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EARLY ONSET OF IgA NEPHROPATHY PRESENTING WITH NEPHROTIC SYNDROME

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ABSTRACT

A 5-year-old boy was admitted to our hospital with the complaint of swelling of his whole body. Urine analysis revealed nephrotic range proteinuria and microscopic hematuria. He was normotensive. Complement C3 and C4 levels were normal. Antinuclear antibodies (ANA) were negative. A percutaneous renal biopsy was performed because of the persistent proteinuria despite a full course of 4 weeks of steroid treatment. The renal biopsy was consistent with IgA nephropathy. Then cyclophosphamide was added to the treatment. Proteinuria disappeared after 12 weeks of cyclophosphamide treatment. This case of IgA nephropathy is reported because of the early age of onset and because of presenting with nephrotic syndrome.

Key Words: Children, IgA Nephropathy, Nephrotic Syndrome.

ERKEN YAŞTA NEFROTİK SENDROM KLİNİĞİ İLE ORTAYA ÇIKAN IgA NEFROPATİSİ

ÖZ

5 yasında erkek hasta hastanemize vucudunda sislik nedeniyle basvurdu. İdrar analizinde mikroskopik hematüri ve nefrotik düzeyde proteinüri saptandı. Kan basıncı normal sınırlardaydı. Kompleman 3 ve 4 düzeyleri normal, ANA negatifti. Hastaya 4 hafta süreyle prednizolon tedavisiverilmesine rağmen proteinürisi sebat ettiği için perkütan böbrek biyopsisi yapıldı. Biyopsi IgA nefropatisi ile uyumluydu. Tedaviye siklofosfamid eklendi. Proteinuri 12 haftalık siklofosfamid tedavisinden sonra düzeldi. Bu IgA nefropati olgusu erken yasta nefrotik sendrom kliniği ile ortaya çıkması sebebiyle rapor edilmistir.

Anahtar Kelimeler: Çocuk, IgA Nefropati, Nefrotik Sendrom.

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INTRODUCTION

In 1968 Berger and Hinglais reported for the first time a form of glomerulonephritis (GN) characterized by mesangial deposition of IgA.[1] Electron microscopy showed the presence of dense deposits between the glomerular basement membrane and the mesangial cells. IgA-nephropathy (IgAN) is the most common form of primary GN. It was initially considered a benign disorder, but recent data revealed that renal failure occurs in about 20-50% of cases.[2] The pathogenesis is unknown and there is no consensus about treatment. In some cases, at any age, a nephrotic or a nephritic syndrome may constitute the first sign.[3] Age at the onset of the first clinical manifestations of primary IgAN ranges between 15 and 30 years and this is often 7 to 10 years before a definitive diagnosis is made by means of biopsy.[4] We report a patient with an early age of onset presenting with nephrotic syndrome.

CASE REPORT

A 5-year-old boy was admitted to our hospital with the complaint of coughing and swelling of his whole body. He had a 10-day history of upper respiratory infection with mild coughing before admission. His past history revealed no hematuria, proteinuria, rash, abdominal pain, or arthritis/arthralgia, and no family history of renal disease. On physical examination there were periorbital edema and bilateral pitting edema of both legs. He was normotensive. Laboratory studies revealed the following data: hemoglobin 11.7 g/dl, white blood cell count 10,900/mm3, platelets 192,000/mm3, erythrocyte sedimentation rate 108 mm/h, total protein 3 g/dl, albumine 1.49 g/dl, cholesterol 329 mg/dl, triglyceride 448 mg/dl, and serum IgA 163 mg/dl. Serum electrolytes, AST, ALT, urea, and creatinine levels were within the normal ranges. Urinalysis revealed nephrotic range proteinuria (118 mg/m2/h) and microscopic hematuria. Complement C3 (138 mg/dl) and C4 (26 mg/dl) levels were normal and tests for antinuclear antibodies (ANA), HBsAg, and Anti HCV were negative. A percutaneous renal biopsy was performed because of the persistent proteinuria despite a full course of 4 weeks of steroid treatment. The renal biopsy showed an increase in the mesangial matrix, thickening of basement membrane, and different degrees of hypercellularity without tubulointerstitial changes (Fig. 1). Immunofluorescence microscopy showed IgA, IgG, and fibrinogen deposition diffusely in the mesangium and basement membrane (Fig. 2). The findings were consistent with IgAN. Then cyclophosphamide was added to the treatment. Proteinuria disappeared after 12 weeks of cyclophosphamide treatment.

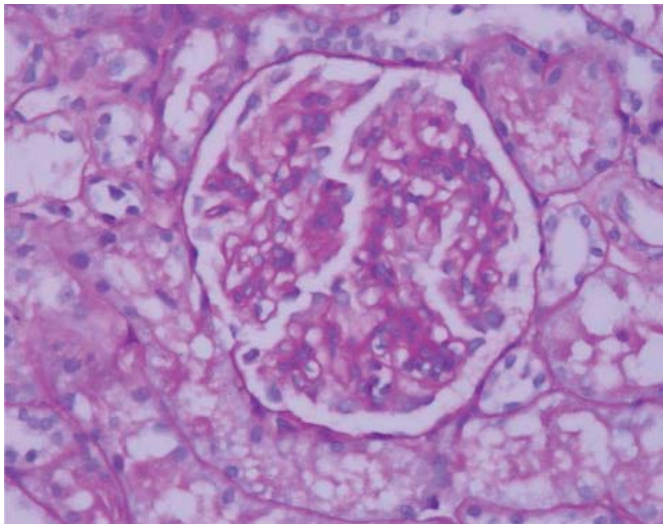

Figure 1: Mild mesangial matrix expansion with mild increase in mesangial cellularity (PAS, Original magnification: x400).

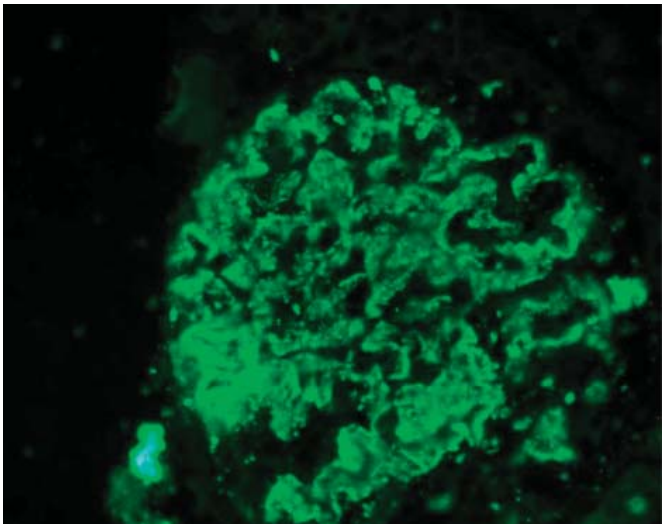

Figure 2: IgA staining in the mesangium with extension to peripheral capillary loops (anti-IgA immunofluorescence, original magnification: x400).

DISCUSSION

IgA nephropathy is a form of glomerular disease usually diagnosed in patients with recurrent macroscopic hematuria or microscopic hematuria following a respiratory tract infection. Although its etiology and pathogenesis remain unclear, there is substantial evidence suggesting that it is an immune complex associated disease.[5] Its prevalence varies from one country to another. In France, Japan, Australia, and Italy it accounts for between 18% and 40% of all primary glomerular diseases, whereas in England, America, and Canada it is responsible for only 2-10%.[6] Affected children do not present with symptoms before the age of 3 years.[3] Ozkaya et al. reported 392 Turkish children who were diagnosed with nephrotic syndrome.[7] Kidney biopsy was performed in 112 patients and only one patient with IgAN was above 6 years old. Our patient showed an early age of onset, presenting at 5 years old.

Henoch-Schönlein purpura (HSP) and chronic liver disease should be considered in patients who show mesangial IgA deposition on kidney biopsy. There is a close relationship between IgAN and HSP. Although there are similarities in their pathologic and immunologic features, the two conditions are clinically different, and the pathogenesis is not clear.[4] While HSP nephritis is an acute disease with glomerular lesions nonprogressive after onset, occurring mostly in young children, IgAN is a chronic, slowly progressive glomerular lesion, which may eventually lead to chronic renal failure, affecting mainly older children and adults.[8] Our patient did not have a clinical history of HSP previously.

Patients with end-stage liver disease are prone to hemodynamic and immunologic renal injury, the latter at times manifesting as glomerulonephritis. Elevated serum IgA levels and mesangial IgG-IgA deposits are common in these patients, but are often clinically silent. Singri et al. reported a patient with autoimmune hepatitis and secondary IgA nephropathy (IgAN) who presented with nephrotic syndrome.[9] Our patient's IgA levels and liver function tests were within the normal ranges and ANA, HBsAg, and Anti HCV were negative.

In children, several studies have shown that the degree of proteinuria correlates with the severity of morphological glomerular lesion, and heavy proteinuria at the time of the biopsy predicts a poor outcome.[3,10,11]Patients showing diffuse mesangial proliferation have been reported to have a significantly worse prognosis than those with focal proliferation or with minimal lesions by light microscopy.[12] Levy et al. found that mesangial proliferative glomerulonephritis with crescents was associated with poor prognosis in children.[3] Yoshikawa et al. showed that 10% of children with IgAN developed chronic renal failure 20 years after diagnosis.[13] Although, among the pathologic features analysed in our patient, diffuse mesangial proliferation, absence of macroscopic hematuria, and the onset with nephrotic syndrome are associated with poor outcome, early age of onset, normal blood pressure, absence of tubulointerstitial changes, and non-persistent proteinuria are good indicators for the prognosis.

The treatment modalities of IgAN include prophylactic administration of antibiotics or tonsillectomy to prevent potential entry of microbial agents, glucocorticoids, immunosuppressive drugs, phenytoin, danazol to manipulate the abnormal immune response, and plasma exchange to remove IgA immune complexes.[2] Although prophylactic antibiotics and tonsillectomy may reduce the frequency of pharyngitis and macroscopic hematuria episodes, the effect on the progression to renal failure remains controversial. Glucocorticoids are beneficial in few patients with nephrotic syndrome and minimal mesangial lesions. A controlled trial performed by the Japanese Pediatric IgAN Treatment Study Group indicated that the treatment of severe pediatric IgAN with prednisolone, azathioprine, heparin/warfarin, and dipyridamole for two years early in the course of the disease prevents progression.[14] Omega-3-polyunsaturated fatty acids and angiotensin converting enzyme (ACE) inhibitors are found to be beneficial in

the treatment of IgAN. Omega-3-polyunsaturated fatty acids are used to limit the production or the action of cytokines and eicosonoids elicited by the initial renal injury. ACE inhibitors reduce glomerular hypertension, and studies showed a favorable effect on reduction in proteinuria and the rate of renal function decline after 1 year.[15] Proteinuria persisted in our patient despite a full course of four weeks of steroid treatment. Twelve weeks of cyclophosphamide treatment were necessary to resolve the proteinuria in our patient.

We reported this case of IgAN because of the early age of onset and because of presenting with nephrotic syndrome.

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