**Case Reports**

**Recovery from Pulmonary Mucormycosis and Candidiasis in Diabetic Ketoacidosis**

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Pulmonary mucormycosis is an unusual opportunistic fungal infection which is often diagnosed post mortem. Simultaneous infection of the lung with mucormycosis and candidiasis has been reported once in an adult (1). This case report is of a child with diabetic ketoacidosis (DKA) and pulmonary infection with mucormycosis and candidiasis who survived after a stormy and eventful stay in the hospital.

**Case Report**

A nine-year-old girl with diabetes of three years duration, presented with low grade fever, cough, chest pain, poor blood sugar control for five weeks and deep sighing respiration for two days. On examination she was malnourished, pale, febrile, dehydrated, with acidotic breathing and oral candidiasis. Chest examination revealed dullness on percussion and reduced air entry on auscultation on the entire left hemi thorax.

Investigations revealed anemia and leukocytosis (hemoglobin 6.5 g/dl, total leukocyte count 15.4 x 10^9/l with 60% neutrophils), hyperglycemia (blood sugar >16.5 mmol/l) and metabolic acidosis. Serum electrolytes and hepatic and renal parameters were normal. Urine tested positive for ketones and sugar. Previous chest X-rays showed a progressively increasing homogeneous opacity in the left lower lobe; which had increased to involve the entire left hemithorax suggestive of a massive consolidation. A pleural tap did not yield any fluid.

Therapy included supportive care with fluids, use of insulin for DKA and coverage with antibiotics. On day 7 of hospital stay she expectorated a grey black cylindrical piece of tissue which was followed by copious purulent expectoration.

*Candida albicans* was grown on culturing this tissue and histopathological examination revealed necrotic cartilage and bronchial mucosa. Enmeshed in this were numerous fungi histologically of two types: one morphologically consistent with phycomycetes or mucormycosis (broad non-septate hyphae with branching at right angles) and the other with pseudohyphae characteristic of *Candida* (Fig. 1).

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Repeated blood fungal cultures were sterile. Chest X-ray had two air fluid levels and ultrasound revealed a solid lung with areas of breakdown.

Intravenous amphotericin-B was initiated in a daily dose up to 30 mg/kg and thereafter on alternate days till a cumulative dose of 41 mg/kg. Metronidazole was added to cover anaerobes. In addition rifampicin was also given for 3 weeks in a dose of 10 mg/kg daily for its additive antifungal effect. Two weeks after starting rifampicin, she developed persistent hyperglycemia and glucosuria. There had been no dietary indiscretion, change in insulin brand or new infection on screening. With stoppage of rifampicin the patient became euglycemic.

As the child did not improve on medical therapy, surgical therapy was undertaken. An extra-pleural pneumonectomy was performed. The histopathological examination showed fibrous tissue with areas of necrotic inflammatory granulation tissue and occasional multinucleated giant cells but no acid fast bacilli or fungi. The rest of the post-operative course was uneventful.

Discussion

Pulmonary mucormycosis is a life threatening complication of DKA. Mucor belongs to the class Zygomycetes, a ubiquitous fungus whose commonest route of entry into the human body is the respiratory tract(2). Other predisposing conditions for this fungus include neutropenia or neutrophil dysfunction, malignancy and desferrioxamine therapy(2). Pulmonary mucormycosis presents as a rapidly progressive pneumonia often with hemoptysis. The radiological picture is not diagnostic and includes nodular or lobar infiltrates, mediastinal widening, bronchopneumonia, cavitation and fungal ball(3).

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Fig. 1. Histopathological appearance of the grayish black piece of tissue. The transverse arrow shows broad nonseptate hyphae with branching at right angles suggestive of mucor and the curved arrow shows pseudo-hyphae with budding suggestive of candida.
The patient reported here had progressive pneumonia complicated with abscesses. Histopathological identification of wide, nonseptate hyphae, branching at right angles with tissue invasion is diagnostic though one may fail to culture the pathogen(4). Propensity for larger airway involvement in diabetics is well documented(3) and was also seen in the present case. Combined pulmonary involvement with mucormycosis has been reported(1,5-7).

Treatment of pulmonary mucormycosis rests on successful control of underlying illness, prolonged therapy with IV amphotericin-B and early and repeated surgical intervention(2). Fluconazole has not been useful(8). A case reportedly resistant to amphotericin has been treated with ketoconazole(9).

Christenson et al.(10) reported a diabetic child with pulmonary mucormycosis who showed clinical improvement on addition of rifampicin to amphotericin. Based on this report rifampicin was added. Rifampicin has been reported to cause early phase hyperglycemia in patients with pulmonary tuberculosis which resolves immediately on stopping the drug(11). Hyperglycemia was noted in this patient and reverted to normal on stopping the drug. Augmentation of intestinal absorption of glucose is the probable mechanism of action(11). Rifampicin is also known to induce several hepatic microsomal enzymes and is known to increase the metabolism of a large number of drugs including oral hypoglycemic agents. However, insulin is metabolized by cytoplasmic hydrolases, more in the kidney than liver(12). More careful study of the use of rifampicin in diabetics would be useful.

Survival in patients with mucormycosis has improved with amphotericin-B and surgical intervention (13). A recent review of 225 cases of pulmonary mucormycosis calculates the in-hospital mortality as 65% for patients with isolated pulmonary mucormycosis, 96% for those with disseminated disease and 80% overall (14). The mortality in those treated surgically was 11%, significantly lower than the 68% mortality in those treated medically (p=0.0004) though there may have been a selection bias.

This case of pulmonary co-infection with mucormycosis and candidiasis highlights the need for aggressive surgical and medical management. Deterioration in diabetic control may be related to the use of rifampicin and hyperglycemia may revert to normal with withdrawal of this drug.

REFERENCES


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