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Remembering the Basics: A Patient with Sickle Cell Disease and Proteinuria

Temel İlkeleri Hatırlamak: Orak Hücreli Anemisi ve Proteinürisi Olan Bir Hasta

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ABSTRACT

Patients with sickle cell disease (SCD) tend to develop many renal abnormalities, including concentration defect, renal papillary necrosis, and glomerulopathy which often presents with proteinuria. In this paper, we have reported a case of a patient presenting with sickle cell crisis and proteinuria. A diagnosis of SCD glomerulopathy was confirmed with renal biopsy. Treatment with angiotensin-converting enzyme inhibitor was started and proteinuria rapidly reduced to 0.27 g/day. For a clinician, it is crucial to recognize this important complication and take necessary precautions to delay the progression to end-stage renal disease.

KEY WORDS: Sickle cell disease, Sickle cell nephropathy, Proteinuria

ÖZ

Orak hücreli anemisi olan hastalar, konsantrasyon defekti, renal papiller nekroz ve genellikle proteinüri ile baş gösteren glomerülopati gibi birçok renal anomali geliştirme eğilimi taşır. Bu yazıda orak hücre krizi ve proteinüri ile başvuran bir hastayı bildirdik. Orak hücre glomerülopatisi tanısı böbrek biyopsisi ile doğrulandı. Anjiotensin dönüştürücü enzim inhibitörü ile tedaviye başlandı ve proteinüri hızla 0.27 g/gün'e düştü. Bir klinisyen için bu önemli komplikasyonu tanımak ve son dönem böbrek yetersizliğine ilerleyişi geciktirmek için gerekli tedbirleri almak çok önemlidir.

ANAHTAR SÖZCÜKLER: Orak hücreli anemi, Orak hücre nefropatisi, Proteinüri

INTRODUCTION

Patients with sickle cell disease (SCD) may develop various renal structural and functional abnormalities, including concentration defect, renal papillary necrosis, and glomerulopathy which often presents with proteinuria (1-3).

Average life span of a patient with SCD has been extended in the modern era of medicine, and consequently the prevalence of chronic kidney disease has increased creating an important risk factor of death among these patients (3). Thus, it is crucial to recognize this important complication and its effects on patients with SCD. Therefore, we present a case of a patient with sickle cell disease glomerulopathy (SCDG) in this report.

CASE REPORT

A 48-year-old female applied to our emergency department with low back pain for 4 days. She had a medical history of SCD (hemoglobin SS) and related pulmonary hypertension, and was on acetyl salicylic acid (ASA), hydroxyurea, iloprost, and folic acid.

Laboratory evaluation showed a white blood cell count of 11900/mm^3 with a neutrophil count of 7600/mm^3, hemoglobin level of 7.7 g/dl, platelet count of 538000/mm^3, and lactate dehydrogenase (LDH) level of 773 IU/l (normal range: 135 – 250 IU/l). Urinalysis demonstrated 3+ protein, and the urine protein to creatinine ratio (UPCR) revealed 3.21 g/day of proteinuria.

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Serum creatinine and albumin levels were 0.9 mg/dl (normal range: 0.7-1.4 mg/dl) and 3 g/dl (normal range: 3.2-5.5 g/dl), respectively. Serologic analyses for hepatitis B surface antigen, antibodies of hepatitis C and human immunodeficiency viruses, antinuclear antibodies and anti-neutrophil cytoplasmic antibodies remained negative. Her serum complement levels were normal, and no monoclonal proteins were detected on serum protein electrophoresis. Abdominal ultrasonography revealed neither renal abnormalities nor splenomegaly.

Intravenous hydration, acetaminophen and tramadol were initiated. Her hemoglobin level further decreased to 5.5 g/dl with a serum haptoglobin of 20 mg/dl (normal range: 30–200 mg/dl), a reticulocyte count of 3.45% (normal range: 0.5–1.5%), and a total bilirubin level of 2 mg/dl. Direct Coombs test and Parvovirus B19 DNA were negative. A diagnosis of sickle cell crisis was made and the patient was admitted for exchange transfusions and differential diagnosis of proteinuria. Her hemoglobin level increased to 8 g/dl with the help of transfusions. After stabilization of the anemia and cessation of ASA, a renal biopsy was performed.

Evaluation of light microscopy demonstrated 16 glomeruli, two of which had global sclerosis. Two glomeruli showed thickening of Bowman's capsule, collapse, and early sclerotic changes. Hypertrophy was predominantly seen in all other glomeruli, and basement membranes of these glomeruli contained segmental thickening and duplications. Tubular epithelial cells included intracytoplasmic brown granules, which were found to be hemosiderin with Prussian blue positivity. Focal interstitial nephritis and occasional sickled erythrocytes in the capillary lumen were noted. Congo staining remained negative, and immunofluorescence microscopy showed no depositions. Endothelial swelling and foot process effacement were seen on electron microscopy (Figure 1A-D).

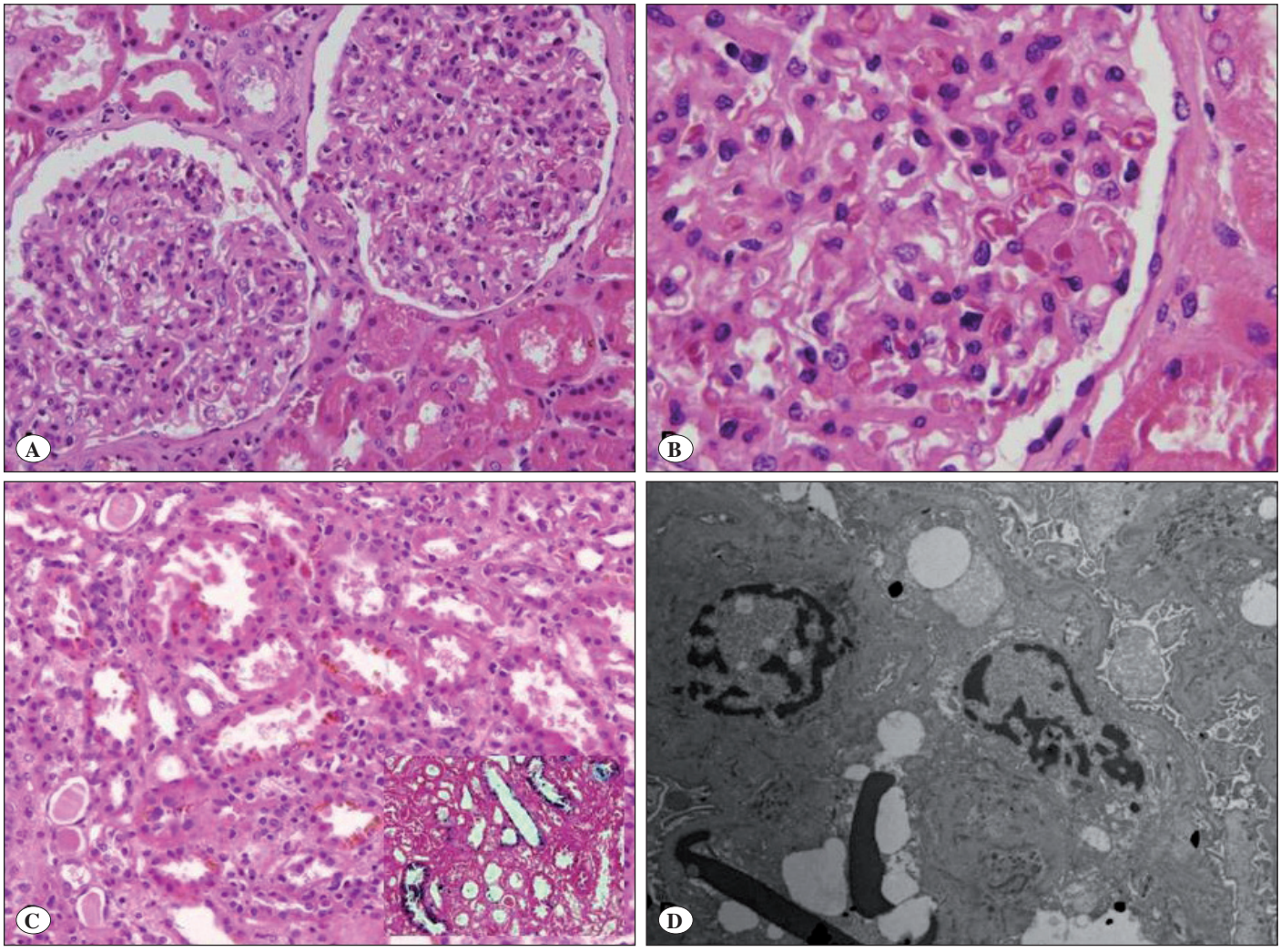

Figure 1: A) *Glomerular hypertrophy, mesangial increase and basement membrane thickness (HE 200x),* ***B)*** *Sickled erythrocytes within glomerular capillaries and basement membrane duplication (HE 400x),* ***C)*** *Brown granular pigment within tubular epithelial cells showing positivity for Prussian blue (inset) (HE 100x, Prussian blue 200x),* ***D)*** *Electron microscopy demonstrating endothelial swelling, foot process effacement and sickled erythrocytes (bottom left).*

Along with these pathological findings, the patient was diagnosed with specific SCDG and started on ramipril 5 mg/day. At the end of six months of treatment, proteinuria (measured with UPCR) substantially decreased to 0.27 g/day.

DISCUSSION

Sickle cell nephropathy is a well-characterized, complex entity and an increasing cause of morbidity and mortality in patients with SCD (4, 5). Hypertonicity and relative hypoxia in the renal medulla cause sickling of red blood cells, and consequently an increase in blood viscosity leading to renal ischemia and infarction (5, 6). Patients tend to develop many abnormalities, such as concentrating defects, renal papillary necrosis, and glomerular diseases (3, 6).

A wide spectrum of glomerular lesions may be seen in patients with SCD, including focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis (MPGN) with or without immune deposits, thrombotic microangiopathy (TMA), and specific SCDG (3, 6-12). Typical lesion in most of the patients is the perihilar variant of FSGS with glomerulomegaly but rare cases with collapsing pattern are reported (5, 6, 8). SCDG contains glomerular hypertrophy without typical FSGS, MPGN, or TMA lesions, and is often encountered in the early stages of glomerular disease (3, 12). Although patients with glomerular disease usually present with proteinuria, most of them display neither a severe renal impairment nor nephrotic syndrome at the time of diagnosis (3, 9). Nevertheless, long-term prognosis is often quite dismal in all patients with glomerulopathies (9).

Unfortunately, specific treatment approaches have not been validated so far in SCD-related glomerulopathies. In disease pathogenesis, it is postulated that renal ischemia leads to increased prostaglandin levels causing medullary vasodilation and glomerulomegaly (4). Consequently, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists are preferred for treatment because of their effects on lowering intraglomerular hypertension and proteinuria (8).

In our case, even though collapse and early sclerotic changes were demonstrated in two glomeruli, absence of typical focal and segmental sclerotic lesions and podocyte hyperplasia was not consistent with collapsing or any other variant of FSGS (6, 13). Segmental thickening and duplications of basement membranes suggest an MPGN-like pattern, but these findings are not adequate for a definitive MPGN diagnosis (10). Along with these features, the prominent glomerular hypertrophy, intracytoplasmic hemosiderin granules, and capillaries containing sickled red blood cells indicate the SCDG (3, 12). In order to reduce proteinuria and delay the progression to end-stage renal disease, early treatment with an ACE inhibitor was initiated (8).

For a clinician, we believe it is important to recognize this particular complication in patients with SCD and take necessary precautions during the disease course.

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Ethical Statement: This article does not contain any studies with human participants or animals performed by any of the authors.

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