A rare case of acute renal failure due to massive renal allograft infiltration with Candida glabrata∗

Nadia Wasi1, Venkata Reddivari2, Luis Salinas-Madrigal3, Paul Garvin4 and Bahar Bastani1

1Division of Nephrology, Saint Louis University School of Medicine, Saint Louis, MO, USA, 2Department of Internal Medicine, Saint Luke’s Hospital, Saint Louis, MO, USA, 3Department of Pathology, Saint Louis University School of Medicine, Saint Louis, MO, USA and 4Division of Abdominal Transplant, Saint Louis University School of Medicine, Saint Louis, MO, USA

Keywords: acute renal failure; alemtuzumab; candida glabrata; renal transplantation; urinary tract infection

Introduction

Renal transplant patients remain at risk of graft loss due to acute rejection, calcineurin inhibitor toxicity and chronic allograft nephropathy. Less frequent causes include opportunistic infections related to immunosuppressive therapy. However, infections are a major clinical issue in the field of renal transplantation, impacting on graft and patient survival. Fungal infections account for about 5% of infections in renal transplant recipients [1]. Candida species are the most common fungal pathogen, and the most common forms of infection are oral and esophageal candidiasis, vascular access device-related and urinary tract infections [2]. The incidence of candidiasis of the renal allograft is rare and not very well documented.

Case report

A 50-year-old white female with a prior medical history of hypertension, end-stage renal disease secondary to type II diabetes, for which she was on haemodialysis for 31/2 years, underwent a renal transplant from a deceased donor in March 2006. The patient received induction therapy with alemtuzumab 30 mg intravenously (IV) and three doses of IV solumedrol around the time of transplantation. The surgery and post-op course were uneventful. A silastic stent was inserted into the pelvis of the kidney and into the bladder at the time of transplantation. The surgery and post-op course were uneventful. A silastic stent was inserted into the pelvis of the kidney and into the bladder at the time of surgery. Her maintenance immunosuppressive regimen included tacrolimus and mycophenolate mofetil. On post-op day 4 her serum creatinine was 2.0 mg/dL (177 µmol/L) with an estimated GFR of 28 mL/min/1.73 m² using the MDRD equation, her vital signs were stable and she was discharged from the hospital. Eight weeks later, the patient was presented to a local emergency room with dehydration and was found to have a serum creatinine value of 7.1 mg/dL (628 µmol/L). The patient was transferred to Saint Louis University Hospital for further evaluation. On initial examination at our institution, she was febrile with a fever of 38.2°C, blood pressure was 130/72 mmHg, RR 20/min and she had dry mucus membranes. She had coarse breathing sounds bilaterally; cardiac exam and abdominal exam were normal. There was absence of oedema, focal neurological deficits or cutaneous lesions. Laboratory evaluation revealed white blood cell (WBC) count 1600/mm³ (89% neutrophils, 3.8% lymphocytes, 0.6% eosinophils), haemoglobin 7.5 g/dL, haematocrit 24%, and platelet count 131 000/mm³. Urinalysis showed trace protein, small leucocyte esterase, WBC 18/high power field (HPF), red blood cells (RBC) 5/HPF and occasional yeasts. Renal ultrasound with Doppler study showed patent vessels with no evidence of hydronephrosis or perinephric fluid collection. Her tacrolimus dose was held because of a high serum trough level of 19.2 ng/mL. The patient was hydrated overnight with normal saline and her serum creatinine decreased to 5.9 mg/dL. However, over the next 2 days her serum creatinine did not improve further, prompting a transplant renal biopsy on hospital day 3.

Renal biopsy findings

The renal biopsy specimen consisted of two cores containing up to eight glomeruli. Some of the glomeruli were extensively destroyed by the presence of a massive yeast infection, which was also present in many tubules and the interstitium (Figure 1A). There was significant interstitial oedema and a granulomatous response around these large clusters of yeast. No hyphae were identified. The electron microscopy confirmed the presence of large aggregates of small spherical yeasts (blastospores), infiltrating...
Fig. 1. (A) Bowman capsule is infiltrated with yeast forms of *Candida glabrata*, also seen in adjacent glomerular tubules and interstitium (Periodic Acid Schiff staining; original magnification ×60). (B) Electron microscopy showing the Bowman capsule with yeast forms of *Candida glabrata* (magnification ×51,000).

tubular epithelium, interstitial and glomerular capillaries (Figure 1B).

**Hospital course**

After the initial histology report, the patient was thought to have renal allograft failure due to infection with cryptococcus. She was started on IV fluconazole 400 mg daily, which after 2 days was switched to IV liposomal amphotericin B at 300 mg/day. On hospital admission day 4 she developed respiratory failure requiring intubation and she was also started on intermittent haemodialysis. A CSF exam, CT scan and MRI of her head showed no abnormalities. The CT scan of the chest showed mild to moderate bilateral pleural effusions and patchy infiltrates. Her abdominal CT scan was negative for any pathology. On hospital day 7 she was extubated, renal function improved and haemodialysis was discontinued. Her ureteral stent was also removed. Subsequently, all the blood and urine cultures became positive for *Candida glabrata*. After 14 days of liposomal amphotericin B, she was switched to oral voriconazole at 200 mg BID for an additional 4 weeks. Her serum creatinine continued to improve and on a follow-up visit 3 months post-treatment, the value was down to 0.9 mg/dL (69 µmol/L).

Though rare, fungal infections portend a higher mortality as compared to bacterial and viral infections, and therefore need special attention. The prime time for fungal infections in transplant recipients is 1 to 6 months post-transplant. Our case developed a severe candida infection of her transplanted kidney 8 weeks after transplantation. In a study by Abbott *et al.*, evaluating USRDS data with regard to fungal infections in renal transplant recipients, most fungal infections (66%) had occurred by 6 months post-transplant, and only 22% by 2 months. An increased risk for fungal infections was associated with induction with OKT3, maintenance immunosuppression with tacrolimus, allograft rejection, recipients with DM, and prolonged pre-transplant dialysis time [3]. In a recent study by Safdar *et al.*, looking at 1738 renal transplant recipients, candiduria was noted in only 11% of the patients and more than half of these patients were asymptomatic [4]. Since asymptomatic candiduria may be the only manifestation of invasive disease, and since significant morbidity has been associated with fungal UTI, it presents a major challenge to the physicians because it is usually unclear whether candiduria represents colonization or active infection.

The present case had received induction therapy with alemtuzumab, a humanized monoclonal antibody directed against CD-52 expressed on B and T lymphocytes, monocytes and natural killer cells. The risk of infection associated with alemtuzumab use as an induction agent in the organ transplant population is reported to be low [5]. However, a recent report by Peleg *et al.* [6] showed that patients who received alemtuzumab as an induction agent had a low risk of developing opportunistic infections, but those who received it as an anti-rejection therapy were five times more likely to develop an opportunistic infection.

In our patient, the presence of yeast on admission urinalysis was a surrogate marker of candida infection of her allograft. To the best of our knowledge, this is the first report of candida infection of renal allograft presenting with severe acute renal failure. A similar presentation has been reported in a case of cryptococcal infection in renal allograft [7].

**Conclusion**

This case report suggests that the use of newer immunosuppressive agents in recent years may be associated with some changes in the epidemiology of post-transplant
infections. Frequent surveillance with urinalysis and urine culture, prophylactic measures and aggressive therapy of documented infection can reduce the high morbidity associated with these potentially fatal infections. A new look at the general measures for prevention of fungal infection, particularly in the high-risk groups, is justified.

Conflict of interest statement. None declared.

References


Received for publication: 10.8.07
Accepted in revised form: 7.9.07