CASE REPORTS

Pseudoaneurysm of the Iliac Artery Secondary to Aspergillus Infection in Two Recipients of Kidney Transplants From the Same Donor

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The authors report 2 cases of patients who underwent cadaveric renal transplantation from the same donor in a multiorgan extraction procedure. Both cases showed, during the first 6 months posttransplantation, a worsening in renal graft function and signs of ischemia in the homolateral lower limb. One of the cases was preceded by pain in the sciatic region. In imaging tests, a pseudoaneurysm was detected in the iliac artery in both patients. Grafts had to be removed, and the iliac arteries were ligated with posterior isolation of Aspergillus spp from the arterial vessels but not from the renal tissue. Besides surgery, medical treatment with liposomal amphotericin B was initiated with a different outcome in each patient: patient A died, whereas patient B recovered. The absence of Aspergillus spp infection in liver and heart recipients ruled out a donor-transmitted infection. The graft placements were carried out in different operating rooms, which rules out contamination during the transplantation process. All of this leads us to conclude that the infection must have occurred during the preservation phase of the kidney. Am J Kidney Dis 41: 488-492.

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FOR MANY YEARS, infections have been a frequent cause of death in kidney transplant recipients. More recently, protocolization of the donation process; a tailored immunosuppression; and progress in the prevention, diagnosis, and treatment of infection have led to a consistent decline in the incidence of fatal infections. Infection of the graft before, during, or after kidney transplantation may trigger serious complications in the host, particularly when it occurs by fungi. Currently, exogenous graft infection during the donation process seems to be more frequent than transmission from the donor. This case report shows the importance of graft colonization as a source of infection during the manipulation procedure and the difficulty in diagnosis of insidious fungal infection. The infrequency of the process as well as the need to keep it in mind to establish a rapid diagnosis and therapy is what has driven us to report these 2 cases.

CASE REPORTS

Donor

A 39-year-old woman died of an intracranial tumor found during biopsy to be a benign ganglioma. The patient had been in the intensive care unit (ICU) for 7 days, where she required treatment with vancomycin and cefotaxime. After her death, a multiorgan extraction was performed; the usual microbiologic and serologic assays were negative.

Recipient A

A 53-year-old woman had end-stage renal disease (ESRD) secondary to chronic pyelonephritis and had been undergoing periodic hemodialysis for 5 years. She shared with the donor 2 human leukocyte antigen (HLA)-DR antigens and one type HLA-A antigen. Induction of immunosuppression was accomplished with cyclosporin A (Sandimmune Neoral; Novartis Pharma AG, Basel, Switzerland), initial dose, 10 mg/kg/d, adapting to the target range blood levels of 200 to 300 ng/mL; methyl prednisolone (MP), 500 mg intravenously the first day, 125 mg intravenously the second day; and, thereafter, prednisone orally, tapering to 10 mg maintenance dose and basiliximab (Simulect; Novartis Pharma AG, Basel, Switzerland), 20 mg pretransplantation and on the 4th day posttransplantation, with cyclosporin A and steroids as maintenance therapy. On day 7 posttransplantation, a biopsy was not done because of technical considerations (interposition of the bowel). A satisfactory response was obtained later with 3 bolus doses of 500 mg of MP. The lowest creatinine level recorded was 2.2 mg/dL (194.48 μmol/L).
ASPERGILLUS INFECTION AND KIDNEY TRANSPLANTS

The patient was admitted to the hospital 35 days after the transplantation because of sciatic pain, which did not cease with rest and analgesics. X-ray examination found hyperlordosis and degenerative changes on the dorso-lumbar area of her spine. On day 37 posttransplantation, her graft function deteriorated with creatinine levels of 3.4 mg/dL (300.56 μmol/L). After ruling out a urinary tract obstruction by ultrasonography and toxic cyclosporine A levels, a technetium 99m dietilentaeminopentacetic acid (DTPA) renal scan was performed; this showed a decrease in renal perfusion. In the absence of a renal biopsy, this was interpreted as a second acute rejection episode, and she was treated again with 3 bolus doses of 500 mg of MP. At the same time, her right leg began to show paresthesia, coldness, and a decreased arterial pulse perception. On day 42 posttransplantation, a magnetic nuclear resonance was performed, ruling out neurologic pathology at the lumbar level but disclosing an aneurysm of the common iliac artery (Fig 1). This was confirmed with arteriography, which showed the existence of a pseudoaneurysm with an arteriovenous fistula to the vena cava (Fig 2), compromising the viability of her leg. Accordingly, the pseudoaneurysm and the arteriovenous fistula were resected, the transplanted kidney was removed, and an aortic-iliac bypass with a polytetrafluoroethylene (PTFE) graft was implanted.

Histologic study of the microaneurysm showed the presence of Aspergillus spp; the graft removed was free of contamination. Treatment with liposomal amphotericin B (AmBisome; Nexstar, San Dimas, CA), 4 mg/kg/d, was initiated (patient weight, 69 kg). The patient progressed favorably until the original symptoms reappeared 3 weeks later. An abdominal computed tomography (CT) scan disclosed an image compatible with hematoma, which failed to uptake contrast, and that was displacing the PTFE graft, which remained permeable according to the Doppler study. The hematoma was confirmed by fine-needle aspiration, with no evidence of Aspergillus spp. In view of the patient’s previous history, an arteriography was performed, showing a new pseudoaneurysm that displaced and obstructed the PTFE graft. The patient underwent emergency surgery resecting the aneurysm, but she died of hemorrhagic shock in the postoperative period.

Recipient B
A 56-year-old woman had ESRD secondary to chronic pyelonephritis. She had been on hemodialysis for 2 years. The patient shared a haplotype with the HLA of the donor. She received the same immunosuppressive regimen as patient A with no rejection episodes and was discharged after 12 days. One week later her plasma creatinine level was 1.5 mg/dL (132.6 μmol/L).

During the fourth month posttransplantation, the patient deteriorated clinically, with a serum creatinine level increase to 3.7 mg/dL (327.08 μmol/L) with no signs of urinary tract obstruction or toxic cyclosporine A levels. A kidney biopsy was performed, after which the existence of acute rejection was ruled out. By technetium-DTPA renal scan, a good degree of graft perfusion was observed. Three weeks later, because the graft dysfunction persisted with no apparent cause, a second biopsy was taken, although no changes were observed. The patient was kept on immunosuppressive treatment; however, because of the progressive deterioration of her renal function with a serum creatinine level of 5.9 mg/dL (521.56 μmol/L), but without a specific diagnosis, she was referred for hemodialysis. During the fifth month posttransplantation, she was admitted to the hospital because of a respiratory infection, with an important degree of hypoxemia and infiltration of the right lung. She was treated empirically with cefadizime,
clarithromycin, cotrimoxazol, and liposomal amphotericin B until Acinetobacter baumannii and Mycobacterium tuberculosis were isolated in her bronchoalveolar lavage fluid. Treatment specific to these microorganisms was initiated with an improvement in the patient’s health status over the ensuing month. During the fifth week after her admission to the hospital (the sixth month posttransplantation) she began to show paraesthesia, coldness, and a decreased arterial pulse perception in her right leg. Ultrasonography showed pyelocaliectasis with an adjacent solid-liquid mass, which was confirmed by abdominal CT scan. A pseudoaneurysm was suspected and was confirmed by arteriography (Fig 3).

The pseudoaneurysm was resected, the graft was removed, and the internal iliac artery was ligated. Later, Aspergillus spp was isolated from the renal artery but was not present in the kidney. Treatment with liposomal amphotericin B, with an initial dose of 4 mg/kg/d intravenously the first week, and 3 mg/kg/d for 3 more weeks, was administered (patient weight, 61 kg) followed by itraconazole (Sporanox; Janssen-Cilag, Madrid, Spain), 200 mg/d, for 5 months with a favorable evolution.

**DISCUSSION**

Infections are one of the most frequent causes of morbidity-mortality in solid organ transplant recipients. Infections may occur at different phases of the transplantation process: (1) donor: especially in patients who have died of cranioencephalic trauma accompanied by abdominal trauma and in those who have spent prolonged periods in the ICU (more than 7 days); (2) extraction: mainly in multiorgan donation; har-vesting kidneys from non–heart-beating donors may facilitate bacterial colonization from the digestive tract; (3) during the time of organ preservation and graft implantation, depending on the duration of surgery, which would facilitate colonization by bacteria. Rubin has established a 3-phase calendar of infections in patients who have undergone transplant from day 1 to the end of the first month (surgical infections, pneumonia, HSV); from the first to the sixth month (opportunistic infections); and as of the sixth month (similar to the risk in the general population).

The frequency of accidental contamination during organ extraction, preservation, or implantation varies from 5% to 23%, depending on the series. In general, the infection is caused by pathogenic bacteria from the normal flora with few clinical repercussions. Infections caused by *Staphylococcus aureus*, gram-negative bacteria, and fungi are much more severe. Among these, invasive aspergillosis in renal graft generally has a fatal outcome because of its insidious presentation.

Various reasons may explain the unequal evolution of the process in the 2 patients reported here. In case A, the patient received very high doses of steroids, which would have facilitated the development and propagation of the infection. Also, a bypass with a PTFE graft was placed in this patient. At the time, the implantation of this type of prosthesis was the motive of considerable debate among us, because the presence of the aneurysm favored the possibility of colonization by fungi. The absence, however, of a microbiological confirmation at that moment and the absence of other foci of fungal infection (mainly *Aspergillus* spp) prevented this diagnosis from being confirmed. Faced with this dilemma and the severity of the situation, it was decided to implant the prosthesis. Later events confirmed that when dealing with the presence of a pseudoaneurysm, even with negative microbiological data, the diagnosis of aspergillosis is correct. Despite this, the alternative in this case would have been more hazardous: the choice between an extracorporeal bypass or amputation of the patient’s leg.

The second patient did not receive antirejection steroidal treatment that could explain the late appearance of the clinical picture, although it
also should be stressed that there were other factors that may have favored the development of aspergillosis, such as the intense antibiotic treatment administered after the patient's respiratory infection. Our earlier experience with the first patient, together with the suspicion of a similar clinical picture in the second one, were key determinants in initiating prompt medical-surgical treatment, which favored a more positive outcome.

There were several reasons for the delay in diagnosis in the first case: (1) The onset with sciatric pain, along with the radiologic evidence of signs of deterioration in the dorso-lumbar region of the spine were suggestive of an osteo-articular problem. (2) The technical impossibility of performing a renal biopsy when graft function deteriorated. A negative biopsy result for the diagnosis of graft rejection would have led us to perform other tests to determine the cause of renal dysfunction. The appearance of the peripheral vascular deficit associated with persistent renal dysfunction suggested a vascular pathology; hence, the appropriate investigations were carried out, leading to the diagnosis of a pseudoaneurysm caused by Aspergillus infection. This case taught us that pain in the sciatic region in a patient without any background of interest and with no radiologic lesions pointing to an osteo-articular process should lead the physician to suspect a pathologic process in adjacent structures, such as vessels.

One unresolved issue is the origin of the aspergillosis. The possibility of transmission of the infection from the donor is remote because no hyphae were seen on the graft, and there was absence of infection in the other organ recipients. The fact that the renal transplantations were carried out by 2 different teams in 2 different operating rooms rules out surgical contamination. These data suggest that contamination probably occurred during preservation or storage. Another possibility is that the infection might have occurred in the posttransplantation period, although the absence of lung pathology and the specific vascular location at graft level almost completely rule out this possibility. The aggressive immunosuppressive therapy in our patient (cyclosporine, basiliximab, and MP), in addition to the antirejection treatment in the first case, could be a risk factor for fungal infection.

The use of liposomal amphotericin B, a new formulation, should be the treatment of choice in this type of patient in which the nephrotoxicity of classic amphotericin must be avoided. Moreover, the high concentrations reached in the reticulo-endothelial system and at inflammatory foci seem to offer greater therapeutic efficacy in fungal infection in immunosuppressed patients.

From the cases reported here, the following conclusions may be drawn. Patients subjected to renal transplantation are exposed to important infections. Some of these infections, such as that caused by aspergillus spp, are of low incidence, difficult to diagnose, have poor prognoses, and are extremely aggressive. The 2 cases described here show that once the most frequent causes of graft dysfunction (rejection, urinary tract obstruction, drug toxicity) have been ruled out, physicians should consider other less-frequent alternatives, such as vascular processes of different origins, among them, fungal infection. The insidious debut and clinical course require a high degree of suspicion to make a correct diagnosis.

REFERENCES