Transpl Int (1999) 12: 297–298

LETTER TO THE EDITOR

Davide Mazza
Jean Gugenheim
Edoardo Baldini
Jean Mouiel

Gastrointestinal mucormycosis and liver transplantation; a case report and review of the literature

Received: 17 September 1998
Accepted: 1 March 1999

Sir: Mucormycosis is a rare but highly invasive fungal infection occurring in the immunocompromised patient [5]. Rhinocerebral, pulmonary, and cutaneous are the most common forms in solid organ recipients, however, only one case of gastric localisation has been described in the literature [10].

In December 1996, a 35-year-old man underwent orthotopic liver transplantation for alcoholic cirrhosis, stage C by Child-Pugh classification. The patient and the donor were seropositive for cytomegalovirus, herpes zoster varicella virus, and Epstein-Barr virus; and seronegative for human immunodeficiency virus, hepatitis A, B, C viruses. Serological tests for candidosis, aspergillosis, and cryptococcosis were negative. The immediate postoperative course was uneventful, immunosuppression regimen (cyclosporine, corticosteroids, and azathioprine) was started on the first postoperative day, and there was no episode of rejection. Systematic postoperative haemocultures were positive for *Staphylococcus epidermidis.* An antibiotic treatment by teicoplanine and fucidine was started. Twenty days after transplantation, azathioprine administration was stopped because of leukopenia (1.8×10^9/L) with lymphocytopenia (0.02×10^9/L), without any clinical or laboratory findings of viral infection. On the twenty-third postoperative day the patient suddenly developed septic shock and diffuse abdominal pain. Emergency laparotomy showed generalised peritonitis, and a perforation of the caecum, that was sutured after resection of the lesion wedges. The liver graft was normal at exploration. In the immediate postoperative period, the patient died of irreversible multiple organ failure. Bacteriological and mycological culture of peritoneal liquid showed *Escherichia coli* and *Lactobacillus suppurans.* Histological examination of the tissue surrounding the caecal perforation showed several leukocyte-infiltrates including non-septate, thick-walled hyphae, as well as a granulomatous lesion with giant cells containing fragments of such hyphae. At necropsy, 3 liver abscesses, measuring from 1 to 2 cm, with a necrotic center, were found. Several broad, non septate, right angle branching hyphae were found after hematoxylin-eosin staining. Their affiliation to the *Mucorales* species was further confirmed by PAS and Grocott silver stains.

The term mucormycosis is used for those acute opportunistic mycoses caused by the thermotolerant, ubiquitous fungi belonging to the order of *Mucorales,* commonly found in soil and decaying organic matter. The *Mucorales* belong to the class of *Zygomycetes,* and they include the family *Mucoraceae,* with *Rizhopus, Mucor,* and *Absidia* as the most common pathogen genera [5]. Predisposing conditions are diabetes mellitus, cancer chemotherapy, organ transplantation [6, 7], use of Elastoplast (Beiersdors Inc. Norwalk, Connecticut) bandages [4], corticosteroid administration in patients with hematological malignancies [11], burns [2], renal failure [11], and prolonged postoperative course [1]. Mucormycosis is characterized by a rapid spread of hyphae in tissues, and invasion of vessel walls, with subsequent infarction, combined with the production of black necrotic pus. The most common mode of infection is by inalation, ingestion, direct inoculation or hematogenous spread of spores [5]. The incidence of mucormycosis in the transplant patient varies from 1 to 9 per cent. The male : female ratio is 3 : 1. Eighty per cent of cases occurr within six months of transplantation; the median time of onset of the infection is 2 months after surgery. The overall mortality is 56 per cent. Most cases of mucormycosis after organ transplantation have been of rhinocerebral localisation, but disseminated, pulmonary, cutaneous and soft tissue forms have also been described. There is only one case of the gastrointestinal form, which developed in a liver graft recipient [10]. Three other cases of mucormicosis after liver transplantation have been reported: a disseminated form, and 2 cutaneous and soft-tissue infections [3, 8, 12]. Only one patient with cutaneous mucormycosis survived. Time of onset of the mycotic infection in such patients, as in the one we reported, is much shorter (7 days in two cases, 30 days in another), than that reported for other organ recipients.

The clue to successful mucormycosis therapy lies in early diagnosis, which can be obtained by a biopsy of the involved area, for histopathological demonstration and culture of the fungus. Once mucormycosis is diagnosed, extensive surgical resection combined with amphotericin B therapy and reduction of immunosuppressive drugs should promptly be realized. The experimental allylamine antifungal agent SF 86-327 (Exoderil; Sandoz, Vienna) has been successfully used to treat a renal graft recipient in which amphotericin B had failed to cure soft tissue mucormycosis [9]. Other antifungal drugs are ineffective.

In conclusion, it must be kept in mind that visceral perforation can be the first manifestation of mucor-

mycosis in the transplant recipient; thus, in case of unexplicated gastrointestinal perforation, an immediate search for fungal hyphae may allow prompt therapy and better outcome.

References

1. Agger WA, Maki DG (1978) Mucormycosis: a complication of critical care. Arch Intern Med 138: 925–927
2. Bruck HM, Nash G, Foley FD, Pruitt BA Jr (1971) Opportunistic fungal infection of the burn wound with phycomycetes and Aspergillus: a clinical-pathogenic review. Arch Surg 102: 476–482
3. Chen YS, Chen CL, Liu PP, Chiang YC, Sun CK, Eng HL (1996) Successful treatment of invasive mucormycosis following liver transplantation. Transplant Proc 28: 1708–1709
4. Keys TF, Haldorson AM, Rhodes KH, Roberts GD, Fifer EZ (1978) Nosocomial outbreak of Rhizopus infections associated with Elastoplast wound dressing. Minnesota Morbid Mortal Weekly Rep 27: 33–34
5. Leherer RI, Howard DH, Sypherd PS, Edwards JE, Segal GP, Winston DJ (1980) Mucormycosis. Ann Intern Med 93: 93–108
6. Meyer RD, Kaplan MH, Ong M, Armstrong D (1973) Cutaneous lesions in disseminated mucormycosis. JAMA 225: 737–738
7. Meyer RD, Rosen P, Armstrong D (1972) Phycomycosis complicating leukemia and lymphoma. Ann Intern Med 77: 871–879
8. Nimmo GR, Whiting RF, Strong RW (1988) Disseminated mucormycosis due to Cunninghamella bertholletiae in a liver transplant recipient. Postgrad Med J 64: 82–84
9. Norden G, Bjorek S, Persson H, Svalander C, Li X, Edebo L (1991) Cure of zygomycosis caused by a lipase-producing Rhizopus rhizopodiformis strain in a renal transplant recipient. Scand J Infect Dis 23: 377–382
10. Singh N, Gayowski T, Singh J, Yu VL (1995) Invasive gastrointestinal zygomycosis in a liver transplant recipient: case report and review of zygomycosis in solid-organ transplantation. Clin Infect Dis 20: 617–620
11. Straatsma BR, Zimmerman LE, Gass JDM (1962) Phycomycosis: a clinicopathologic study of fifty-one cases. Lab Invest 11: 963–985
12. Wajszczuk CP, Dummer JS, Ho M, Van Thiel DH, Starzl TE, Iwatsuki S, Shaw B Jr (1985) Fungal infections in liver transplant recipients. Transplantation 40: 347–353

D. Mazza (✉)
Department of Digestive Surgery,
"Font Pre" Hospital,
B. P. 1412,
F-83056 Toulon,
Fance

J. Gugenheim · E. Baldini · J. Mouiel
Department of Digestive Surgery and
Liver Transplantation,
University of Nice – Sophia Antinopolis,
"L'Archet 2" Hospital,
B. P. 3079 – F-06202, Nice, Cedex 3, France