Isolated urinary aspergillosis in a renal transplant recipient

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Introduction

In spite of the increased incidence of invasive aspergillosis in transplant recipients, urinary tract infections caused by *Aspergillus* species are uncommon and are usually part of a systemic hematogenous dissemination [1]. The origin of this hemogenous spread is usually the immunosuppressed transplant recipient but recently the transmission of an invasive renal aspergillosis from an immunosuppressed and subclinically infected donor to two different transplant recipients has been reported [2]. We describe here an unusual case of isolated urinary aspergillosis in a renal transplant recipient.

Case

The donor was a 53-year-old man, with a past history of diabetes and heavy alcohol consumption who presented to the hospital complaining of headaches. He was soon found in coma and a computed tomography (CT) scan of his head revealed massive intracranial bleeding with blood in the ventricular system. He remained apyretic, renal function was normal, urine, blood and abdominal fluid cultures were negative, no sputum was produced and the chest X-ray was clear. Brain death was diagnosed later in the day and he was considered for kidney donation.

A 43-year-old man in hemodialysis from a glomerulopathy of unknown origin and with a residual diuresis of 500 ml/day received one of the two kidneys. Cold ischemia was 33 h. The immunosuppression regimen was antithymocyte globulin (Merieux) during the first 11 days associated with methylprednisolone (1 g in the operating room, 60 mg on day 2 then 20 mg from day 3 to 11), prednisone 40 mg/day, cyclosporine from day 8, 4 mg/kg/day (usually 300 mg/day adjusted to blood levels) and azathioprine 2 mg/kg/day (usually 150 mg/day). In the post-operative course, renal function did not improve and diuresis remained between 700 ml and 1.5 l/day. Doppler ultrasound and renal scintigraphy showed a good arterial flow with no increased resistance, no signs of renal vein thrombosis and no dilatation of the pyelocaliceal system. The patient was considered to have acute tubular necrosis. From the first day, his temperature was between 38°C and 39°C with no obvious infection. Cultures of blood and urine for bacteria, CMV and fungi were negative. The chest X-ray was clear.

On day 15, after four negative urine cultures, the urine culture was positive for *Escherichia coli* and *Aspergillus fumigatus*. On further evaluation, no overt focus of *Aspergillus* infection could be found in the lungs (sputum, bronchoscopy with cultures of bronchioloalveolar fluid), nasal sinuses or skin. *Aspergillus* antigen and antibodies in the serum were negative. When urinary aspergillosis was diagnosed, the allograft was traced back to the other renal transplant recipient in which transplant nephrectomy was performed within 48 h because of an arterial thrombosis. No fungal hyphae were found histologically.

Itraconazole 400 mg/day was begun on day 18 associated with flucytosine 500 mg three times daily from day 51. Fever persisted and urine cultures remained positive for *A. fumigatus*. A graft biopsy on day 22 and on day 39 showed prominent interlobular chronic endarteritis with focal glomerular ischemia, mild diffuse glomerulosclerosis with scanty mesangial IgA and C3 deposits, and tubulointerstitial fibrosis. No acute rejection and no fungal hyphae were found. A contrast CT scan of the abdomen and pelvis, and a renal ultrasound were normal. On day 53, cystourethroscopy showed a macroscopically normal overlying mucosa except for hypertrophic mucosa at the implantation site of the ureter which, under light microscopy, showed abundant fungal hyphae with underlying necrotic submucosal areas.

Nephrectomy was performed on day 60 because of the persistence of the fever, the positive urine cultures for *A. fumigatus* and the impaired renal function. On gross appearance, the kidney was normal in size with necrotic papillae still attached. Histologically, these nec-
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Necrotic papillae were covered and invaded by fungal hyphae mixed with polymorphonuclears, and were separated from the adjacent living medulla by a dense zone of granulocytes and, occasionally, collections of giant cells (Figure 1). In the adjacent inner medulla, fungal abscesses were present. Cortical extension of the lesions was seen along very few tracts with polymorphs in the lumen of the tubules and interstitial giant cell granulomas containing *A. fumigatus*. The cortex exhibited marked fibrosis with tubular atrophy and sclerotic glomeruli.

The patient became apyretic within 4 days of the transplantectomy. Until he left hospital on day 67, the urine cultures were positive for *Aspergillus fumigatus*. He then quickly became anuric.

**Discussion**

To our knowledge the case reported here is the first of an isolated renal aspergillosis in a kidney transplant recipient. Several arguments have indicated that the invasive aspergillosis in our patient is limited to the kidney and that the route of infection is an ascending one: other infected sites have been ruled out in the recipient on many occasions; no abscesses on gross appearance and no fungal hyphae invasion of the cortex under light microscopy in both kidney grafts at the time of transplantectomy; no evidence for an hematogenous spread from a subclinically infected donor. Urinary fungal infection by ascension has been described in diabetic patients and patients with obstruction of the ureteropelvic junction. Two different patterns were seen: panurothelial infection and an isolated renal infection producing aspergilloma and/or papillary necrosis [3–5]. The histopathologic findings in our patient are consistent with these patterns combining papillary necrosis with inflammatory infiltrates extended focally in cords from the renal papillae into the adjacent medulla, medullary abscesses and an almost uninvolved cortex. This renal aspergillosis could correspond to a nosocomial infection, a pre-existing subclinically infected recipient or a donor-transmitted infection.

*Aspergillus* species are ubiquitous saprophytes in nature and are opportunistic fungi. The hospital may be the source of micro-epidemic outbreaks, most cases being the result of airborne transmission [6]. At the time of transplantation, no increased incidence of *Aspergillus* species infection was reported in the hospital or in the renal unit. Multiple samples were taken from the operating rooms and the donor’s and recipient’s rooms and all were negative for *Aspergillus* species. The culture of the storage solution was negative and we cannot exclude a peroperative infection.

A pre-existing latent infected recipient’s bladder seems unlikely since this patient was not diabetic, had no previous history of urinary tract infection and urine cultures during early days of transplantation were negative.

Several arguments suggest that this case corresponds to a donor-transmitted infection. The donor was a diabetic and alcoholic man, conditions associated with both papillary necrosis and *Aspergillus* infection. The negative urine culture obtained from the donor does not rule out renal aspergillosis, similarly normal renal function does not rule out papillary necrosis. Moreover in some cases, papillary necrosis in diabetic patients progresses slowly as in analgesic nephropathy [6]. In these cases, the renal cortex may exhibit tubular loss and atrophy with increased interstitial fibrosis and focal segmental glomerulosclerosis. These histopatho-

![Fig. 1. (A) Gross appearance of cut surface of the renal transplant: necrotic papillae are yellow (X) and friable. (B) Histologic section showing necrotic papilla. Large medullary area of necrosis (●) underlined by a zone of inflammatory reactions (★); on the other side, the mucosa is preserved (original magnification ×20 HES). (C) Microscopic aspect of fungal hyphae mixed with necrotic fragmented tissue and polymorphonuclear neutrophils (original magnification ×320 HES).](image)
logic findings of the cortex were noticed in all the graft biopsies of our patient and later in the transplantectomy-ized kidney, and are therefore compatible with a chronic papillary necrosis.

Whatever the route of contamination, the use of immunosuppressive drugs, corticosteroids and broad-spectrum antibiotics is associated with a greater incidence of invasive and disseminated *Aspergillus* infections [7]. Corticosteroids at an average daily dose above 1.25 mg/kg/day are known as a very reliable predictor of subsequent invasive aspergillosis [9]. Such doses were not reached in our patient.

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**References**


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