An Unusual Case of Acute Myeloid Leukemia Cell Infiltration of the Renal Allograft: A Case Report and Review of Literature

S. Manohar[a], I.J. Sathick[b], J. Grande[c], Z. El-Zoghby[a], and N. Leung[a,*]

[a]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [b]Division of Nephrology and Hypertension, Memorial Sloan Kettering Cancer Center, New York, New York, USA; and [c]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota, USA

ABSTRACT

Kidney transplant recipients are at a high risk for developing malignancies with dermatologic cancers and lymphomas making up the bulk of these. Leukemia is rare in this cohort of patients. Kidney infiltration by leukemic cells is seen in about 34% of native kidneys based on autopsy studies. But leukemia infiltration of the kidney allograft has not been described much in the literature. Here we discuss the case of a 59-year-old kidney transplant recipient with acute myeloid leukemia (AML) who presented with acute kidney injury and his transplant kidney biopsy showed leukemic cell infiltration of the renal cortex. We also present a comprehensive literature review of post–kidney transplantation AML.

NATIVE kidney involvement of hematologic malignancies is common and can often be the presenting feature. A study of autopsy cases of patients with myeloproliferative and lymphoproliferative disorders done by Xiao et al [1] showed native kidney involvement in 34% of the cases. When it comes to kidney transplant recipients, it is well known that these patients are at a higher risk of developing malignancies and this is likely from their long history of immunosuppression. Dermatologic cancers and lymphomas make up the bulk of these malignancies, but leukemia is less common. The Cincinnati Transplant Tumor Registry of 1991 noted 2.7% of the cancers to be due to leukemia, of which 43% were acute myeloid leukemia (AML) [2]. The incidence of AML in kidney transplant recipients is low and estimated by various studies to be between 0.1% and 0.2% [3]. We present an interesting case of secondary AML in a kidney transplant recipient 14 years post-transplantation with evidence of leukemic infiltration of the allograft on biopsy. We also review the literature for prevalence, pathophysiology, and treatment options.

CLINICAL HISTORY AND INITIAL LABORATORY DATA

A 59-year-old white male presented initially to the Hematology Clinic for a second opinion regarding the management of his recently diagnosed AML. He had a long-standing history of diabetes mellitus with biopsy-proven diabetic nephropathy. He slowly progressed to end-stage renal disease and started on hemodialysis. After 2 years, he underwent a deceased donor kidney transplantation at an outside facility. His nadir creatinine level was 1.3 mg/dL during the first year post-transplantation. His maintenance immunosuppression consisted of prednisone 5 mg daily and Cyclosporine 75 mg twice daily. For the next 14 years, his clinical course was unremarkable with stable allograft function.

About a year prior to presentation, he was noted to have a gradual decrease in his platelet count down to 50–60 $\times$ 10^9 cells/L as well as a concurrent increase in creatinine level from 1.3 mg/dL to 1.7 mg/dL. His urine sediment was bland and unchanged, but a kidney biopsy was deferred until a thorough evaluation of the low platelets could be completed. Of note, he had a prior history of thrombocytopenia before kidney transplantation. At that time his platelet count was as low as 102 $\times$ 10^9 cells/L. A bone marrow biopsy had revealed a normocellular bone marrow for age (50%–60%) with slight erythroid hyperplasia and a modest increase in bone marrow lymphocytes (15%). No definitive diagnosis was reached, and his platelet counts spontaneously improved. Upon his current presentation, a bone marrow biopsy was done and showed a hypercellular marrow (95%). The erythroid precursors and

*Address correspondence to Nelson Leung, MD, Mayo Clinic, 200 1st SW, Rochester, MN 55905, USA. E-mail: leung.nelson@mayo.edu

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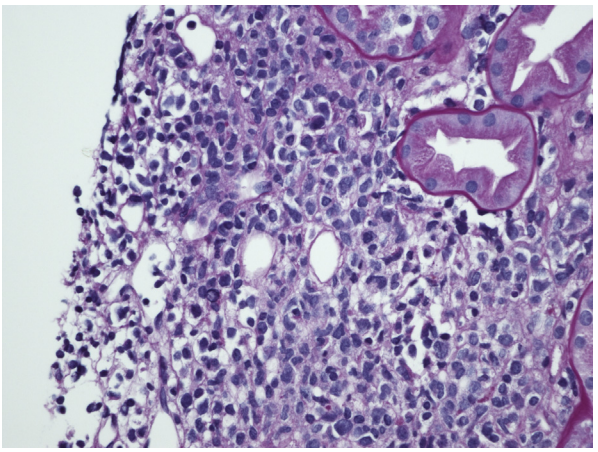

Fig 1. Kidney transplant biopsy. Periodic acid-Schiff stain showing multifocal interstitial infiltrates consisting of large myeloid cells with enlarged nuclei and increased numbers of mitotic figures.

megakaryocytes were unremarkable, but there were increased myeloid precursors with increased blasts (29%). The morphological features were consistent with the diagnosis of AML. The patient elected to seek a second opinion in our center.

He was initially seen in our Hematology Clinic and was immediately hospitalized for chemotherapy initiation. Clinically he was asymptomatic except for occasional tiredness. His vital signs were normal, and his physical examination was unremarkable. His renal allograft in the right lower quadrant of his abdomen was palpable and nontender. His urine output was satisfactory. Blood work was notable for a serum creatinine level of 2.7 mg/dL. His urinalysis revealed mild hematuria of 3–10 red blood cells/high-power field (HPF) with a urine protein of 953 mg/g of creatinine. He did not report recent medication changes; his cyclosporine drug levels were at goal at 67 ng/mL (his target range was 50–70 ng/mL), and he did not have any hypotensive episodes, diarrhea, or evidence of volume depletion. A computed tomography (CT) scan of the abdomen showed mild inflammatory stranding around the renal allograft. A trial of intravenous fluids did not improve his serum creatinine values. Due to the unclear nature of his acute kidney injury, he underwent a kidney allograft biopsy.

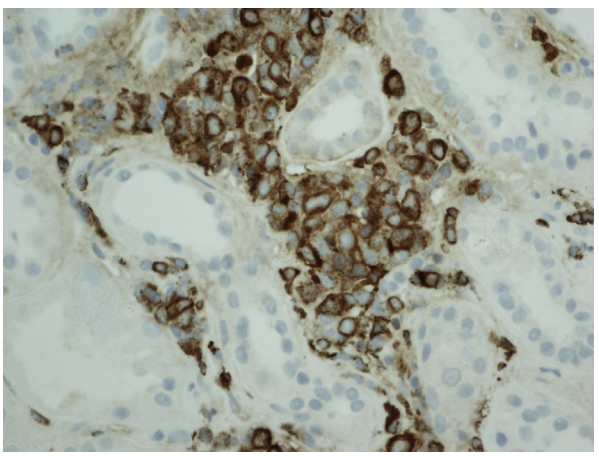

Fig 2. Kidney transplant biopsy. Immunoperoxidase staining for myeloperoxidase shows strong diffuse positivity within the infiltrating cells consistent with myeloid leukemic cells.

KIDNEY BIOPSY

The biopsy showed the renal cortex with multifocal interstitial infiltrates consisting of large myeloid cells. These cells had enlarged nuclei and increased numbers of mitotic figures. The immunoperoxidase staining for myeloperoxidase showed strong diffuse positivity within the infiltrating cells (Fig 1 and Fig 2).

DIAGNOSIS

His diagnosis was AML with renal allograft infiltration of leukemic cells.

CLINICAL FOLLOW-UP

He was started on chemotherapy on a 7 + 3 regimen of cytarabine and dose-adjusted idarubicin. His creatinine level improved after the first cycle of chemotherapy, and by day 10 it was at his baseline at 1.4 mg/dL. Unfortunately, he subsequently developed hospital-acquired pneumonia with hemodynamic compromise. He progressively deteriorated and died a month later.

DISCUSSION

We present a case of AML with allograft infiltration 14 years post–kidney transplantation. Post-transplantation AML is possibly a different disease entity compared with primary AML. The cytogenetics and clinical presentation are quite different from de novo primary AML [2]. Fortunately, it is a rare disease in patients with a kidney transplant, but the exact incidence is unknown.

The Cincinnati Transplant Tumor Registry of 1991 reports that 2.7% of the cancers in this population are due to leukemia, of which 43% were AML [4]. Offman et al [3] reviewed the Collaborative Transplant Study data from 1985 to 2004 and noted that 56 of 153,528 recipients of a kidney transplant had AML. The relative risk for AML in kidney transplant recipients compared with controls who did not undergo transplantation after matching for age, gender, and geographic region was 2.1 (95% confidence interval [CI], 1.6–2.7; $P < .0001$). The risk was higher in heart/lung transplant recipients with a relative risk (RR) of 5.5 (95% CI, 4.0–7.7). Interestingly they noted that the incidence is low during the first 4 years after transplantation but subsequently increases significantly [3]. The other large study looking at epidemiological data from the same registry was by Gale et al [5] who studied 217,219 patients with kidney transplants and