AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES

CKD and Nephrotic Syndrome After Allogeneic Hematopoietic Cell Transplantation

CLINICAL PRESENTATION

A 21-year-old Hispanic man with a medical history of myelodysplastic syndrome underwent related HLA-identical allogeneic stem cell transplantation at the age of 11 years. His conditioning regimen included cyclophosphamide, cytarabine, and total-body irradiation. The posttransplantation course was complicated by chronic graft-versus-host disease (cGVHD) involving the liver, skin, and oral mucosa, for which he was prescribed tacrolimus for the last 8 years with a slow taper.

Ten years after the transplantation, at the age of 21 years, the patient was referred to nephrology for evaluation of an elevated serum creatinine (Scr) level and proteinuria. Scr level had been 0.8 to 1.0 mg/dL (corresponding to estimated glomerular filtration rate [eGFR] of 107-128 mL/min/1.73 m^2 as calculated using the CKD-EPI [Chronic Kidney Disease Epidemiology Collaboration] equation) until 18 months prior to presentation, when it increased to 1.2 mg/dL (eGFR, 86 mL/min/1.73 m^2). Urinalyses by dipstick gave negative results for blood and protein until 5 years prior to presentation. Since then, his urine dipsticks were increasingly positive for protein (initially trace, increasing to 3+ over time). No past urine microscopies were available.

At the patient's initial nephrology evaluation, the only manifestation of cGVHD was chronically mildly elevated liver function test results, but he was otherwise asymptomatic. He had developed hypertension over the previous few months, with average home blood pressure readings of 140/90 mm Hg. He reported occasional mild bilateral ankle edema. On examination, he was afebrile, office blood pressure was 132/78 mm Hg, and findings were otherwise unremarkable except for trace pitting ankle edema bilaterally.

Laboratory evaluation revealed the following values: Scr, 1.6 mg/dL (eGFR, 58 mL/min/1.73 m^2); serum albumin, 3.4 (reference range, 3.5-5.5) g/dL; aspartate aminotransferase, 81 (reference range, 15-41) U/L; alanine aminotransferase, 144 (reference range, 17-63) U/L; alkaline phosphatase, 202 (reference range, 38-125) U/L; total cholesterol, 286 mg/dL; triglycerides, 652 mg/dL; high-density lipoprotein cholesterol, 50 mg/dL (low-density lipoprotein cholesterol not determined); white blood cells, 4,400/μL; hemoglobin, 15.5 g/dL; and platelets, 217,000/μL. Laboratory urinalysis showed protein (3+), trace heme, and 4 to 10 red blood cells per high-power field without red blood cell casts. A 24-hour urine collection revealed 7,500 mg of protein. The most recent trough tacrolimus levels were 3 to 5 ng/mL, obtained while the patient was on a regimen of 1 mg of the drug every 12 hours. A serologic workup included normal serum protein electrophoresis pattern and C3 and C4 levels, negative results for serum immunofixation, and undetectable serum antinuclear and anti-PLA_2R antibody levels. A kidney biopsy was performed (Fig 1).

- **What is the differential diagnosis for CKD after allogeneic hematopoietic cell transplantation?**
- **Does the presence of nephrotic-range proteinuria influence your differential diagnosis?**
- **What does the kidney biopsy show?**
- **How should the patient be treated?**
- **What is the clinical follow-up for this patient?**

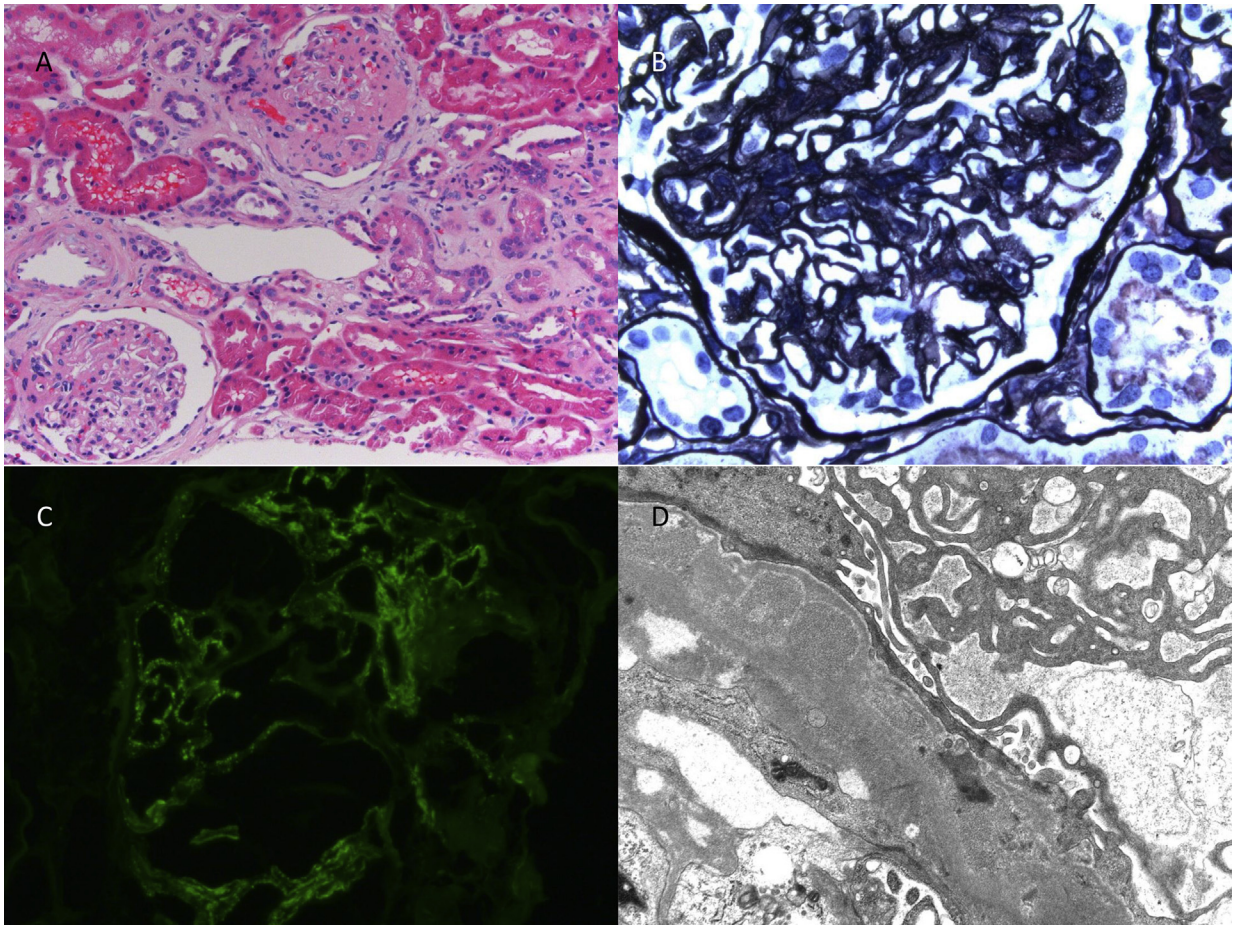

Figure 1. Kidney biopsy images. (A) Light microscopy (hematoxylin and eosin; original magnification, ×200). (B) Jones silver stain (original magnification, ×600). (C) Immunofluorescence is positive for immnoglobulin G (IgG) (anti-IgG antibody; original magnification, ×400). (D) Electron microscopy (original magnification, ×10,000).