A renal transplant recipient with acute paraparesis due to an Aspergillus epidural abscess

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Introduction

In immunocompromized patients, such as renal transplant recipients, spores of Aspergillus, which are ubiquitous in the environment, are dangerous opportunistic pathogens. The brain, lungs, and sinuses are the main targets of this fungal infection, with a high rate of mortality due to difficulties in diagnosis and therapy. We describe here a rare epidural location of invasive aspergillosis in a renal transplant recipient.

Case report

In March 1995 a 66-year-old man with chronic renal failure due to glomerulonephritis of undetermined aetiology received a cadaveric renal transplant. Immunosuppressive regimen comprised cyclosporin A (4 mg/kg/day), azathioprine (2 mg/kg/day), and methylprednisolone tapered from 120 mg/day to 4 mg/day over 2 months. The initial postoperative course was unremarkable, apart from an Enterococcus faecalis urinary tract infection, which was treated with amoxicillin, and the patient was discharged with a well-functioning graft (serum creatinine 130 μM/l).

In May 1995 he was hospitalized for fever and leukopenia (2100/mm³). CMV antigen pp65 was present in the patient’s leukocytes. Blood and urine cultures were positive for CMV, as well. He was treated successfully with ganciclovir (10mg/kg/day for 14 days).

In June 1995 he was admitted again for renal function degradation. Graft biopsy showed acute cellular rejection of grade I in the Banff classification. He was treated with boluses of methylprednisolone (4.5 g over 9 days) and serum creatinine stabilized at 170 μM/l.

In October 1995 the patient presented right intercostal nerve pain, without any neurological deficit, for which he was treated symptomatically. However, in February 1996, he was hospitalized for a sudden increase in intercostal pain. The patient was afebrile and neurological examination was normal. Plain films of the spinal column did not show any abnormality. Two days later he presented with an acute weakness of both legs, loss of sensation below T9, and slight sphincter dysfunction. There was no Babinski reflex. A spinal MRI-scan was performed (Figures 1–3). It showed a large posterior epidural fusiform mass (3 cm long) at level T8–9, compressing the cord, which was...

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Following injection of gadolinium, the enhancement was seen in periphery whereas two central zones were not enhanced. A decompressive laminectomy permitted the drainage of an epidural abscess containing purulent material. Culture analysis revealed fungi identified as *Aspergillus fumigatus*. At that time, specific aspergillar antibodies directed against the three antigens tested (metabolic, catalase, somatic) were highly positive, whereas previous serologic results had always been negative. Laboratory findings showed neither neutropenia nor inflammatory syndrome. Following laminectomy, the recovery of neurological deficit was complete. Medical treatment was started immediately with itraconazole (400mg/day), and serial serum itraconazole level determinations showed proper therapeutic concentrations. The immunosuppressive regimen was not changed.

The search for locations in the brain and lungs was negative. The finding of a right maxillary sinus opacity led to meatotomy allowing the isolation of *Aspergillus fumigatus*. Follow-up MRI in April and August 1996 showed no sign of recurrence (Figure 4). Moreover, aspergillar antibodies were no longer detectable after July 1996. The same month, sinus CT scan and ENT examination suggested a possible relapse involving the maxillary sinus. A second meatotomy was performed and both histology and direct examination were unable to identify fungi. During the period necessary for culture growth, amphotericin B was introduced for 22 days until a cumulative dose of 1.3 g was reached. At that
time cultures were still negative for *Aspergillus fumigatus* and amphotericin B was replaced by itraconazole at the previous dose. However, probably because of amphotericin B toxicity, renal function deteriorated and haemodialysis was required.

In August 1996, the patient was admitted to intensive care for acute respiratory failure. Bronchoalveolar lavage specimens revealed CMV and bacterial superinfection (*Pseudomonas aeruginosa*, *Staphylococcus aureus*). *Aspergillus fumigatus* was not found in bronchoalveolar samples (direct examination and culture) and specific serological testing remained negative. In September, while still in intensive care, he presented massive rectal haemorrhage, necessitating rectal resection. Pathology revealed ischaemic necrosis, but the search for fungus using specific colorations or CMV inclusions was negative and no other infectious etiology was found. Presenting septic shock and diffuse gastric bleeding for which surgical abstention was decided, the patient died in October 1996. No necropsy was performed.

**Discussion**

Invasive aspergillosis occurs mainly in immunosuppressed individuals, including HIV-positive patients. In autopsy series of patients with AIDS its overall frequency is estimated at around 4% [1]. In renal allograft recipients it probably constitutes the greatest infectious risk because of its high mortality rate, close to 100%, with an incidence around 2% [2]. In our department we have observed five cases of invasive aspergillosis out of more than 1400 renal transplantations carried out over the last 20 years. This is the first case we have observed with an epidural location, and we found only two cases previously reported in the literature [3,4]. In renal transplantation Aspergillus infection usually affects the lungs, central nervous system, sinuses, skin, and occasionally the gastrointestinal tract, the liver, or kidney [2,3].

The highest rate of occurrence of invasive aspergillosis is during the first year after renal transplantation [2,5,6]. In our case, the diagnosis was made at month 11. Lungs are the major portal of entry and secondary haematogenous dissemination is frequent [5,6]. The peculiarity of our observation was the unusual route of infection with a probable primary focus involving the sinuses and subsequent haematogenous spread into the epidural area. In spite of extensive CT investigations including the lungs and brain, we detected no other foci. Of note is that our patient had never undergone a lumbar puncture nor epidural anaesthesia, as in previously reported case that may have had an iatrogenic origin [3].

This case illustrates the usual paucity of physical examination which renders early diagnosis difficult [2,5]. Chronic pain should alert the clinician, even in the absence of objective evidence such as fever, neurological signs, or laboratory findings of inflammation, and should prompt complementary investigations. We underscore the excellent and non-invasive mode of exploration of such cord lesions provided by MRI [7]. In this context, three factors which favour tissue invasion by Aspergillus have considerable value. Indeed, our patient successively presented all of them, i.e. CMV infection, leukenaemia, and pulse corticosteroid therapy for acute rejection [2,6]. To confirm diagnosis, the gold standard remains histological examination and culture of a biopsy specimen. Although in our case there was a clear correlation between clinical course and results of aspergillar serology, this is not always the case in immunosuppressed patients.

Our patient was first treated surgically, then with itraconazole for 7 months, except for a short course of amphotericin B. This well-tolerated antifungal drug offers several advantages including oral administration, lower renal toxicity compared to amphotericin B, and similar minimum inhibitory concentrations [8,9]. Due to this prolonged and pharmacologically monitored treatment, we have good reason to believe that aspergillar foci were sterilized. Indeed, (i) no recurrence was observed by MRI examination, (ii) the second sinus biopsy was found to be free of Aspergillus by both histology and cultures, and (iii) aspergillar serology became negative following treatment. However, this assumption was unfortunately not submitted to confirmation by necropsy.

In conclusion, *Aspergillus fumigatus* epidural abscess should be considered in renal transplant recipients with chronic back pain. MR imaging offers the most reliable means of examining and monitoring this kind of lesion. Itraconazole is an effective alternative to amphotericin B for long-term treatment of these patients with compromised renal function.

**References**


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