A Case of Celiac Disease with Focal Segmental Glomerulosclerosis Leading to End-Stage Renal Disease

Son Dönem Böbrek Yetmezliğine İlerleyen Fokal Segmental Glomerülosklerozlu Bir Çölyak Hastalığı Olgusu

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ABSTRACT In this case report a 5-year-old girl is presented who had Celiac disease and presented with nephrotic syndrome due to focal segmental glomerulosclerosis. Her intestinal biopsy which had been performed 2 years previously had revealed chronic duodenitis characterized by total villous atrophy and crypt hyperplasia. She presented with abdominal cramps, diarrhea, nausea, vomiting, failure to thrive and generalized edema while she was on gluten-free diet and in clinical remission for the disease. Kidney biopsy was performed considering the probable diagnoses of nephrotic syndrome and renal failure. The histopathological diagnosis was a cellular type focal segmentary glomerulosclerosis. A progressive deterioration could not be prevented in renal functions despite all therapeutic approaches including pulse methylprednisolone and cyclophosphamide administration. An end-stage renal disease (ESRD) developed within eight months, and the patient died due to the cardiovascular complications of ESRD 18 months after the initial presentation of renal findings. Very rare association of progressive glomerular disease and Celiac disease should be kept in mind during the follow-up of any child with Celiac disease

Key Words: Renal insufficiency; celiac disease; glomerulosclerosis, focal segmental

ÖZET Bu yazıda, çölyak hastalığı olan beş yaşında bir kız olguda nefrotik sendrom ile prezente olan fokal segmental glomerüloskleroz olgusu sunulmuştur. Olgunun iki yıl önceki intestinal biyopsisinde total villus atrofisi ile birlikte kript hiperplazisi gözlenmiş idi. Hasta glutensiz diyet ile hastalık klinik remisyonda iken abdominal kramplar, diyare, bulantı, kusma, gelişme geriliği ve genel ödem ile başvurdu. Böbrek biyopsisi nefrotik sendrom ve böbrek yetmezliği ile uyumlu olarak rapor edildi. Histopatolojik tanı selüler tip fokal segmental glomerüloskleroz olarak sonuçlandı. Pulse metilprednizolon ve siklofosfamid dâhil yapılan tüm tedavi girişimlerine rağmen olgudaki ilerleme önlenemedi. Son dönem böbrek yetmezliği sekiz ay içinde gelişti ve hasta ilk başvurusundan 18 ay sonra son dönem böbrek yetmezliğinin kardiyovasküler komplikasyonlarından dolayı kaybedildi. Çölyak hastalıklı çocuklarda ilerleyici glomerüler hastalık ve çölyak hastalığı birlikteliği akıldan çıkarılmamalıdır.

Anahtar Kelimeler: Böbrek yetmezliği; çölyak hastalığı; glomerüloskleroz, fokal segmental

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Celiac disease (CD) is one of the most common chronic disorders encountered during childhood. Its prevalence is reported as 0.5-1%.[1] Diagnosis of focal segmental glomerulosclerosis (FSGS) is based on the kidney biopsy findings. The classical lesion of FSGS is characterized by the presence of a scarring lesion in a segment of some, but not all glomeruli.[2] There are two forms of FSGS; idiopathic and secondary forms. Focal prolif-

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erative glomerulonephritis (such as IgA nephropathy, lupus nephritis, pauci-immune focal necrotizing and crescentic glomerulonephritis) is a cause of secondary FSGS.[3] IgA nephropathy, immune complex-associated or membranoproliferative glomerulonephritis are the most common forms of renal involvement in patients with Celiac disease.[4] Secondary forms of FSGS are generally considered to result from maladaptive responses that occur due to loss of functioning nephrons, hyperfiltration or increased glomerular pressure. It was demonstrated that loss of podocytes which starts with injury to the podocytewas pivotal in FSGS resulting from these maladaptive responses.[5] The damaged podocytes detach from the glomerular basement membrane (GBM), ultimately followed by loss of entire cell into Bowman's space. Next, parietal epithelial cells covering Bowman's capsule attach to the bare GBM, leading to the formation of an adhesion between capillary tuft and Bowman's capsule. At the site of the adhesion, a gap develops in the parietal epithelium. To our knowledge, no studies have reported the association of focal segmental glomerulosclerosis with CD so far.

We herein report a 5-year-old girl who had Celiac disease and presented with nephrotic syndrome and renal failure due to biopsy-proven cellular type focal segmental glomerulosclerosis.

CASE REPORT

A 5-year-old girl presented with abdominal cramps, diarrhea, nausea, vomiting, failure to thrive and generalized edema.

Physical examination was revealed pallor and edema of the patient. Other systems examinations were not found pathologic signs. Case of height 102 cm (3%) and weight 14.8 kg (3%) were detected. Laboratory testresults were as follows: Hgb: 9.8 g/dL, Hct: 28%, platelet count 154 000 mm^3, AST: 78 IU/L, ALT: 102 IU/L, pH: 7.38, HCO_3: 22, Base excess (BE): 4.7. She had been under the follow up of the Department of Pediatric Gastroenterology with the diagnosis of biopsy proven CD for two years. Results of the laboratory investigations on admission were normal except for hypertriglyceridemia, hypercholesterolemia, hypoalbuminemia (2.1 g/dL), metabolic acidosis and severe proteinuria (4.5 g/m^2/day). On the follow-up of Gastroenterology department, the patient was given a dietary treatment and on the control visit of case it was seen that her compliance to diet was not good. In addition, it was learned that she did not come her follow-up visits until 5 years of age. Titers of HBs Ag, anti HBs, anti HBC, anti-HCV, anti-HIV antibodies, and serological screening for anti-nuclear antibodies (ANA), anti ds-DNA, anti ss-DNA, glomerular basement membrane antibodies (Anti-GBM), anti-neutrophyl cytoplasmic antibodies (ANCA) and anticardiolipin antibodies were all negative. Serum immunoglobulines, complement 3 (C3) and 4 (C4) levels were normal, while the titers of lgA and lgG type antigliadine antibodies were found as positive. Microscopic examination of the biopsy specimens revealed focal segmental sclerotic lesion with cellular type in seven of 16 glomeruli (Figure 1, 2). Immunofluorescence microscopy showed a mild degree of granular type lgG, lgM and C3 deposition on the mesangium, but there were no lgA, C_4 or fibrinogen deposits. Electron microscopic evaluation revealed segmental endocapillary hypercellularity occluding lumens, and glomerular basement membrane was moderately thickened. Her renal function tests deteriorated progressively, and end-stage renal disease (ESRD) developed within eight months. Peritoneal dialysis and other supportive renal replacement therapies were performed after development of end- stage renal failure.

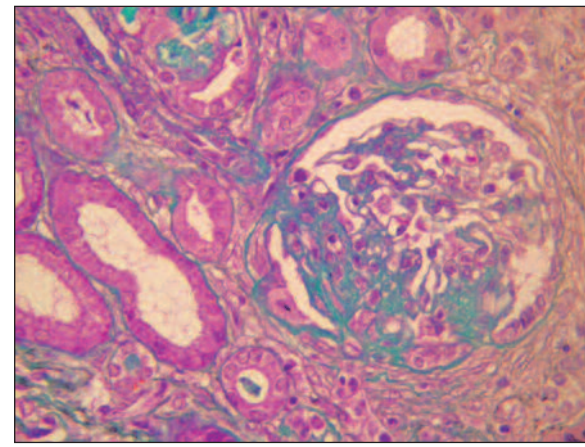

FIGURE 1: Segmental sclerotic lesion (Masson-Trichrome stain, x310).
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

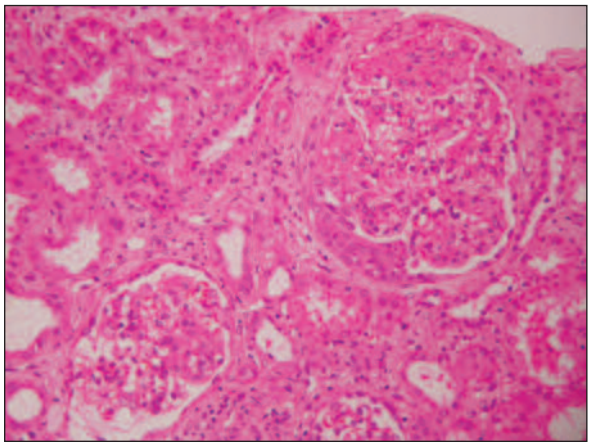

FIGURE 2: Segmental sclerosis (HE, x125).
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

DISCUSSION

The association of Celiac disease with immune complex glomerulonephritis has been reported previously.[6] The most common renal manifestations of CD are hematuria and/or proteinuria with normal renal functions. The presentation of CD with renal failure due to cellular type FSGS is a very rare condition in children.[7] The renal presentation of our patient was nephrotic syndrome and renal failure, which has rarely been reported in the literature.[7,8] Prognosis has reportedly been poor in patients with FSGS, and more than 50% of the patients develop ESRD within five years. Cellular forms of FSGS are relatively rare in childhood, and the association of this type of FSGS with CD has not been reported in children before. The evidence-based data on treatment are very limited in children.[9,10] Our treatment of choice for the present patient was high dose intravenous methylprednisolone pulses and intravenous cyclophosphamide, as described previously.[11] We suggest that rapidly progressive crescentic type FSGS should be taken into account as a possibility in patients with CD, and renal biopsy should be promptly performed in patients presenting with renal failure. Although the incidence of typical Celiac disease appears to be decreasing, and there is an increase in the atypical forms, we suggest that the possibility of the development of several forms of glomerular disease and the rapidly progressive course associated with typical or atypical (occult) Celiac disease should be kept in mind during the follow-up of any child with Celiac disease.

REFERENCES

1. Catassi C, Rätsch IM, Fabiani E, Rossini M, Bordicchia F, Candela F, et al. Coeliac disease in the year 2000: exploring the iceberg. Lancet 1994;343(8891):200-3.
2. Schwartz M. Focal segmental glomerulosclerosis. In: Jennette J, Olson J, Schwartz M, Silva F, eds. Heptinstall's Pathology of the Kidney. 6th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2007. p.155-204.
3. D'Agati VD, Fogo AB, Brujin JA, Jennette JC. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. Am J Kidney Dis 2004;43(2):368-82.
4. Johnston SD, Watson RG, McMillan SA, Sloan J, Love AH. Prevalence of coeliac disease in Northern Ireland. Lancet 1997;350 (9088):1370.
5. Kriz W, Gretz N, Lemley KV. Progression of glomerular disease: is podocyte the culprit? Kidney Int 1998;54(3):687-97.
6. Rees AJ, Cameron JS. Crescentic glomerulonephritis. In: Cameron JS, ed. Oxford Textbook of Clinical Nephrology. 1st ed. Oxford: Oxford University Press; 1992. p.418-38.
7. Scholy J, Freeman HJ. Celiac sprue-associated immune complex glomerulonephritis. J Clin Gastroenterol 1986;8(2):181-3.
8. Schwartz MM, Korbet SM. Primary focal segmental glomerulosclerosis: pathology, histological variants, and pathogenesis. Am J Kidney Dis 1993;22(6):874-83.
9. Noel LH. Morphological features of primary focal and segmental glomerulosclerosis. Nephrol Dial Transplant 1999;14(Suppl 3):53-7.
10. Kansu A. [Recent advances in celiac disease]. Turkiye Klinikleri J Pediatr Sci 2007;3(7):18-24.
11. Paydas S. [Focal segmental glomerulosclerosis]. Turkiye Klinikleri J Int Med Sci 2006; 2(21):15-24.