Case Report / Olgu Sunumu

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A Cause of Nephrotic Syndrome Rarely Seen in Adults: IgM Nephropathy

Yetişkinde Nadir Görülen Nefrotik Sendrom Nedeni: IgM Nefropatisi

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Abstract / Özet

IgM nephropathy is one of the rare causes of glomerulonephritis, characterized by a clinical picture ranging from asymptomatic urinary disorders to proteinuria severe enough to cause nephrotic syndrome, and is more frequently seen in children and adolescents. Under a light microscope, there are minor changes and focal segmental glomerulosclerosis (FSGS), like mesangial proliferation in various degrees. Although IgM nephropathy is considered a refractory variant of minimal change disease (MCD), there is no agreement on the treatment of IgM nephropathy, and it seems that the success of treatment with steroids is not as effective as the treatment of MCD. In this report, we will present our experience with the treatment of a case of a patient with primary IgM nephropathy with steroids and cyclosporine. In this case, edema and ascites completely disappeared, and complete remission was obtained within 2 months of treatment with a combination of prednisolone and cyclosporine. We can suggest that a combination of cyclosporine and a steroid, together with recommendations generally made in nephrotic syndrome, can be useful in the absence of contraindications for the treatment of IgM nephropathy, which is rarely seen in adults.

Key Words: Cyclosporine, IgM nephropathy, minimal change disease, nephrotic syndrome

IgM nefropatisi daha ziyade çocuk ve gençlerde görülen asemptomatik idrar bozukluklarından nefrotik düzeyde proteinüriye kadar değişen tablolarla seyreden nadir glomerulonefrit nedenlerinden biridir. Işık mikroskop incelemede minör değişiklikler ve fokal segmental glomeruloskleroz (FSGS) benzeri değişik derecelerde mezangial proliferasyon vardır. Tedavi konusunda uzlaşılmış bir görüş olmasa da minimal değişim hastalığı ve/veya FSGS'de olduğu kadar steroidle tedavi başarısı az görünmektedir. Olgumuzda primer Ig M nefropati tanısı olan erişkin hastada steroid ve siklosporin tedavi deneyimimiz anlatılmaktadır. Siklosporin ve prednisolon tedavi kombinasyonu ile ikinci ayda ödem ve asiti tamamen kaybolan hasta tam remisyona girdi. Yetişkinlerde nadir görülen IgM nefropatisi vakalarında tedavide genel nefrotik sendrom önerileri eşliğinde, kontredikasyon yoksa siklosporin ve steroid kombinasyonlu rejiminin yaralı olacağı kanısındayız.

Anahtar Kelimeler: IgM nefropatisi, minimal değişim hastalığı, nefrotik sendrom, siklosporin

Introduction

IgM nephropathy is one of the rare causes of glomerulonephritis, characterized by a clinical picture ranging from asymptomatic urinary disorders to proteinuria severe enough to cause nephrotic syndrome, and is more frequently seen in children and adolescents. It was first described by Bhasin (1). IgM nephropathy is one of the three conditions in which there are minor changes of minimal change disease (MCD) under a light microscope. The other conditions are C1q nephropathy and idiopathic mesangial proliferative glomerulonephritis (2).

Under a light microscope, there are minor changes and focal segmental glomerulosclerosis (FSGS), like mesangial proliferation, in various degrees. While some claim that IgM nephropathy is a refractory variant of MCD and FSGS, others think that it is a distinct pathological condition (3). What causes primary IgM nephropathy is not known. Secondary IgM nephropathy may appear in such conditions as systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus, paraproteinemia and Alport syndrome (4). Although similar to IgA nephropathy, there is no structural and biochemical abnormality in IgM molecule (5).

IgM nephropathy is characterized by clinical asymptomatic hematuria, macroscopic hematuria attacks, and proteinuria. Evidence available in the literature has mostly been derived from children, and the frequency of hypertension in this condition is related to the course of the disease (6). Myllymaki et al. (7) in their study, showed that 23% of the patients with IgM nephropathy had end-stage renal disease during a 15-year follow-up.

It was previously reported that response to steroids is not satisfactory in this disease (8). In this report, we will present our experience with the treatment of the case of primary IgM nephropathy with a combination of steroid and cyclosporine.

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Case Report

This article has been stared based on patient consent. A 38-year-old female patient without any previous chronic disease presented to our nephrology outpatient clinic with edema in both lower extremities that was present for the last 1 month. The history did not show any remarkable conditions, medication use, allergy, or a systemic disease. The patient did not have accompanying macroscopic hematuria, dysuria, shortness of breath, or high blood pressure. On physical examination, the patient had a good general health status and was conscious, his blood pressure was 130/80 mm Hg, and his heart rate was 76/min, but he had severe bilateral pretibial edema and abdominal ascites. Laboratory investigations showed that hemoglobin was 12 gr/dL, white cell count was 6000/mm^3, platelet count was 320,000/mm^3, erythrocyte sedimentation rate was 30 mm/hour, CRP was 3 mg/dL, urea was 23 mg/dL, creatinine was 0.8 mg/dL, potassium was 4.0 mEq/L, sodium was 140 mEq/L, and serum albumin was 2.3 g/dL. Urinalysis showed that urine density was 1015, protein was 500 mg/dL, white cell count was 1/HPF (high-power field), and erythrocyte count was 10/HPF. Since the patient was found to have hematuria and proteinuria, she was hospitalized. Analysis of the 24-hour urine revealed that daily protein excretion was 6990 mg. Renal ultrasonography revealed that the sizes of the kidneys and thickness and echogenicity of the parenchyma were normal, and there was no obstructive lesion or hydronephrosis. Renal vascular structures were natural, and there were no signs of arterial or venous thrombosis in the renal Doppler ultrasonographic examination. Further investigations showed that serum C_3, C_4, IgA, and IgG levels were normal but that serum IgM level was high at a rate of 3.15 g/L (0.46-3.04 g/L). Tests for HBsAg, anti-HCV, ANA, anti-DNA, RF, p-ANCA, c-ANCA, and anti-GBM antibodies were all negative. Urine culture was negative. Urine and serum immunofixation electrophoresis and serum light chain levels were normal.

Renal biopsy was performed to elucidate the etiology of nephrotic syndrome. Light microscopic examination was normal with the absence of endo- or extracapillary proliferation, mesangial hyperplasia, necrosis or karyorrhexis, segmental sclerosis, and a normal glomerular capillary wall. Immunofluorescence examination showed diffuse global granular IgM staining (+2) in mesangial areas and a low degree of fine granular C_3 staining. Based on the findings mentioned above, the patient was diagnosed as primary IgM nephropathy.

She was prescribed a diet restricted in salt and protein, ramipril 5 mg/day, prednisolone 1 mg/kg/day, and cyclosporine 5 mg/kg/day. Second-hour serum cyclosporine levels were 350-400 ng/mL. Within 1 month of the treatment, ascites and edema regressed, proteinuria decreased to 950 mg/day, and serum albumin increased to 3.2 g/dL. The dose of the steroid decreased by 4 mg weekly. Within 2 months of treatment, proteinuria was 150 mg/day, serum albumin was 4 g/dL, and edema and ascites completely disappeared. Serum creatinine levels were normal and ranged from 0.8 to 0.9 mg/dL from the beginning to the end of the treatment. The patient is still under steroid (methylprednisolone 4 mg/day) and calcineurin inhibitor (cyclosporine 250 mg/day) treatment and is being followed monthly.

Discussion

Although primary IgM nephropathy is most commonly seen in children and adolescents, it is rarely observed in adults. An experienced nephropathologist is needed for the diagnosis of this condition (9). It is treated with a salt- and protein-restricted diet and with rennin-angiotensin-aldosterone system blockers, as in other nephrotic syndromes. There is no agreement on the immunosuppressive treatment of IgM nephropathy, and although there has not been a randomized study on the treatment of IgM nephropathy, it seems that treatment with steroids is not as effective as treatment of MCD. Many studies have revealed steroid resistance or dependence in 50% of the cases (8, 10). There are little data on the use and response rates of immunosuppressive agents in patients with IgM nephropathy (11, 12).

In a Hamed study, pediatric patients with steroid-resistant IgM nephropathy were treated with cyclophosphamide and cyclosporine. Cyclosphosphamide 2.5 mg/kg body weight/day had been prescribed to one steroid-resistant patient for 13 weeks but was ineffective. Seventeen patients with steroid-resistant received cyclosporine A (CsA). CsA was started in eligible children at a dose of 5 mg/kg body weight per day. Eight patients responded to CsA, and seven patients showed no response to CsA, two of whom developed gradual loss of renal function and eventually died from end-stage renal failure. CsA was offered to these patients for periods varying from 4 to 29 months (11).

In a Swartz study that was conducted in a pediatric group of patients, the response to cyclophosphamide was reported to be similar to that obtained with steroids, but the response to cyclosporine was good. In their study on 23 children with IgM nephropathy, they compared the efficacy of adjuvant treatment with cyclophosphamide and CsA. Few of the children (18%) responded to cyclophosphamide. Response to CsA was significantly better, with 88% achieving complete or partial remission (12).

Conclusion

In light of the previous literature data about the unfavorable response to steroids in IgM nephropathy, initial combination treatment with cyclosporine and steroids may be appropriate. However, further controlled studies with a large sample size are needed.

Informed Consent: Written informed consent was obtained from the patient who participated in this case.

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