Late-Onset Allograft Aspergillosis in an HIV-Positive Renal Transplant Recipient: A Case Report

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ABSTRACT

Aspergillus infection of the allograft in renal transplant patients is rare and associated with a high mortality. We report a case of a 21-year-old, human immunodeficiency virus–positive, deceased-donor kidney recipient who presented 1 year after transplant with oliguric kidney injury. A nuclear medicine renal scan revealed absence of flow to the transplanted kidney, and a urine fungal culture was positive for *Aspergillus flavus*. The diagnosis was confirmed with the presence of fungal hyphae along with thrombosis in the vascular structures in renal allograft pathology. We found no evidence of disseminated aspergillosis or involvement of any other organ in the patient. To our knowledge, this case is the first reported in the literature of late-onset non-disseminated renal-limited aspergillosis in a human immunodeficiency virus–positive renal transplant patient.

INFECTION is a frequent complication seen in transplant recipients due to the use of immunosuppression. Invasive aspergillosis after kidney transplantation can lead to graft loss and death. Isolated involvement of the allograft with aspergillosis is rare. We present a case of allograft aspergillosis in a human immunodeficiency virus (HIV)-positive patient 1 year after renal transplantation.

CASE REPORT

A 21-year-old white man presented with a 1-day history of fever, allograft pain, and oliguria 12 months after receiving a deceased-donor kidney transplant. Before the transplantation, the patient had end-stage renal disease secondary to HIV-associated nephropathy.

One year ago, at the time of transplantation, the patient received induction therapy with 4 doses of antithymocyte globulin 1.5 mg/kg and was maintained on a regimen of tacrolimus and mycophenolate mofetil. He was sensitized with 4-antigen mismatch to the donor who had a Kidney Donor Profile Index of 23%. The recipient was positive for cytomegalovirus and received prophylaxis with valganciclovir for 3 months. His HIV infection was treated with combination antiretroviral therapy comprising abacavir, dolutegravir, and rilpivirine.

The patient's post-transplant course was complicated by recurrent episodes of rejection, leukopenia, and diarrhea. Two weeks after the transplant, the patient developed antibody-mediated rejection that was confirmed on biopsy. Donor-specific antibodies were negative at the time. He underwent treatment for rejection, as per our institutional protocol, with a single dose of rituximab 375 mg/m^2 and 4 sessions of plasmapheresis and bortezomib 1.3 mg/m^2. Eight months after the transplant, the patient was diagnosed with acute cellular rejection grade 1A, which was treated with 3 doses of intravenous methylprednisone 500 mg, followed by a rapid taper. Results of a repeat biopsy revealed persistent acute cellular rejection 1A, for which he was given 4 doses of antithymocyte globulin 1.5 mg/kg. Throughout this course, the patient also continued to experience chronic, intermittent diarrhea for which mycophenolate mofetil was replaced with azathioprine at 10 months. He underwent a colonoscopy, which was grossly unremarkable and revealed chronic mild colitis on pathology.

One year after the transplant, the patient presented with fever, oliguria, and pain at the site of allograft for 1 day. Vital signs were within normal ranges. On physical examination, there was tenderness to palpation at the site of the allograft. Results of laboratory testing were remarkable for an elevated serum creatinine level of 9.3 mg/dL with an estimated glomerular filtration rate of 8 mL/min/1.73 m^2 (baseline creatinine level was 2.5 mg/dL with an estimated glomerular filtration rate of 35 mL/min/1.73 m^2), potassium level of 6.4 mmol/L, bicarbonate level of 18 mmol/L, white blood cell count of 12,400/μL, hemoglobin level of 10.4 g/dL, and platelet levels of 136,000/μL. Urinalysis revealed 5 red blood cells, 9 white blood cells and no bacteria per high-power field.

At the time of admission, a urinary catheter was placed, with urine output of 100 mL over the next 24 hours. Urine and blood

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cultures were collected, and the patient was empirically started on broad-spectrum intravenous antibiotics (vancomycin, cefepime, and metronidazole). A kidney ultrasound revealed mild hydronephrosis with intact blood flow to the allograft on Doppler imaging. A computed tomography (CT) scan of the abdomen without contrast confirmed hydronephrosis, and a percutaneous nephrostomy tube was placed. Hemodialysis was performed for hyperkalemia, which was refractory to medical management.

On day 2 of admission, the patient underwent allograft biopsy, which revealed diffuse necrosis of the renal parenchyma. A nuclear medicine study was performed with Technetium-99m mercaptoacetyltriglycine, which showed absence of flow in the allograft. Results of a urine culture collected from the nephrostomy tube started growing *Aspergillus flavus* on day 4 of admission, and the patient was started on intravenous voriconazole 400 mg twice daily. On day 6 of admission, the patient underwent a graft nephrectomy. Allograft pathology revealed severe cellular rejection with extensive renal infarction and vascular thrombosis. Fungal hyphae consistent with *Aspergillus* species were found in a few vessel structures (Figs 1 and 2). Computed tomography scans of the sinuses and chest performed to look for source did not show any characterisitic findings compatible with aspergillosis. The patient was discharged on a 4-week course of oral voriconazole.

DISCUSSION

Aspergillus species are ubiquitous in the environment and are the most common invasive pathogenic mold in humans. Of the ~200 known species, only a few are pathogenic to man, primarily *Aspergillus fumigatus*, *A flavus*, and *Aspergillus niger*. It is known for its propensity to invade blood vessles, leading to thrombosis and tissue infarction [1]. Among solid organ transplantation, invasive aspergillosis is more commonly seen in lung and heart/lung transplants with a reported incidence of up to 14% [2]. It is relatively rare after kidney transplantation, in which the incidence is 0.7% to 4%. Invasive disease isolated to the allograft, without involvement of any other organ, is even more rare. To the best of our knowledge, only 10 cases have been reported in the literature.

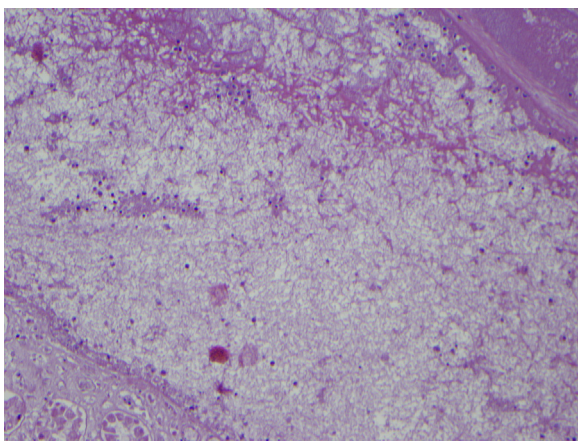

Fig 1. Hematoxylin and eosin stain: vessel thrombus with fungal hyphae and fibrin.

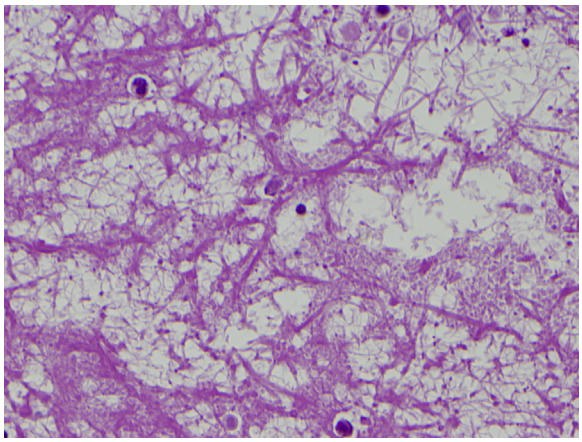

Fig 2. Periodic acid–Schiff stain: fungal structures, some with well-defined septae and acute angle branching.

We present a rare case of isolated aspergillosis of the allograft in a kidney transplant recipient presenting 12 months' post-transplantation with oliguric acute kidney injury resulting from thrombosis of the graft. There was no evidence of disseminated disease. In this patient, the infection occurred later in the post-transplant course than all previously reported cases. Another unique aspect of this case is that the recipient was HIV positive.

Among kidney transplant patients, invasive aspergillosis has been reported in 0.7% to 4% of the cases, leading to higher morbidity, graft loss, and death [2]. Invasive or cavitary forms of pulmonary aspergillosis and infection of the central nervous system are the most common clinical manifestations in this population [3]. Risk factors include high doses and prolonged duration of corticosteroids, graft failure requiring hemodialysis, and potent immunosuppressive therapy [2]. Heylen et al [4] identified other risk factors in their case-control study of 41 adult kidney transplant patients with invasive aspergillosis. A longer duration of renal replacement therapy pretransplantation and the occurrence of leukopenia (white blood cell count <3000/μL) were risk factors for early disease (occurring within 3 months after the transplant), whereas donor cytomegalovirus seropositivity increased the risk for late-onset invasive aspergillosis.

Several factors may have contributed to the development of disease in our patient. He was treated with rituximab, bortezomib, and plasmapheresis for antibody-mediated rejection 2 weeks' post-transplantation. Later, the patient underwent treatment with high-dose glucocorticoids and antithymocyte globulin for acute cellular rejection. In addition, he developed leukopenia 6 weeks' post-transplantation, with a leukocyte count dropping intermittently to <3000/μL in the following months. Acquired immunodeficiency syndrome has been identified as an independent risk for invasive aspergillosis. Our patient reported compliance with antiretroviral therapy, and his HIV viral load remained undetectable during his