Letters to the Editor

Staphylococcus aureus Bacteraemia, Absidia corymbifera Infection and Probable Pulmonary Aspergillosis in a Recipient of Orthotopic Liver Transplantation for End Stage Liver Disease Secondary to Hepatitis C

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Sirs.

In recent years, several reports have underlined the emerging role of invasive fungal infections as a cause of morbidity and mortality in recipients of orthotopic liver transplantation. The incidence of this complication varies from 5% to 42% with a case fatality rate as high as 69% in some reports.1-3 Although the most common pathogens remain Candida albicans and Aspergillus, there are increasing reports of infections caused by non-albicans candida and by Cryptococcus, Pseudallescheria boydii, Trichosporon beigelii and other uncommon microorganisms.4-6 We have recently seen a case of fatal Absidia corymbifera bacteraemia and accompanied by probable pulmonary aspergillosis, in a recipient of orthotopic liver transplantation for liver cirrhosis and hepatocarcinoma consequent to HCV infection.

The patient, a 55-year-old man with a history of hepatic carcinoma and cirrhosis secondary to hepatitis C, underwent orthotopic liver transplantation in January 1994. Choledochocholedochostomy was performed and a T-tube stent was placed intraoperatively across the biliary anastomosis. Perioperative antibiotic prophylaxis consisted of teicoplanin (he was a nasal carrier of MRSA) and azthreonam. Initial post-transplant immunosuppressive therapy included cyclosporin A (5 mg/kg/day, tapered to 2.5 mg/kg/day) and prednisone (1 g bolus on day 1, then tapered to 150 mg/day). In addition, the patient received intestinal decontamination with polymixin B, gentamycin and nystatin, as well as antiviral prophylaxis with acyclovir (750 mg tid intravenously). The early post-transplant course was complicated by the appearance of acute hepatic failure due to histologically documented rejection. For this reason, cyclosporin was discontinued on day 3 and the patient was put on intravenous OKT3 monoclonal antibodies, together with intravenous gancyclovir for VMC prophylaxis. In the meantime, because of the repeated isolation of MRSA from nasal and respiratory secretions, the decision was taken of not discontinuing prophylactic intravenous teicoplanin. On day 6 post-transplant, the patient developed high fever, renal and hepatic insufficiency and respiratory failure due to pleural effusion and pneumonia. Despite teicoplanin prophylaxis several blood cultures yielded MRSA. Teicoplanin was then replaced with vancomycin with slight improvement of both clinical conditions and respiratory parameters, as well as of renal and hepatic functions. However, the patient was still intubated and on assisted ventilation. On day 9 from transplant, OKT3 and gancyclovir were discontinued and cyclosporin was restarted (2 mg/kg/day, then tapered to 1 mg/kg/day), in combination with azathioprine (2 mg/kg/day) and prednisone (300 mg bolus for 3 days, then tapered to 0.1 mg/kg/day). On day 11, a red maculopapular lesion with a black centre was first noticed on the patient's right shoulder, located under an electrode used for vital signs monitoring. Within 24 h the shoulder lesion reached a diameter of about 10 cm and became frankly necrotic, surrounded by a bluish halo of vasculitis (Fig. 1). Subsequently, several other lesions with the same aspect and the same diameter became apparent throughout the patient's body (Fig. 2). The patient was highly febrile, with hypotension and signs of multiple organ failure. Lesions were biopsied and cultures were taken. Specimens for histology (2 fragments 1 cm x 1 cm) were put in 10% buffered formalin and stained with eosin, periodic acid Schiff and methanamine-silver. Microscopic examination showed small granulomatous infiltrates.
with several sporelike elements and non-septate fungal hyphae spreading among fat lobules and invading blood vessels (Fig. 3). At the microbiology laboratory both Gram and blue-lactophenol stains showed the presence of fungal hyphae. Culture on blood and Sabouraud agar yielded filamentous fungi, provisionally classified as belonging to the Mucorales group. The mould was later identified as *Absidia corymbifera* at the Pasteur Institute, Mycology Unit, Paris, France. All blood cultures remained negative. Antifungal therapy with amphotericin B (0.5 mg/kg/day) was immediately started as soon as the first lesion was noticed, because of its similarity with skin lesions commonly associated with disseminated fungal infections, such as, for example, fusariosis. Nevertheless the patient’s clinical conditions continued to deteriorate, with progressive enlargement and increase in number of the skin lesions and with appearance of several new pulmonary infiltrates. Bronchoalveolar lavage was then performed and culture yielded *Aspergillus fumigatus*. Lung biopsy was not taken because of the patient’s critical condition. The patient died on day 24 after transplant for cardiorespiratory arrest secondary to respiratory insufficiency and irreversible shock, after having received a total dose of 560 mg of amphotericin B.

Invasive fungal infections due to uncommon pathogens are increasingly reported among immunocompromised patients, especially those receiving chemotherapy for the treatment of neoplastic diseases. Among patients undergoing solid organ transplantation, orthotopic liver graft recipients are at the highest risk of developing these infections due to several reasons, including prolonged operation time, frequent need of reoperation and reintubation, generous use of antibacterial drugs, need of immunosuppressive therapy and, possibly, previous colonization. The present case might be instructive both because of the rarity of *A. corymbifera* infection and because of its occurrence in association with other infections, such as *S. aureus* bacteraemia and *A. fumigatus* pulmonary infection. Since post-mortem examination was not performed and since the mould did not grow in the blood, we are unable to definitively prove deep organ involvement. However, the fact that the skin lesions rapidly spread all over the body from the initial one (Fig. 2) and that clear signs of systemic infection were concomitantly present, suggests that the infection was actually disseminated. Similarly, pulmonary aspergillosis was not documented with absolute certainty, because no histological documentation of lung tissue invasion was obtained. However, the isolation of *A. fumigatus* from respiratory secretions obtained by bronchoalveolar lavage in association with pulmonary infiltrates in a liver transplant patient has been found to be closely associated with pulmonary aspergillosis.

*Absidia corymbifera* is a rare cause of human disease even in immunocompromised hosts. As recently reviewed by Manso, infections due to this mould have been documented mainly in patients with neoplastic diseases, especially those with haematological malignancies. Other cases have been reported in patients with AIDS, with a single case in a renal transplant recipient. More recently, two other cases have been reported, one in an AIDS patient and another in a patient with acute leukaemia. Clinical presentation included cutaneous lesions, rhinocerebral infarctions, surgical wound infections, pulmonary localizations and kidney infections. Rarely has this infection been diagnosed before death. To the best of our knowledge, *A. corymbifera* has never been reported as cause of infection in liver transplantation, although liver cirrhosis is often accompanied by iron overloading, which is thought to facilitate mucormycosis. The occurrence of zygomicotic infections (but not absidiomycosis) under elastoplast bandages over operative wounds has been described.
and it seems that moist and humid conditions created by occlusive dressing may facilitate these infections. In the present case the primary infection developed under an electrode for vital signs monitoring (and not under an elastoplast bandage), but then spread to other skin sites (excluding the operative wound) that were free of any bandage. Little is known about the treatment of choice. Amphotericin B is generally used but it is almost always unsuccessful, probably due to host and pathogen-related factors. Recovery from the underlying immunodeficiency is probably essential for survival.

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References

Tonsillar Actinomycosis Presenting as Expectorated Debris

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Sir,

We wish to report a case of tonsillar actinomycosis discovered in an asymptomatic patient attending for routine D.C. cardioversion for persistent atrial fibrillation.

At routine clerking the patient handed over a small mass of white material (approximately 1 mm3) which he claimed to have expectorated shortly prior to arriving on the ward. Nothing similar had happened to him previously. On further questioning, the patient reported no symptoms suggestive of tonsillar disease. However, he had been troubled by a productive cough over the preceding 3 months. There was a history of childhood asthma.

On examination, the patient was apyrexic, his chest was clinically clear and his oral cavity was unremarkable. There was no cervical lymphadenopathy. His chest radiograph was clear and sputum cytology was negative.

The sample was sent for histological examination and was reported to comprise of a colony of Actinomyces spp, consistent with a tonsillar origin. The patient was