Successful Treatment of Pulmonary Mucormycosis in a Renal Transplant Recipient with Limited Pulmonary Reserve by Combined Medical and Surgical Therapy

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Mucormycosis is a rare opportunistic fungal infection in renal transplant recipients which is associated with exceedingly high mortality when inadequately treated. Risk factors for this infection include diabetes, neutropaenia and immunosuppression. We report a case of pulmonary mucormycosis in a renal allograft recipient with type 2 diabetes and limited pulmonary reserve. The patient was successfully treated with lobectomy and liposomal amphotericin B with preservation of pulmonary and allograft functions. Early recognition of this infection is warranted before dissemination, which carries a poor prognosis.

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Introduction

Mucormycosis, which is also known as zygomycosis, is a rare opportunistic fungal infection that complicates various chronic diseases and immunosuppressed solid organ transplant recipients. The common genera causing mucormycosis include Rhizopus, Mucor and Absidia.1 The main clinical presentations are pulmonary, rhinocerebral, and disseminated forms. The incidence of mucormycosis in renal transplant recipients is estimated to be 0.4–0.5 per 1000 patients and pulmonary involvement is most common (25%).2 The pathogen is highly invasive and carries an extremely high mortality and morbidity.3,4 We report a case of pulmonary mucormycosis in a renal allograft recipient with limited pulmonary reserve treated with combined medical and surgical therapy which led to a favourable outcome.

Case Report

A 47 year-old Aboriginal lady, who had received a cadaveric renal transplant 9 months earlier, presented with a 1-month history of persistent productive cough not responding to oral antibiotics. Her medical history included type 2 diabetes of 20-years duration treated with insulin (HbA1c, 9.8%), and hypertension. Her end-stage renal disease was caused by diabetic nephropathy. Post-transplantation, she had an episode of early vascular rejection which was successfully treated with a course of antithymocyte globulin. She also had a 4 pack-year history of smoking but ceased 20 years ago. Her maintenance immunosuppression included tacrolimus 2 mg twice a day, mycophenolate 1000 mg twice a day and prednisolone 10 mg daily.

Physical examination revealed an ill-looking woman with respiratory rate of 22 min−1, oxygen saturation of 91% on air, and temperature of 37.8 °C. Bronchial breath sounds were present at the right lung base. The remainder of the physical examination was non-contributory.

Investigations revealed mild anaemia, leucocytosis and neutrophilia. C-reactive protein was 210 mg/L (RR: <10). Serum urea and creatinine were 9.4 mmol/l and...
143 μmol/L, respectively, which were stable. Trough tacrolimus level was 8.7 μg/L. The chest X-ray (Fig. 1) revealed a thick-walled cavity with air-fluid level in the superior segment of the right lower lobe. Computed tomography (CT) of the chest (Fig. 2) showed changes of consolidation in the apical segment of the right lower lobe with a 6.4 cm cavitating lesion. A clinical diagnosis of bacterial pneumonia and abscess was made. Intravenous clindamycin 150 mg four times per day and metronidazole 500 mg three times per day were initiated. Bronchoscopy and broncho-alveolar lavage (BAL) was performed. Culture of the lavage did not yield any specific causative organism. A CT-guided percutaneous drain was inserted into the cavitation. Rhizopus and Bacteroides species were cultured from the abscess fluid. Intravenous liposomal amphotericin 250 mg daily was commenced while continuing metronidazole. The dose of mycophenolate was reduced to 500 mg twice a day. However, there was no significant clinical improvement. As a result, treatment with lobectomy was contemplated. Spirometry revealed that the forced expiratory volume at one second (FEV₁) and forced ventilatory capacity (FVC) were 1.42 L (55% of predicted) and 1.76 L (56% of predicted), respectively. No improvement was observed with bronchodilator use. The corrected diffusion capacity for carbon monoxide was 7.96 mL/min/mmHg (35% of predicted). Arterial blood gas on air revealed pH 7.36, pO₂ 65.5 mmHg and pCO₂ 44.5 mmHg. These findings raised concerns about the viability of performing a lobectomy. After discussing with the patient the risks and benefits of this procedure, she underwent right lower lobe lobectomy. Post-lobectomy, she required prolonged mechanical ventilation but was successfully weaned off after 5 weeks. During this period, she was maintained on a stress dose of hydrocortisone only (50 mg three times a day). She received in total 11.2 g of liposomal amphotericin over a duration of 7 weeks. After a period of convalescence, she was discharged home without the need for supplementary oxygen and her graft function was preserved (serum creatinine 170 μmol/L) while on pre-operation immunosuppressive regimen. Twenty months after lobectomy, she remained well and was functioning independently.

Discussion

Pulmonary mucormycosis is a rapidly progressive infection that carries a mortality rate of greater than 80% in 12 months. The cause of death is related to pulmonary haemorrhage, overwhelming sepsicaemia, respiratory failure secondary to soiling of other previously unaffected areas of lung, or progression to invasive fungal infection. This infection is most frequently seen in patients with poorly controlled diabetes, recurrent ketoacidosis, solid organ and allogenic stem cell transplant, acquired immunodeficiency syndrome and haematological malignancies. The subject of this report had two of these risk factors.
The diagnosis of pulmonary mucormycosis can be difficult because it can mimic more common bacterial infections. In addition, many patients have a secondary bacterial infection, as seen in this case, leading to delay in diagnosis of the underlying pathogen as treatment with standard antibacterials is used. Lipid formulations of amphotericin have been used effectively as they exhibit reduced nephrotoxicity compared to conventional amphotericin B.

Amphotericin B and its lipid derivatives remain the front-line agents for this pathogen because resistance has been shown with all currently available azole antifungal agents. Lipid formulations of amphotericin have been used effectively as they exhibit reduced nephrotoxicity compared to conventional amphotericin B.

One observational study suggested that a better outcome was achieved when surgery was combined with amphotericin B, compared with amphotericin alone. In this study, the mortality was 11% in patients treated surgically compared to 68% in those treated medically. This study's findings are consistent with previously reported studies. Computed tomography-guided biopsy or abscess drainage are required.

In summary, we report a case of pulmonary mucormycosis in a diabetic renal transplant recipient who responded favourably to intravenous liposomal amphotericin B therapy in conjunction with surgical resection of infected lung tissue despite limited pulmonary reserve. Since clinical and radiological features of pulmonary mucormycosis are non-specific, a high index of suspicion and prompt diagnostic studies should be performed to achieve diagnosis.

Conflict of Interest
No conflict of interest or financial support to declare by all authors.

References