Gangrene of the anterior abdominal wall after orthotopic liver transplantation: invasive cutaneous candidiasis

M. Rela, N.D. Heaton, V. Vougas, N. Rolando, J. Wade, B. Portmann, Roger Williams and K.C. Tan

Department of Liver Transplant Surgery and Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS, UK

Summary: Fungal infections following liver transplantation are not uncommon and may be life-threatening. Superficial candidal infections of the bronchus, oesophagus and urinary tract are the most common mode of presentation. Invasive cutaneous and subcutaneous candidiasis is, however, very rare. We report two patients with invasive cutaneous and subcutaneous candidiasis after orthotopic liver transplantation.

Introduction

Invasive fungal infections have become an increasingly important problem following orthotopic liver transplantation (OLT), being reported in up to 42% of these patients.^{1,2} Eighty-five per cent of these infections develop within 2 months of transplantation.¹ Fungal infections appear to be a particular problem following liver transplantation compared with heart, lung and renal transplants, and are a significant factor in determining outcome. Although superficial fungal infections of the bronchus, oesophagus and urinary tract are not uncommon after liver transplantation, there has been no report of invasive cutaneous and subcutaneous fungal infection associated with skin necrosis. We report two patients with histological evidence of skin necrosis secondary to invasive candidal infection.

Patients

Case 1

A 48 year old man presented in 1980 with alcoholic cirrhosis and hepatic decompensation precipitated by bleeding oesophageal varices and was successfully treated by injection sclerotherapy. He was readmitted in 1990 with jaundice and hepatic encephalopathy and was referred for orthotopic liver transplantation (OLT) which he underwent in March 1991. The total operative time was 7 hours

and the operative blood loss was 3 litres. His postoperative recovery was complicated by continuing bleeding requiring 2.5 litres of blood transfusion, pulmonary hypertension, renal failure and confusion. He developed early severe acute cellular rejection which did not respond to conventional boluses of methyl prednisolone and because of deteriorating liver function was retransplanted as an emergency on day 10. The explanted liver appeared cholestatic and the left hepatic artery was thrombosed. Following the retransplant he received standard immunosuppressive therapy of cyclosporin A, azathioprine and methyl prednisolone.

Seven days after retransplantation a rapidly progressive necrotic area appeared at the site of the abdominal drain. Despite treatment with vancomycin, ciprofloxacin, amoxycillin and metronidazole, the superficial gangrene spread rapidly. A necrotic tissue covering an area 20 cm × 15 cm was excised. *Staphylococcus epidermidis*, *Enterococcus faecalis* and *Candida albicans* were isolated from the cultures of the excised material. Histological examination revealed *Candida* invading the skin and subcutaneous tissue (Figure 1). *Candida* was also isolated from swabs from the oral cavity, the left axilla and an indwelling urinary catheter tip. He was treated with intravenous amphotericin B, vancomycin, flucloxacillin, metronidazole and gentamicin and he subsequently recovered. The wound was closed by secondary suture and it healed over a period of 3 weeks. The patient was discharged 8 weeks post-transplant with good graft function.

Figure 1 Histology of subcutaneous tissue showing the wall of totally necrotic vessel infiltrated by elongated fungi (Grocott silver method, $\times 250$).

Case 2

A 45 year old man was referred for liver transplantation for cirrhosis related to hepatitis B infection. Standard orthotopic liver transplantation was performed with an operative time of about 7 hours and operative blood loss of 8 litres. The bile duct anastomosis was by end-to-end choledocho-choledochostomy with a T-tube. The initial post-operative course was complicated by persistent cholestasis and the development of multiorgan failure which was managed by mechanical ventilation, haemofiltration, inotropic support, antibiotics, amphotericin and transfusion of blood, fresh frozen plasma and platelets.

A necrotic area developed at the site of the abdominal drain 10 days after OLT which rapidly enlarged to 7 cm $\times$ 8 cm in size. The necrosed skin and subcutaneous tissue was excised to healthy tissue and samples were sent for culture and histology. The cultures grew *Candida albicans*, *Achromobacter xylosoxidans* and *Pseudomonas* species. Histology showed invasive candida in the necrotic tissue. *Candida albicans* had previously been isolated from the T-tube, penile swabs, wound drainage, and from a catheter specimen of urine. The patient subsequently deteriorated and began to bleed from the distal gastrointestinal tract which was difficult to control due to thrombocytopenia and coagulopathy. He died 3 weeks post-transplant due to multiorgan failure.

Discussion

Invasive fungal infections are associated with significant morbidity and mortality after OLT.¹⁻³ The most frequent pathogens are *Candida* and *Aspergillus* species, but occasionally *Cryptococcus*, *Fusarium* species or other unusual fungi may be responsible for infection in debilitated or immunosuppressed patients. *Candida* accounts for approximately two thirds of infections after OLT, but *Aspergillus* infection appears to carry a worse prognosis.² The usual source of the fungi is from the gastrointestinal tract and infection is associated with deranged reticulo-endothelial function.⁴ Fungal invasion is invariably preceded by evidence of colonization of the upper respiratory tract, urine, wound, abdominal drains and urinary catheters.⁵ Fungal infection has also been reported as a common but often unrecognized complication of acute liver failure.⁶ This population has defective cell-mediated immunity which predisposes to infection and there is an association with the use of invasive monitoring and broad-spectrum antibiotic therapy. Early diagnosis of fungal infection is often difficult and definitive diagnosis of invasive fungal infection depends on the histological demonstration of the organism in the affected tissue.⁷

Identified risk factors for fungal infection after liver transplantation include retransplantation, tracheal reintubation, bacterial infection, massive intra-operative blood transfusion, urgent-listed cases, the number of steroid boluses, vascular complications, the use of Roux loop for biliary reconstruction,¹ prolonged courses of systemic antibiotics and prolonged length of operation.² Several of the above factors were present in both these cases.

Bronchial, oesophageal and urinary tract are the common sites of superficial fungal infection. A review of recent literature showed no cases of invasive cutaneous and subcutaneous candidiasis, although disseminated systemic infection was found in a significant percentage of patients.^{2,3,5,7} These two cases are reported to highlight a rare manifestation of a common fungal infection in the post-transplant patient.

References

1. Castaldo, P., Stratta, R.J., Wood, P., Martin, R.S. *et al.* Clinical spectrum of fungal infection after orthotopic liver transplantation. *Arch Surg* 1991, **126**: 149-156.
2. Wajsazuk, C.P., Dummer, J.K.S., Ho, M., Van Thiel, D.H. *et al.* Fungal infections in liver transplant recipients. *Transplantation* 1985, **40**: 347-353.
3. Schroter, G.P.J., Hoelscher, M., Putnam, C.W., Porter, K.A. & Starzl, T.E. Fungus infections after liver transplantation. *Ann Surg* 1977, **186**: 115-122.
4. Harlon Stone, H., Kolb, L.D., Currie, C.A., Geheber, C.E. & Guzzell, J.Z. *Candida* sepsis: pathogenesis and principles of treatment. *Ann Surg* 1974, **179**: 697-711.

5. Kusne, S., Dummer, J.S., Singh, N., Iwatsuki, S. *et al.* Infections after liver transplantation. An analysis of 101 consecutive cases. *Medicine* 1988, **67**: 132–143.
6. Rolando, N., Harvey, F., Brahm, J., Philpott-Howard, J. *et al.* Fungal infection: a common unrecognised complication of acute liver failure. *J Hepatol* 1991, **12**: 1–9.
7. Tollemar, J., Ericzon, B.G., Holmberg, K. & Andersson, J. The incidence and diagnosis of invasive fungal infections in liver transplant recipients. *Transplant Proc* 1990, **22**: 242–244.