Focal Segmental Glomerulosclerosis in a Patient Associated with Kappa-Light Chain Disease

Bir Hastada Kappa Hafif Zincir Hastalığıyla İlişkili Fokal Segmental Glomerüloskleroz

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ABSTRACT

Focal segmental glomerulosclerosis is a non-inflammatory glomerulopathy associated with nephrotic syndrome and end-stage renal failure. Focal segmental glomerulosclerosis related to plasma cell disorder is not common. A 46-year-old man presented to our outpatient clinic with lumbar pain that had been present for two years. He had been taking non-steroid anti-inflammatory drugs for two years because of his pain. He had no history of any systemic disease. Physical examination revealed a body mass index of 20 kg/m^2, blood pressure of 150/90 mmHg, 2+ bilateral lower extremity pitting edema and lumbar vertebrae sensitivity. We described a patient found to have nephrotic syndrome on the first medical examination, and lytic bone lesion and monoclonal gammopathy of the kappa light-chain type later on. A renal biopsy was performed and the histopathological findings were consisted with FSGS. Monoclonal gammopathy should be considered as the underlying disease in any patient diagnosed with focal segmental glomerulosclerosis.

KEY WORDS: Focal segmental glomerulosclerosis, Light chain disease, Multiple myeloma, Nephrotic syndrome

ÖZ

Fokal segmental glomerüloskleroz nefrotik sendrom ve son dönem böbrek yetmezliğiyle ilişkili inflamatuvar olmayan bir glomerülopatidir. Monoklonal gamopatiye ikincil gelişen fokal glomerüloskleroz yaygın bir durum değildir. Kırk altı yaşında erkek hasta 2 yıldır devam eden bel ağrısıyla kliniğe başvurdu. Ağrı nedeniyle 2 yıldır non-steroid anti-inflamatuvar ilaç kullanım dışında sistemik bir hastalık öyküsü yoktu. Fizik muayenede, vücut kitle indeksi 20 kg/m^2, kan basıncı 150/90 mmHg, bilateral alt ekstremitede 2+ gode bırakan ödem ve lomber vertebralarda duyarlılık mevcuttu. Burada ilk tıbbi incelemede nefrotik sendrom, daha sonra litik kemik lezyonları ve kappa hafif zincir monoklonal gamopati tespit edilen bir hasta tanımlanmıştır. Renal biyopsi sonrasında histopatolojik inceleme fokal segmental glomerülosklerozla uyumlu bulundu. Fokal segmental glomerüloskleroz tespit edilen hastalarda altta yatan ikincil neden olarak monoklonal gamopati düşünülmelidir.

ANAHTAR SÖZCÜKLER: Fokal segmental glomerüloskleroz, Hafif zincir hastalığı, Multipl miyelom, Nefrotik sendrom

INTRODUCTION

Focal segmental glomerulosclerosis (FSGS) is a non-inflammatory glomerulopathy associated with nephrotic syndrome and end-stage renal failure (1). FSGS related to plasma cell disorder is not common. Development of FSGS after administration of biphosphanate treatment in multiple myeloma is well documented (2) but the literature contains few cases of secondary FSGS due to multiple myeloma (3,4).

Multiple myeloma is the most common plasma cell proliferative disease affecting renal functions through various factors such as monoclonal proteins, hypercalcemia, infection, uric acid nephropathy, infiltration of the kidneys by plasma cells, and amyloidosis (5).

We described a case of secondary FSGS associated with kappa light- chain disease in which the diagnosis was supported by renal biopsy.

Received: 27.04.2010
Accepted: 02.06.2010

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CASE SUMMARY

A 46-year-old man presented to the outpatient clinic with lumbar pain that had been present for two years. He had been taking non-steroid anti-inflammatory drugs for two years because of his pain. He had no history of any systemic disease. Physical examination revealed a body mass index of 20 kg/m^2, blood pressure of 150/90 mmHg, 2+ bilateral lower extremity pitting edema and lumbar vertebrae sensitivity.

Serum tests on admission showed hemoglobin: 9.8 g/L, blood urea nitrogen (BUN) 16 mg/dL, and serum creatinine 1.7 mg/dL. The complete blood count with differential and serum electrolytes (including sodium, potassium, calcium, chloride, and bicarbonate), total protein, albumin, alkaline phosphates, lactic dehydrogenase levels, and sedimentation rate were normal. Examination of urine sediment showed no white or red cells, and casts. Repeated urine cultures were sterile. Twenty-four hour urine collection revealed proteinuria of 21.3 g/day, and creatinine clearance rate was estimated at 49 ml/min.

Serological tests for anti-nuclear antibodies, double stranded DNA antibodies were normal and viral serology including HIV, hepatitis B surface antigen and core antigen and hepatitis C antibody were negative. Serum complement levels (C3, C4) were normal.

Renal ultrasound showed normal-size kidneys with increased grade I parenchymal echogenicity. A renal biopsy was performed in March 2008 to determine the cause of the patient's nephrotic syndrome. Histopathology examination revealed an infiltrate containing monocytes in the interstitium and focal segmental glomerulosclerosis in some glomeruli. No immune complex deposits or vascular pathology was detected in the glomeruli. Interstitial fibrosis, tubular atrophy and hyaline droplets were seen in the tubular lumen. Tissues sampled for immunofluorescence were negative IgG, IgM, IgA, C3, C1q, and kappa-lambda (κ-λ) light chain (Figure 1A,B,C).

The patient was accepted to have κ-light-chain disease and treated with immunosuppressive treatment. The plasma cell count decreased from 80% to 1-2% in the bone marrow after this treatment and patient was accepted to be on remission and autologous bone marrow transplantation was performed. Serum beta$_2$ microglobulin and κ-light chain levels were normal and protein extraction on urine decreased to the normal range (100 mg/day), the Hb level was 14 g/dL, and creatinine was 1.4mg/dL on the 4th month of the bone marrow transplantation. Renal and hematological parameters were still stable after the first year of bone marrow transplantation (creatinine was 1.2 g/dL, proteinuria was 100mg / day, and Hb level was 13.3 gr/dL).

DISCUSSION

Focal segmental glomerulosclerosis has become an important lesion found to underlie the nephrotic syndrome in adults. It is not a disease but a lesion initially affecting the podocyte. Various

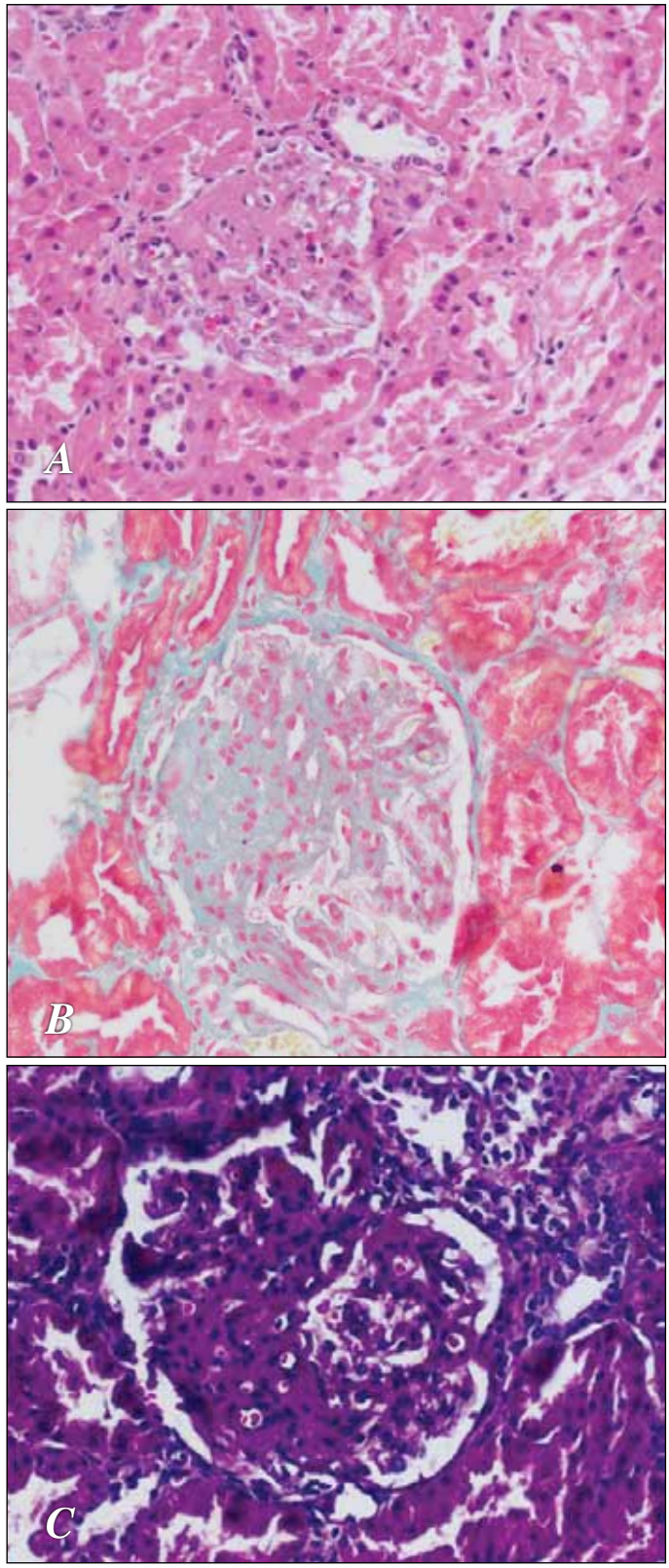

Figure 1A,B,C: *The glomeruli shown contain peripheral foci of segmental sclerosis X 400 in hematoxylin and eosin* ***(1A),*** *masson's trichrome* ***(1B)*** *and periodic acid schiff stain* ***(1C)****.*

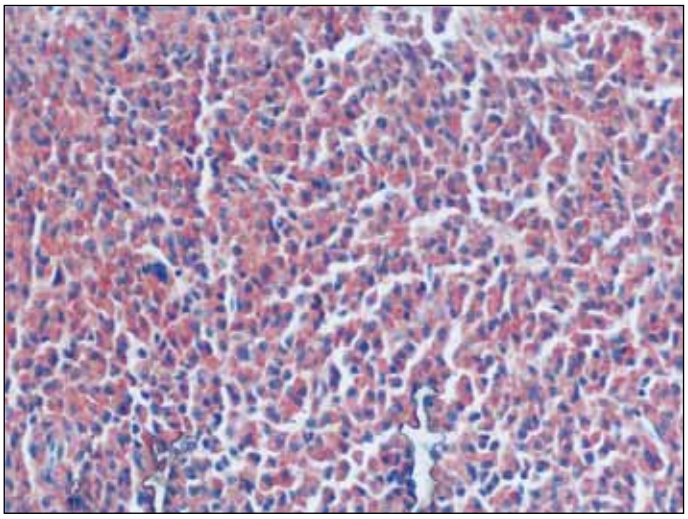

Figure 2: *Bone marrow biopsy demonstrating sheets of malignant plasma with kappa.*

factors may induce 'secondary' FSGS, including familial, virus-associated, drug toxicity, decreased renal mass, obesity, sickle cell anemia, hypertension, and atheroembolic vascular diseases, and malignancy (1).

Focal segmental glomerulosclerosis is not classically considered a paraneoplastic glomerular lesion. This glomerulopathy has rarely been reported in association with solid tumours, including non-Hodgkin lymphoma, large granular cell lymphoproliferative disorders, and non-small cell lung cancer. Patients with monoclonal gammopathy can develop a variety of related renal lesions or possibly have kidney disease unrelated to their monoclonal gammopathy. Paueksakon et al. found that 63.2% of 121 patients with monoclonal gammopathy had various kinds of renal disease unrelated to monoclonal gammopathy. The frequency of FSGS was found to be 18.1% in this study (3). Similarly, Dingli et al. described 4 patients with both multiple myeloma and FSGS (4).

Multiple myeloma is a monoclonal B cell malignancy which accounts for 1% of all malignancy. The characteristic findings in multiple myeloma are renal insufficiency, anemia, hypercalcemia, lytic bone disease, and immunodeficiency. Any of these findings should alert the clinician to the possibility of multiple myeloma and warrant further clinical investigation. The standard evaluation of a patient with suspected multiple myeloma includes; complete blood count with differential, serum calcium, creatinine, lactate dehydrogenase, albumin, beta$_2$ microglobulin levels, serum free light-chain assay with kappa/lambda ratio, serum and urine electrophoresis with immunofixation, bone marrow aspirate and biopsy, and skeletal survey (5).

The renal insufficiency, anemia, and lytic bone disease in our case increased the possibility of multiple myeloma and κ-light-chain disease was diagnosed when we performed further investigations (serum immonufixation, bone marrow biopsy, and skeletal survey).

The presence of a monoclonal protein on serum or urine electrophoresis suggests that the patient may have primary amyloidosis or light chain deposition disease (5). The nature of the light chain is fundamentally κ type in light-chain deposition disease then amyloidosis. In this case, renal tissue sampled showed no kappa-lambda (κ-λ) light chain and amyloid accumulation and was negative for immunocomplexes for IgG, IgM, IgA, C3, and C1q. Histopathology findings were consistent with FSGS. Based on histopathology examination, the underlying etiology of nephrotic syndrome was associated with unrelated monoclonal gammopathy.

The nephrotic range protein extraction decreased to normal range after the immunosuppressive treatment and autologous bone marrow transplantation.

Clinically, the patient had shown nephrotic syndrome on the first medical examination, and later was found to have the lytic bone lesions and monoclonal gammopathy of the κ-light- chain type. Monoclonal gammopathy should be considered as the underlying disease in any patient diagnosed with FSGS.

REFERENCES

1. Kitiyakara C, Eggers P, Kopp JB: Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am J Kidney Dis 2004; 44(5): 815-825
2. Markowitz GS, Appel GB, Fine PL, Fenves AZ, Loon NR, Jagannath S, Kuhn JA, Dratch AD, D'Agati VD: Collapsing focal segmental glomerulosclerosis following treatment with high-dose pamidronate. J Am Soc Nephrol 2001; 12(6): 1164-1172
3. Paueksakon P, Revelo MP, Horn RG, Shappell S, Fogo AB: Monoclonal gammopathy: Significance and possible causality in renal disease. Am J Kidney Dis 2003; 42(1): 87-95
4. Dingli D, Larson DR, Plevak MF, Grande JP, Kyle RA: Focal and segmental glomerulosclerosis and plasma cell proliferative disorders. Am J Kidney Dis 2005; 46(2): 278-282
5. Katzel JA, Hari P, Vesole DH: Multiple myeloma: Charging toward a bright future. CA Cancer J Clin 2007; 57(5): 301-318