Renal Sarcoidosis: A Case with Granulomatous Interstitial Nephritis, Renal Failure and Moderate Proteinuria

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Abstract

Sarcoidosis is a multisystem disease of unknown etiology characterized by the development of epithelioid granulomas in different organs. Most cases show pulmonary and mediastinal lymph node involvement whereas renal involvement in sarcoidosis is rare. We present the case of a female patient with extra pulmonary sarcoidosis (i.e. abdominal lymph node involvement) without calcium metabolism abnormalities but with renal involvement consisting of interstitial granulomatous nephritis and moderate proteinuria, complicated by renal failure. Oral administration of corticosteroids was successfully applied.

Key words: extra pulmonary sarcoidosis, granulomatous interstitial nephritis, proteinuria renal failure

Introduction

Sarcoidosis is a multisystem disease of unknown etiology represented by noncaseating epithelioid-cell granulomas that is a common finding developed in the affected tissues. In most cases the mediastinal lymph nodes and the lungs are involved (in >95% of patients) [1]. Extra pulmonary sarcoidosis (liver, spleen, skin, parotid gland, peripheral lymph nodes, central nervous system and so on) is reported with a variable frequency (16.6 to 80%) [2,3]. Renal involvement in sarcoidosis has been reported with variable prevalence, in some recent studies in up to 48% of the patients [4]. The renal involvement in sarcoidosis includes abnormal calcium metabolism (nephrocalcinosis, kidney stones), interstitial granulomatous nephritis, and glomerulonephritis [13]. Glomerulonephritis (GN) associated with sarcoidosis has been reported in few cases, represented mainly by membranous GN [5], focal segmental glomerulosclerosis [6], IgA nephropathy [7], or extracapillary proliferative GN [8]. In most cases at least two of the renal changes associated with sarcoidosis have been identified. We present the case of a patient with interstitial granulomatous nephritis and renal failure with a history of heavy proteinuria and no glomerular lesions on light microscopy in the renal biopsy.

Case report

A 49 years old female patient was admitted to the Nephrology Department with reduced diuresis, malaise, vomiting, fever 38.5°C, back pain, mild edema and elevated serum urea (72 mg/dl) and serum creatinine (3.9 mg/dl). The blood pressure was normal 115/70 mmHg. She had a history of repeated upper urinary tract infections. No peripheral lymph nodes, pulmonary or cardiac findings were observed in the physical examination. However, there was tenderness in the perinephric area of both sites. Chest X-ray was normal. She presented proteinuria of 2.45 g/24h and mild hematuria with dysmorphic red cells (22 RBC/HPF). Serum and urine calcium levels were normal. A marked elevation of serum IgG (3099 mg/dl) and a slight elevation of IgA (416 mg/dl) were found. Inflammatory markers were elevated with ESR of 51 mm/h and CRP 13.4 mg/dl. The patient turned out to be negative for hepatitis B and C virus markers and the investigations for SLE were also negative. Abdominal ultrasound and abdominal CT scan revealed enlarged kidneys with cortical irregularity, mild spleen enlargement and retro-peritoneal lymph nodes enlargement.

Fig. 1. Abdominal lymph node (HE staining, X200): Epitheloid cell granulomas, giant cells and Schaumann bodies
Surgical abdominal lymph node biopsy was performed and the light microscopy revealed effacement of the normal structure by numerous non-caseating epitheloid cell granulomas, giant cells and frequent Schaumann bodies (Figure 1-HE staining, x 200).

Taking in account the presence of proteinuria and impairment of renal function, a kidney biopsy was also performed. On light microscopy (HE, PAS, Trichrome and silver staining) 15 normal structured glomeruli were recognized (Figure 2-HE staining, x200) along with well defined, interstitial, noncaseating epitheloid cell granulomas. In the interstitium chronic infiltration, fibrosis and tubular atrophy were also present. (Figure 3-HE staining, x 400) Immunofluorescence for IgG, IgM, IgA and C3 was negative in the glomeruli. EM was not performed.

Under these circumstances we concluded that the patient presented an extra pulmonary sarcoidosis with interstitial granulomatous nephritis and proteinuria (2.45g/24h) complicated with renal failure. These findings raised a logical question whether proteinuria was due to minimal changes disease (since EM microscopy was not performed). Oral prednisone (60mg/day) was administered for 6 weeks, the dose being subsequently reduced gradually. Proteinuria decreased to near normal in 3 weeks and serum creatinine decreased to 1.8mg/dl in two months.

**Discussion**

The most prevalent form of sarcoidosis is the intrathoracic sarcoidosis with lung and mediastinal lymph node involvement (>90%), but peripheral lymph nodes are also frequently affected [2]. That is why, in the absence of any clinical signs for chest and peripheral lymph node sarcoidosis, the abdominal lymph node biopsy result with epitheloid noncaseating granulomas suggesting sarcoidosis was quite unexpected.

Renal involvement in sarcoidosis is clinically a rare and protean feature and significant renal failure appears in less than 2% of cases. Renal failure is mainly related to various associations of hypercalcemia and hypercalciuria with interstitial granulomatous nephritis (IGN) [1,14]. Though IGN is frequent in sarcoidosis (>20% of the cases) [8], the development of renal failure in the absence of hypercalcemia is rare (<2%) [1]. In our patient renal failure was related to biopsy proven IGN whereas abnormal calcium metabolism was detected.

In most of the IGN cases proteinuria is absent or mild [15], and the presence of proteinuria may suggest glomerular involvement. In our patient glomerular proteinuria was associated with mild dysmorphic hematuria.

Anomalous immune reactions are characteristic for sarcoidosis. Though patients do not develop predisposition to viral or fungal infections or to malignancies, depressed hypersensitivity to various antigens (tuberculin, mumps virus, Candida, dinitrochlorobenzene), the presence of immune complexes and polyclonal hypergammaglobulinemia are common. In spite of these findings, glomerular involvement in sarcoidosis is rare (less than 100 cases communicated). All types of GN, (proliferative and non proliferative) have been reported but membranous GN was more frequent [8]. Such findings raise the as yet unanswered question of whether or not the reported GNs can be linked to sarcoidosis. We have found only 4 reports about minimal changes disease associated with sarcoidosis [9-12] and in 2 of them other pathology was also involved (Graves' disease [10] and Hashimoto's thyroiditis [12]). With glomerular proteinuria and mild dysmorphic hematuria, normal glomeruli in the light microscopy and negative IF we may consider our case a minimal changes disease.

**Conclusion**

To conclude, we can say that our case supports the idea of the protean face of renal sarcoidosis, as suggested by Carmichael. Corticosteroids have been used successfully in the treatment of renal involvement in sarcoidosis and the clinical course of our patient confirmed their efficacy.

**Statement:** We have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated.

**Conflict of interest statement.** None declared.
References