nephritis had been established, further investigation was carried out to examine evidence for systemic sarcoidosis. Ophthalmologic examination was suggestive of chronic iridocyclitis, X-ray of the chest was normal. Calcium homeostasis was checked by serum calcium, 1:25 dihydroxy vitamin D, urine calcium/creatinine ratio which was normal. The serum angiotensin-converting enzyme (ACE) levels were increased at 65 (normal 8-52). CT guided biopsy of abdominal nodes was negative for tuberculosis and fungus.

Patient was given 6 pulses of dexamethasone followed by daily oral prednisolone at 2 mg/kg/day. Renal function started to improve by 6 weeks but the child became severely cushingoid and hypertensive. Mycophenolate was added at 1200 mg/m² as a steroid sparing agent and steroids were made alternate day at 1.5 mg/kg. The rate of renal recovery was very slow and at completion of 1 year of therapy, creatinine has settled down to 1.7 mg/dl. His serum calcium is still normal.

Fig 1: 10x dense tubule interstitial infiltration by lymphocytes

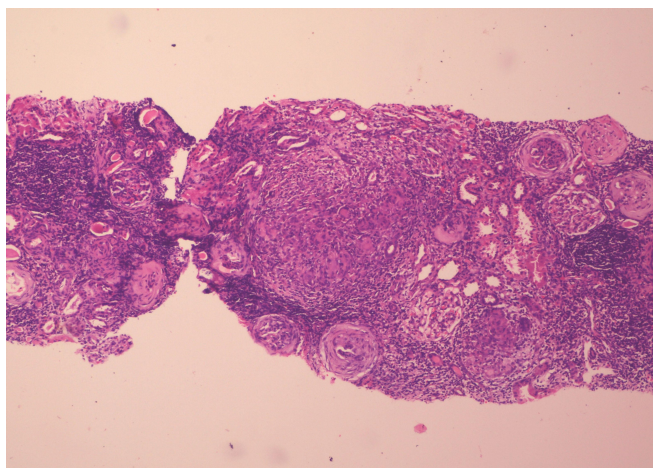
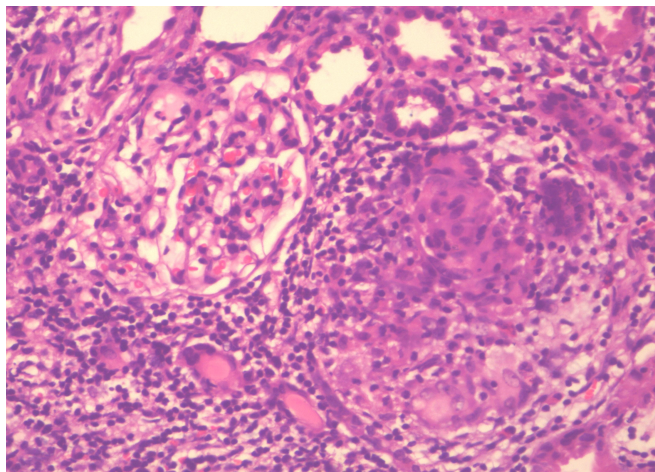


Fig 2: 40x Granuloma with multinucleated giant cells



3. Discussion

Sarcoidosis is a multi-system disorder of unknown etiology characterized by the presence of non-caseating epithelioid granulomas in multiple organs.¹ It usually manifests itself in young adults around 20-40 years of age. It is uncommon in children, with a reported incidence of 0.22–0.27 cases per 100,000 children under the age of 15 years.³ The clinical expression of the disease is dominated by the involvement of the lung which is involved in upto 90% cases. Other organs involved most often are eyes, skin, lymph nodes and liver in 25-30% cases.⁴ Kidney involvement is reported in 10% patients.⁵ Significant renal involvement leading to renal failure is uncommon⁶. It is very rare to have a young child presenting with advanced renal failure secondary to renal sarcoid without any lung involvement and hence this case is being reported.

Diagnosis of sarcoidosis is based on a combination of suggestive clinical features, with histologically documented noncaseating granuloma, in the absence of other known causes of granuloma formation. The presentation of the index case

was with renal failure secondary to granulomatous interstitial nephritis. GIN is a distinct renal pathology but is not pathognomonic of sarcoidosis. It is an uncommon histological diagnosis. A large retrospective study of native kidney biopsies found GIN in <1% of patients over a 15-year period⁷. GIN may be seen with mycobacterial and fungal infections, Wegener's Granulomatosis and drugs⁸. We concluded the diagnosis of sarcoidosis by documenting evidence of ophthalmic involvement which was clinically silent, intra-abdominal nodes, raised ACE levels and past history unexplained fevers which could be sarcoid related constitutional symptoms. Serum ACE levels are known to be elevated in 40–90% of patients⁹ and can provide useful supportive evidence of sarcoidosis as was seen in the index patient. Our patient did not have evidence of calcium dysregulation which has been common in many previously reported cases. Management of pediatric patients remains empirical, due to the absence of validated criteria of disease activity and severity. Most children with sarcoidosis receive corticosteroids, a reasonable treatment duration being 18 months. MMF¹⁰, Mizoribin¹¹, Infliximab¹² have been used in steroid resistant cases or those who develop severe steroid related side effects. We added MMF at the end of 6 weeks of therapy as a steroid sparing agent. The prognosis is variable, most cases recovering renal function in 1-6 months, others showing incomplete recovery and some progressing to ESRD in spite of immune-suppression. Our patient has shown partial renal recovery at the end of 1 year follow up.

4. Conclusion

Sarcoidosis should be considered in the differential diagnosis of granulomatous interstitial nephritis in absence of significant drug history. Systemic involvement in sarcoidosis is often clinically silent. Cases of advanced renal failure due to sarcoid GIN may stabilize and improve with steroid therapy.

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