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Case Report

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

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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 that often presents with proteinuria. We report a case of a patient who presented with sickle cell crisis and proteinuria. A diagnosis of SCD glomerulopathy was confirmed with renal biopsy. Treatment with angiotensin-converting enzyme inhibitor was initiated, and proteinuria rapidly reduced to 0.27 g/day. It is crucial for a clinician to recognize this important complication and take necessary precautions to delay progression to end-stage renal disease.

Keywords: Sickle cell disease, sickle cell nephropathy, proteinuria

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INTRODUCTION

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

The 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 for 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).

CASE PRESENTATION

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

Laboratory evaluation revealed 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 urine protein to creatinine ratio (UPCR) revealed a 3.21 g/day proteinuria. 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. Serological analyses for hepatitis B surface antigen, antibodies of hepatitis C and human immunodeficiency viruses, and antinuclear antibodies and antineutrophil cytoplasmic antibodies showed negative results. 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 showed negative results. 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 anemia and cessation of ASA, a renal biopsy was performed.

Evaluation of kidney biopsy with light microscopy demonstrated 16 glomeruli, 2 of which had global sclerosis. Further, 2 glomeruli showed thickening of Bowman's capsule, collapse, and early sclerotic changes. Hypertrophy was predominantly observed 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 when stained with Prussian blue. Focal interstitial nephritis and occasional sickled erythrocytes in the lumen of capillaries were noted. Congo red staining showed negative results, and immunofluorescence microscopy showed no depositions. Endothelial swelling and foot process effacement were observed on electron microscopy (Figure 1).

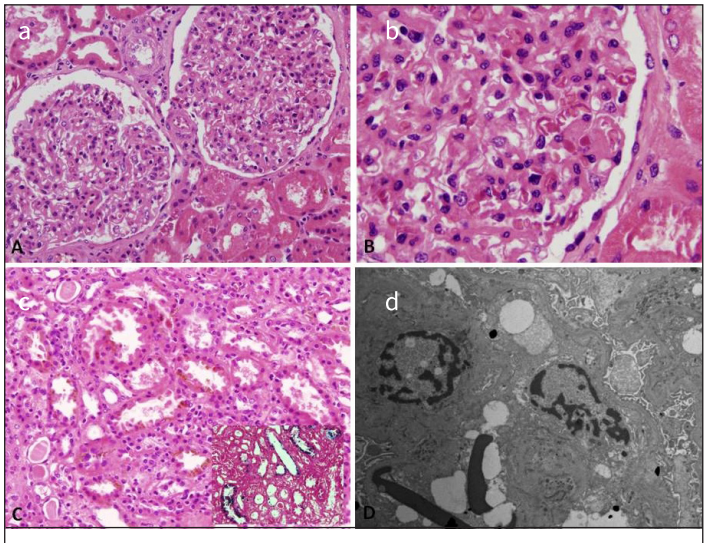

Figure 1. a-d. a) Glomerular hypertrophy, mesangial increase, and basement membrane thickness [hematoxylin and eosin (HE), 200x], b) Sickled erythrocytes within glomerular capillaries and basement membrane duplication (HE, 400x), c) Brown granular pigment within tubular epithelial cells showing positivity 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 initiated on 5 mg/day ramipril. At the end of 6 months of treatment, proteinuria (measured using UPCR) substantially reduced to 0.27 g/day. Informed consent was obtained from the patient who participated in this study.

DISCUSSION

Sickle cell nephropathy is a well-characterized and complex entity and an increasing cause of morbidity and mortality among 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 observed 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; however, rare cases with collapsing pattern have been reported (5, 6, 8). SCDG contains glomerular hypertrophy without typical FSGS, MPGN, or TMA lesions and is often encountered in the early stages of the 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 2 glomeruli, the 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 diagnosis of MPGN (10). Along with these features, prominent glomerular hypertrophy, intracytoplasmic hemosiderin granules, and capillaries containing sickled red blood cells indicate SCDG (3, 12). In order to reduce proteinuria and delay the progression to end-stage renal disease, early treatment with an ACE inhibitor is required (8).

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

CONCLUSION

Patients with SCD may suffer from glomerulopathy, which frequently presents with proteinuria. Hence, for clinical nephrologists, it is an important aspect of this debilitating disease in daily practice. Delaying the diagnosis may endanger the outcomes of patients with SCD and culminate in rapid progression to end-stage renal disease.

Informed Consent: Informed consent was obtained from the patient who participated in this study.

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REFERENCES

1. Ataga KI, Orringer EP. Renal abnormalities in sickle cell disease. Am J Hematol 2000; 63: 205-11. [CrossRef]
2. Ataga KI, Derebail VK, Archer DR. The glomerulopathy of sickle cell disease. Am J Hematol 2014; 89: 907-14. [CrossRef]
3. Maigne G, Ferlicot S, Galacteros F, Belenfant X, Ulinski T, Niaudet P, et al. Glomerular lesions in patients with sickle cell disease. Medicine (Baltimore) 2010; 89: 18-27. [CrossRef]
4. Saborio P, Scheinman JI. Sickle cell nephropathy. J Am Soc Nephrol 1999; 10: 187-92.
5. Ramidi GB, Kurukumbi MK, Sealy PL. Collapsing glomerulopathy in sickle cell disease: a case report. J Med Case Rep 2011; 5: 71. [CrossRef]
6. Nasr SH, Markowitz GS, Sentman RL, D'Agati VD. Sickle cell disease, nephrotic syndrome, and renal failure. Kidney Int 2006; 69: 1276-80. [CrossRef]
7. Bhathena DB, Sondheimer JH. The glomerulopathy of homozygous sickle hemoglobin (SS) disease: morphology and pathogenesis. J Am Soc Nephrol 1991; 1: 1241-52.
8. Falk RJ, Scheinman J, Phillips G, Orringer E, Johnson A, Jennette JC. Prevalence and pathologic features of sickle cell nephropathy and response to inhibition of angiotensin-converting enzyme. N Engl J Med 1992; 326: 910-5. [CrossRef]
9. Bakir AA, Hathiwala SC, Ainis H, Hryhorczuk DO, Rhee HL, et al. Prognosis of the nephrotic syndrome in sickle glomerulopathy. A retrospective study. Am J Nephrol 1987; 7: 110-5. [CrossRef]
10. Pardo V, Strauss J, Kramer H, Ozawa T, McIntosh RM. Nephropathy associated with sickle cell anemia: an autologous immune complex nephritis. II. Clinicopathologic study of seven patients. Am J Med 1975; 59: 650-9. [CrossRef]
11. Vogler C, Wood E, Lane P, Ellis C, Cole B, Thorpe C. Microangiopathic glomerulopathy in children with sickle cell anemia. Pediatr Pathol Lab Med 1996; 16: 275-84. [CrossRef]
12. Pitcock JA, Muirhead EE, Hatch FE, Johnson JG, Kelly BJ. Early renal changes in sickle cell anemia. Arch Pathol 1970; 90: 403-10.
13. D'Agati VD, Fogo AB, Bruijn JA, Jennette JC. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. Am J Kidney Dis 2004; 43: 368-82. [CrossRef]