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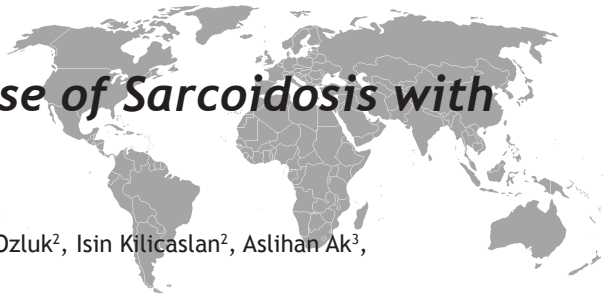
Case Report



IgA Nephropathy in the Course of Sarcoidosis with Multi-Systemic Involvement

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ABSTRACT

Sarcoidosis is a multisystemic inflammatory disease characterized by noncaseating granulomatous inflammation of unknown origin. Although, renal involvement is rare, renal manifestations of sarcoidosis include abnormal calcium metabolism, nephrocalcinosis, nephrolithiasis, nephrotic syndrome and glomerulonephritis. We report a case of sarcoidosis presented with nephrotic syndrome and diagnosed as Ig A nephropathy.

Key words: *IgA Nephropathy, massive splenomegaly, nephrotic syndrome, sarcoidosis*

Multi Sistemik Tutulumlu Sarkoidoza Eşlik Eden IgA Nefropatisi

ÖZET

Sarkoidoz nonkazeifiye granülomatöz inflamasyon ile karakterize, nedeni bilinmeyen, çok sayıda sistemi etkileyebilen, inflamatuar bir hastalıktır. Sarkoidozda böbrek tutulumu nadir olmakla beraber genellikle anormal kalsiyum metabolizması, nefrokalsinozis, nefrolitiazis, nefrotik sendrom ve glomerulonefrit şeklinde olur. Bu yazıda nefrotik sendrom ile başvuran ve renal biyopsi ile IgA nefropatisi tanısı konan bir sarkoidoz olgusu sunulmuştur.

Anahtar kelimeler: *IgA nefropatisi, massif splenomegali, nefrotik sendrom, sarkoidoz*

INTRODUCTION

Sarcoidosis is a multisystemic inflammatory disease characterized by noncaseating granulomatous inflammation of unknown origin. Bilateral hilar lymphadenopathy, pulmonary infiltrates, and skin and ocular lesions are the most frequent manifestations of sarcoidosis (1, 2). Common forms of renal involvement are noncaseating epithelioid granulomas which has been found in 9% to 26% of reported and nephrolithiasis and/or nephrocalcinosis associated with abnormalities in calcium homeostasis. Uncommon forms of renal involvement are various types of glomerulonephritis which include membranous glomerulonephritis, focal and segmental glomerulosclerosis, diffuse mesangial proliferative glomerulonephritis, mesangio-capillary glomerulonephritis, IgA nephropathy, and crescentic glomerulonephritis (1). Bone marrow involvement and massive splenomegaly are quite uncommon in sarcoidosis (3-5). Herein, we report a case of sarcoidosis with multiple organ involvements presented with nephrotic syndrome due to IgA nephropathy.

CASE

A 55 year-old woman admitted with generalized edema, abdominal distention, fatigue and cough. On physical examination, her temperature was 36.6°C, pulse was regular and with a rate of 78 bpm, blood pressure was

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112/74 mmHg, and respiratory rate was 16 breaths/min. Pretibial edema, hepatomegaly of 5 cm and splenomegaly of 10 cm were found. Examination of the chest revealed crepitations throughout basal fields of both lungs. The rest of her examination was unremarkable. Her laboratory investigation on presentation revealed a hemoglobin level of 9.5 g/dL, hematocrit of 31.0%, white blood cell count of 9.6 × 109/L, platelet count of 565 × 109/L, erythrocyte sedimentation rate of 66 mm/h, C-reactive protein of 0,67 mg/dL, blood urea of 44 mg/dL, serum creatinine of 0.77 mg/dL, total protein of 7.45 g/dL, albumin of 2.76 g/dL, corrected calcium of 9.5 mg/dL, phosphorus of 3.23 mg/dL, alanine aminotransferase (ALT) of 61 IU/L (range, 0-38), aspartate aminotransferase (AST) of 51 IU/L (range, 0-31), alkaline phosphatase (ALP) of 353 IU/L (range, 30-120), serum gamma glutamyl transpeptidase (GGT) of 209 IU/L (range, 0-38), total bilirubin of 0.7 mg/dL, direct bilirubin of 0.13 mg/dL, lactate dehydrogenase (LDH) of 328 IU/L (range 0-247) total cholesterol of 250 mg/dL, LDL cholesterol of 166 mg/dL, triglyceride of 80 mg/dL. Protein electrophoresis revealed polyclonal gammopathy. Further blood analysis was normal for prothrombin time and activated partial thromboplastin time, electrolytes, folic acid, vitamin B12, tumor markers, culture and sensitivity. She has nephrotic range proteinuria of 3.5 g / day. ANA, Anti-dsDNA, ANCAs, HBsAg, anti-HCV antibody and anti-HIV were negative. Anti-HBs was positive. Serum complement C3 and C4 were within normal levels. Serum IgA of 614 mg/dL (range 82-453).

In thorax CT, bilateral mediastinal lymphadenopathy and bilateral interstitial infiltrates were detected. Bronchoalveolar lavage (BAL) was negative for acid-resistant bacilles (ARBs), fungal or bacterial growth, and abnormal cytology. BAL cultures remained negative for tuberculosis. Sampling of cells had a lymphocyte predominance. CD4/CD8 ratio was high as 3.77 in the BAL. Mediastinoscopic biopsy of the mediastinal lymph nodes showed granulomatous inflammation. Laparoscopic splenectomy was performed and microscopic examination also showed chronic granulomatous inflammation without caseification necrosis. In bone marrow biopsy, non-caseating granulomatous inlammation was found. Angiotensin converting enzyme activity was high in serum. Echocardiography was normal. Ophthalmological examinations were normal.

Renal biopsy was performed due to proteinuria and hematuria. Renal biopsy were consistent with IgA nephropathy (Figure-1 and 2). Ultimately, the patient was considered as a case of sarcoidosis which has lung, liver, bone marrow and splenic involvement accompanied by IgA nephropathy. The treatment with methylprednisolone 32 mg / day and ramipril 5 mg / day was started. The patient was clinically well-responded to the treatment and proteinuria decreased from 3.5 g/day to 500 mg/day after 2 months. She is still on immunosuppressive therapy (methyprednisolone 5 mg/day) and ramipril without any complaint.

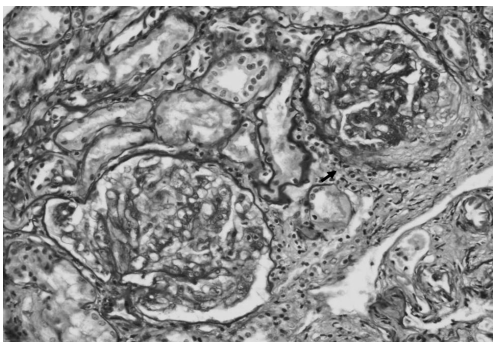

***Figure 1**. Glomeruli show increase in mesangial matrix and cellularity. Note segmental sclerosis and fibrocellular crescent (arrow) (PAS 200x)*

DISCUSSION

Sarcoidosis is a systemic disease of unknown origin characterized by granulomatous lesions in various organs. Two thirds of patients are asymptomatic and are usually diagnosed during a routine check-up via bilateral

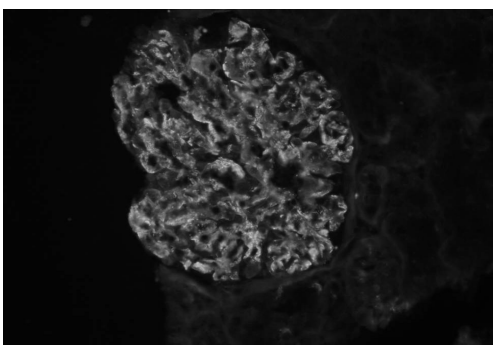

***Figure 2**. Immunofluorescence microscopy revealed positivity for anti IgA antibody in the mesangium and basement membranes (Anti IgA FITC 200x)*

hilar lymph nodes seen on chest film (1). The illness may be self-limited or chronic, with episodic recurrence and remissions. Clinical signs are depends on disease duration, affected organs, the extent of involvement, and activity of granulomatous event. Renal manifestations due to sarcoidosis generally include abnormal urinary calcium metabolism such as hypercalcemia, nephrocalcinosis, and nephrolithiasis (2). The other forms of renal involvement of sarcoidosis are as follows; interstitial granulomatous nephritis, membranous glomerulonephritis, focal segmental glomerulosclerosis, diffuse mesangial proliferative glomerulonephritis, mesangiocapillary glomerulonephritis, IgA nephropathy, and crescentic glomerulonephritis (1,2). Granulomatous tubulointerstitial nephritis may be associated with acute renal failure, and can lead to hemodialysis (1). Renal failure due to sarcoidosis ranges from 0.7% to 4.3% of previous clinical series (6).

The simultaneous presentation of sarcoidosis and IgA nephropathy is rare (7). The relationship between IgA nephropathy and sarcoidosis has been disputed. Both conditions are systemic disorders with unknown origin. Familial clustering has been reported in both IgA nephropathy and sarcoidosis (8,9). Some studies showed a strong association between Ig A nephropathy and sarcoidosis due to the increased Ig A levels in both disease (7,10). Some small-scale studies do suggest an association between sarcoidosis and IgA nephropathy (11). The present case may provide suggestive pathogenetic evidence for a link between sarcoidosis and IgA nephropathy. Corticosteroid treatment is the corner stone of treatment. In refractory cases, other immunosuppressive regimens might be used. Usually the response to corticosteroids is good with improvement in disease activity within 2-3 months. We preferred using steroids in our patient, and had a good response to this treatment.

Sarcoidosis complicated by IgA nephropathy is rare, and thus is of particular interest because common immunological abnormalities might be considered in the disease process of both diseases. The growing evidence and increasing number of cases show an association between sarcoidosis and IgA nephropathy. Meanwhile, it is suggested that this association should be kept in mind while dealing with either of these conditions.

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