The Interesting Case

Pulmonary mucormycosis presenting as fatal massive haemoptysis in a renal transplant recipient

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Introduction

Mucormycosis is a devastating fungal infection which usually occurs in patients with diabetic ketoacidosis, chronic renal failure, haematological malignancies, or solid-organ transplant recipients [1]. The four main clinical presentations recognized are the rhinocerebral, pulmonary, gastrointestinal, and disseminated forms. In renal transplant recipients the most common form is rhinocerebral, while lung involvement may be seen in 10% of patients [2]. Pulmonary mucormycosis may present as an unresolving pneumonia, multiple nodules, or a cavitating abscess, and is associated with an overall 80% mortality [3,4]. A deadly combination is the presence of diabetes mellitus and involvement of large airways [5,6], since in such cases it may result in fatal haemoptysis [7–10].

This report describes the occurrence of fatal massive haemoptysis in a renal transplant recipient who had endobronchial and pulmonary mucormycosis following the development of post-transplant diabetes mellitus and diabetic ketoacidosis.

Case report

A 25-year-old male renal allograft recipient presented to the Emergency department with recurrent bouts of haemoptysis for 10 days before admission. He had had four such bouts, each time bringing up about 50–100 ml of blood, while in between he had cough with streaky haemoptysis. There was no history of accompanying fever or chest pain.

He had been diagnosed to have end-stage renal disease due to chronic glomerulonephritis a year earlier and he had received a live related renal transplant from his father 6 months ago. In the second week after transplantation he had acute rejection from which he completely recovered following therapy with pulse methylprednisolone. He was doing well until 1 month before this admission when he had presented with multiple superficial abscesses and altered sensorium. He was diagnosed to have post-transplant diabetes mellitus with ketoacidosis, septicemia and oesophageal candidiasis. He improved with antibiotics, insulin, and ketoconazole. He was maintained on cyclosporin 4 mg/kg and prednisolone 15 mg daily.

On admission he was afebrile but had moderate pallor, a pulse rate of 96/min and BP of 120/80 mmHg. Chest examination revealed evidence of a consolidation with crepitations over the left infraclavicular area. Other systems were normal.

Investigations revealed a haemoglobin of 8.0 g/dl, total white cell $7 \times 10^9$/l and ESR of 41 mm in 1st hour. Serum biochemistry showed urea 7 mmol/l, creatinine 150 μmol/l, uric acid 520 μmol/l, cholesterol 4.25 mmol/l. Blood sugar levels ranged from 6.3 to 13 mmol/l. Although the liver function tests were normal hepatitis B surface antigen was positive. Chest X-ray showed a thick-walled cavity in the upper zone of the left lung (Figure 1). Sputum was negative for acid-fast bacilli on three occasions.

Even though the Mantoux test was negative he was put empirically on antitubercular treatment in view of the history of haemoptysis, chest X-ray evidence of a cavity, and a wide prevalence of tuberculosis in the area. However, there was no improvement over next few days.

Bronchoscopy revealed that the left upper lobe bronchial mucosa was inflamed and purulent secretions were seen in the apicoposterior bronchus. Bronchial biopsy included fragments of necrotic tissue and inflammatory exudate in which broad aseptate hyphae with right-angled branching characteristic of mucormycosis were identified (Figure 2). With these findings, he was started on amphotericin B. There was no improvement in the patient’s condition over the next
Diabetes mellitus with ketoacidosis, which our patient developed in the post-transplant period, has been known to be the most common predisposing factor for mucormycosis. Although phagocytic and microbicidal defects are well known in diabetes mellitus, it is the acidosis which plays an important role in development of fungal infections. With the fall in the pH of blood, there is increased release of iron from transferrin and enhanced hyphal growth [1].

The combination of pulmonary mucormycosis and diabetes mellitus has been recognized as a well-defined clinical disorder of the bronchus and pulmonary vessels that if unrecognized may result in serious complications including atelectasis, abscess formation, and haemorrhage [5]. Of 11 patients with endobronchial disease reviewed by Bigby et al. [3], nine were diabetic.

Pulmonary mucormycosis presents with cough, fever, pleuritic chest pain or haemoptysis and chest examination may demonstrate rales with evidence of consolidation and pleural friction rub. The radiological findings may be non-specific and include multiple lung nodules, lobar or wedge-shaped infiltrates, cavitating lung abscesses or pleural effusion [3,13]. The ‘air-crescent sign’ has been recently recognized as a rare manifestation of both aspergillosis and mucormycosis [8,13].

Sputum in patients with pulmonary mucormycosis may be white, yellow, blood-tinged, or grossly bloody. Massive haemoptysis is also described in these patients, and rarely may prove fatal, as seen in our patient and mentioned in isolated case reports earlier [6–9]. In a recent review of 255 patients with pulmonary mucormycosis reported in literature, Tedder et al. documented haemoptysis in 22 (16%), and it was fatal in 19 (13%) of the 146 patients who had died. [4]. Because of the angioinvasive tendency of the Mucorales, lung infection leads to the invasion of the pulmonary vessels with consequent thrombosis, infarction, and necrosis of the parenchyma. Rupture of vessel into diseased bronchi leads to massive haemorrhage in the large airways, causing asphyxiation.

Diagnosis of pulmonary mucormycosis is rarely made antemortem because of the acute nature of this illness, lack of awareness of the condition, and the need for tissue to establish the diagnosis. Sputum culture is usually negative but a positive culture is highly suggestive of infection [3]. Definite diagnosis requires histological demonstration of tissue invasion with characteristic broad aseptate hyphae with right-angled branching. Bronchoscopy examination with bronchoalveolar lavage has been recently advocated as a useful, safe, and less invasive technique [14].

While amphotericin B is the mainstay of therapy in pulmonary mucormycosis, patients with endobronchial disease may benefit from early and aggressive surgical resection of the involved lung tissue. As reported recently by Tedder et al. [4], mortality was 65% for patients with isolated lung involvement, 96% for those with disseminated disease, and 80% overall. However
mortality in patients treated surgically was 11%, which is very low compared to 68% in those treated medically.

In conclusion, it is important to recognize the presentation of pulmonary mucormycosis in the form of endobronchial involvement with localized disease in diabetics, as compared to diffuse parenchymal involvement in haematological malignancies. If identified early with the help of various diagnostic aids including bronchoscopy, aggressive treatment with amphotericin B and timely surgical intervention may help in increasing the survival in an otherwise fatal disease.

References