CASE REPORT

Aspergillus thyroiditis in a living donor liver transplant recipient

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KEYWORDS
Aspergillosis; Liver transplantation; Fulminant hepatitis; Living donor

Summary Aspergillosis is increasingly recognized as an important nosocomial pathogen in immunocompromised patients. Infection is difficult to diagnose and typically has a fatal outcome. We describe a liver transplant patient with fulminant hepatic failure, who had persistent fever of undetected origin postoperatively and an increased (1-3)-beta-D glucan level. Gallium-67 citrate scanning showed abnormal uptake in the thyroid bilaterally. Fine needle biopsy of the thyroid revealed thyroidal invasion of Aspergillosis. Total thyroidectomy was performed and the C reactive protein level decreased to 1.01 mg/dl. The patient died of liver sepsis due to Pseudomonas aeruginosa. (1-3)-beta-D Glucan monitoring and systematic radionuclide images are useful modalities for early diagnosis of Aspergillosis.

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Abbreviations: BDG, (1-3)-beta-D glucan; POD, postoperative day.
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Introduction

Invasive aspergillosis, defined as the growth of *Aspergillus* species from tissue obtained by biopsy, surgical resection, or autopsy, is a rare but devastating complication with high mortality rates in immunocompromised patients. Patient survival depends on early diagnosis and prompt initiation of therapeutic measures, which is complicated by the fact that there is no effective antifungal prophylaxis against aspergillosis.

We describe a patient who developed *Aspergillus* thyroiditis following living donor liver transplantation. A detailed description of his clinical course provides important information on the clinical features of thyroid involvement by invasive Aspergillosis.

Case report

A 62-year-old male patient with no past history of liver disease was referred to our hospital for fulminant hepatic failure. Living donor liver transplantation using the left liver graft was performed. The postoperative course was uneventful postoperative day (POD) 60, except for positive cytomegalovirus antigenemia, which was treated by ganciclovir administration. On POD 63, his (1–3)-beta-D glucan (BDG) level had increased to 51 pg/ml (normal range <11 pg/ml). Sputum culture revealed *Candida albicans*. Chest computed tomography revealed a ground glass appearance in the right lower lung, which was suspected to be *Pneumocystis jiroveci* infection. Polymerase chain reaction results of the sputum for *P. jiroveci*, however, were negative. Serum alactomannan *Aspergillus* antigen, which had been checked once a week, was negative (<0.5 ODI). We started fluconazole and trimethoprim on POD 63 because Candidiasis and *P. jiroveci* pneumonia were suspected. Fluconazole therapy was changed to micafungin 2 weeks after beginning the administration. Voriconazole and caspofungin were not approved for this use at the time in Japan. In spite of the antifungal therapy, the BDG level increased to 112 pg/ml on POD 84.

Gallium-67 scintigraphy was taken on POD 108 for systemic screening of the causative site of infection, which showed abnormal uptake bilaterally in the thyroid (Fig. 1A). Fine needle biopsy of the thyroid gland revealed *Aspergillus* invasion. Total thyroidectomy was performed on POD 118, and was followed by administration of Amphotericin B (15 mg/day). A resected specimen of the thyroid showed an extensive abscess with diffuse *Aspergillus* hyphae infiltration (Fig. 1B). Two weeks after thyroidectomy, BDG and C reactive protein levels decreased to 7.2 pg/ml and 1.01 mg/dl, respectively. On the POD125, the patient suddenly suffered from high grade fever of 39.9 °C with an elevated C reactive protein level (29.2 mg/dl). The patient died of sepsis due to abscess formation of *Pseudomonas aeruginosa* in the hepatic graft on POD 159.

Discussion

The lungs are the most common primary site of infection with sinus disease having nearly the same frequency. The thyroid is a relatively frequent
site of infection of invasive aspergillosis. Previous autopsy studies revealed that 9–15% of invasive aspergillosis involves the thyroid. Most patients with thyroidal invasion remain asymptomatic and it is usually difficult to diagnose in the antemortem period. Gallium scintigraphy is useful for the detection of occult thyroid lesions.

To our knowledge, this is the first report of thyroidal involvement of invasive aspergillosis with a detailed description of the clinical course after liver transplantation, although there are reports of invasive aspergillosis after cardiac and renal transplantations. Thyroidectomy, followed by antifungal drug administration, was performed in both patients. One patient died of pulmonary aspergillosis and the other died of myocardial involvement with aspergillosis.

We describe a liver transplant patient with fulminant hepatic failure, who had persistent fever of undetected origin postoperatively with an elevated BDG level. Invasive aspergillosis of the thyroid was detected by gallium scintigraphy. Monitoring BDG is key for early diagnosis of fungal infection and gallium scintigraphy might be a useful modality to determine the causative site of fungal infection.

References