

# A case report on successfully treated invasive pulmonary mucormycosis in a patient with poorly controlled diabetes mellitus

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## Abstract

Although fungal infections are common in clinical practice, usually they are superficial and invasive infections are very rare among immunocompetent people. Invasive fungal infections in immunocompromised people are life threatening if left untreated. Among invasive fungal infections, mucormycosis is uncommon. Pulmonary mucormycosis is rarely seen in clinical practice and is often life-threatening. This case report describes a patient with poorly controlled diabetes who presented with pulmonary mucormycosis and responded well to systemic antifungals.

**Key words:** pulmonary mucormycosis, invasive fungal infections, diabetes mellitus, reversed halo sign, immunocompromised

## Introduction

Mucormycosis is a rare but life-threatening opportunistic infection, which usually occurs in immunocompromised individuals. It is caused by broad aseptate fungi belonging to the subphylum Mucoromycotina, order Mucorales.(1) Rhino-orbito-cerebral and cutaneous involvements are the commonest manifestations. The lung is the third most frequently involved site. Pulmonary mucormycosis (PM) is aggressive with a high mortality rate with medical management alone. A combination of prompt diagnosis, appropriate medical therapy and early aggressive surgical intervention could reduce the mortality.(2) The first line therapy for mucormycosis is amphotericin B-based drugs. Early suspicion and diagnosis would improve survival.(3)

## Case presentation

A 59-year-old woman, with a background history of poorly controlled type 2 diabetes mellitus, was transferred from District General Hospital, Vavuniya for further evaluation of her prolonged respiratory symptoms. She presented with fever, cough with yellowish sputum and right sided pleuritic type chest pain for one month. She had loss of appetite and loss of weight of recent onset. She had complained of exertional shortness of breath for one week. She denied exposure to tuberculosis. She neither smokes nor consumes alcohol. She was not exposed to avian antigens. She did not reveal symptoms of connective tissue disease. On examination, she was afebrile, tachypnoeic and tachycardic. Auscultation of the chest revealed diminished breath sounds and coarse crackles over the right upper zone. Saturation on

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room air was 95%. Other system examinations were unremarkable. Blood investigations showed high erythrocyte sedimentation rate (136 mm/1<sup>st</sup> hour) and c-reactive protein (236 mg/dL). Full blood count revealed a haemoglobin of 9.2 g/dL while other cell lines were normal. Chest x-ray showed a right upper lobe heterogeneous opacification (figure 1). Her liver functions, renal functions tests, urine full report, 12 lead ECG, two dimensional echocardiogram and coagulation studies were normal. Her blood glucose level was 400 mg/dL on admission. But her arterial blood gas revealed no evidence of lactic acidosis. She was initiated on soluble insulin three times daily with isophane insulin at night. The dose was adjusted according to her blood glucose monitoring. She was commenced on a broad spectrum antibiotic, intravenous meropenem 1 g 8 hourly as she continued to have symptoms. Adequate blood glucose control was achieved after adjusting the basal bolus regime. After 5 days her fasting blood sugar level was 102 mg/dL.

Since she had a heterogeneous opacification in the upper lobe of the right lung in her chest x-ray (figure 1-left), she was screened for tuberculosis and invasive aspergillosis which were negative. Blood and urine culture revealed no growth. As she was not improving despite broad spectrum antibiotics, she underwent contrast enhanced computed tomography of the chest which showed ground glass opacification and multiple nodules with reversed Halo sign in the right upper lobe.(figure 2). Even though there are multiple conditions which can give rise to reversed Halo sign, it is most commonly associated with pulmonary mucormycosis. Hence bronchoscopy was done to obtain samples for microbiological confirmation and to rule out the

other possibilities.

Bronchoscopy showed large slough-like material coming out from the right upper lobe bronchus. Biopsy was taken for bacterial culture, tuberculosis PCR, fungal studies and histology. Tuberculosis PCR was negative. Culture yielded a blackish fungal growth suggestive of mucormycosis. Histology of the specimen revealed necrotic debris, partially viable chondroid and fibrosclerotic tissue invaded by abundant broad aseptate fungal hyphae, some of which showed branching at 90° angles (figure 3). Invasive pulmonary mucormycosis was diagnosed.

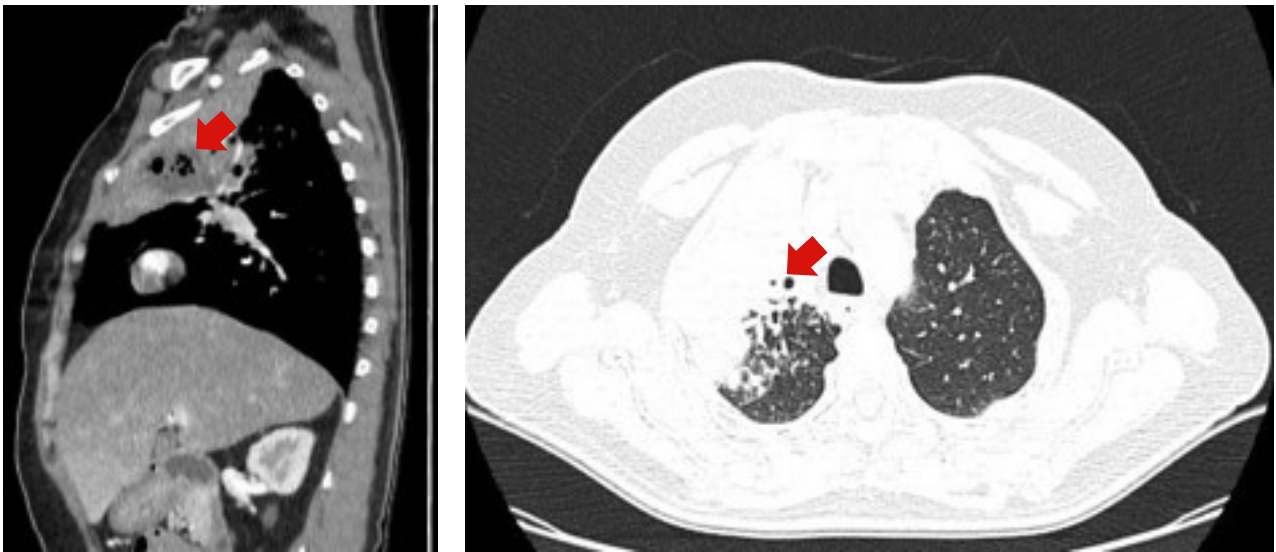
She was treated with liposomal amphotericin 200 mg IV daily for 11 days and amphotericin B 40 mg daily for 6 days. Her renal functions were closely monitored and proper hydration was ensured to avoid acute kidney injury throughout the course of antifungal treatment. Her symptoms and signs were improved following initiation of antifungal therapy and repeat chest x-ray showed remarkable improvement (figure 1).

## Discussion

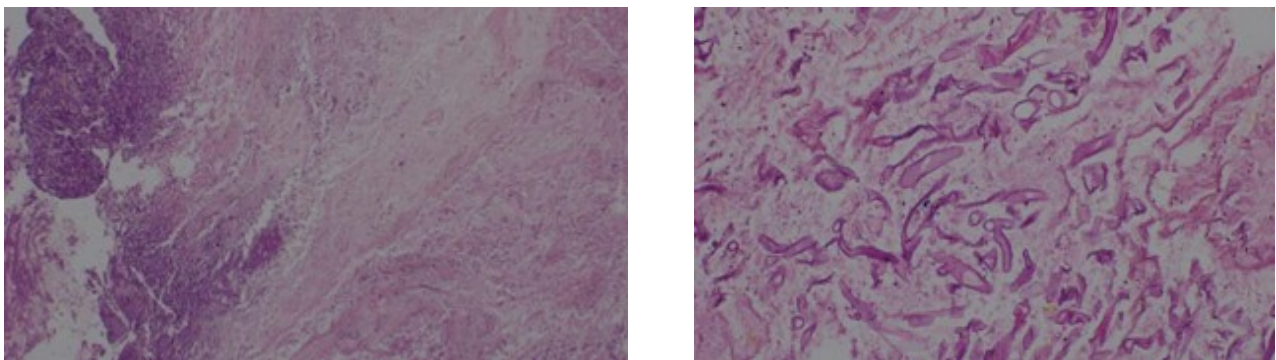
Pulmonary mucormycosis is a rapidly progressive infection and can be life threatening if not treated early. In a patient with poorly resolving pneumonia despite broad spectrum antibiotics we should always suspect a fungal infection like mucormycosis as a differential diagnosis especially if the patient has a risk of being immunocompromised. It is very common to miss this diagnosis because of other usual bacterial infections and tuberculosis.



**Figure 1** - Chest x-ray taken on admission(left) and after treatment(right) showed remarkable improvement



**Figure 2** - CECT of chest sagittal view(left) and axial view in lung window(right) shows ground glass opacification with multiple nodules and reversed halo sign (arrow) in the upper lobe



**Figure 3** - Histology of specimen revealed necrotic debris tissue ,partially viable chondroid and fibrosclerotic tissue(left) and invasion by abundant broad aseptate fungal hyphae ,some show branching at 90° angle(right) suggestive of mucormycosis

The most common organism of mucormycosis are *Rhizopus* spp., *Mucor* spp., and *Lichtheimia*. Other Mucorales, such as *Rhizomucor*, *Saksenaea*, *Cunninghamella*, and *Apophysomyces*, are less common. The most common mode of transmissions result from inhalation of fungal sporangiospores that have been released in the air or from direct inoculation of organisms into disrupted skin or gastrointestinal tract mucosa. The incidence of mucormycosis has been increasing in recent decades, mainly due to a surge in immunocompromised individuals. In developed countries, the disease is mostly seen in patients with haematological malignancies. In contrast, in developing countries, mucormycosis is more common among patients with uncontrolled diabetes mellitus. The most common clinical presentations of mucormycosis encompass

rhino-orbito-cerebral, pulmonary, cutaneous, and disseminated.(3) The common symptoms of pulmonary mucormycosis are fever, cough and shortness of breath.(5) Our patient had all symptoms mentioned above.

The diagnosis of mucormycosis depends on the identification of organisms in the tissue by histopathology with culture confirmation. However, culture often yields no growth, and histopathologic identification of an organism with a structure typical of Mucorales may provide the only evidence of infection. The diagnosis of pulmonary mucormycosis is challenging because the presentation does not differ from pneumonia due to other angio invasive moulds, bacteria or tuberculosis. Treatment must be initiated if mucormycosis agent is isolated in

respiratory specimens of high risk individuals with compatible clinical presentation. Establishing a definitive diagnosis can be difficult because it requires demonstration of the organism in tissue.(5) However our histology of the biopsied tissue revealed the diagnosis of mucormycosis with the support of culture.

Radiologically, multiple ( $\geq 10$ ) nodules, and pleural effusion are reportedly more common in mucormycosis. But they are not always a must. Another finding on computed tomography (CT) scan, which seemed to indicate the presence of mucormycosis, was the reverse halo sign.(6) This sign is more common in patients with mucormycosis than in those with aspergillosis. There are other causes for the reversed halo sign like paracoccidioidomycosis, pneumocystis pneumonia, tuberculosis, community acquired pneumonia, lymphomatoid granulomatosis, Wegener granulomatosis, lipoid pneumonia and sarcoidosis.(6) Direct microscopy of clinical specimens, allows a rapid presumptive diagnosis of mucormycosis. Hyphae of Mucorales have a variable width, are aseptate and show an irregular, ribbon-like appearance. The angle of branching is variable and includes wide-angle  $90^\circ$  bifurcations.(3)

This patient's CT chest showed reversed halo sign over the upper lobe and tissue biopsy revealed necrotic debris, partially viable chondroid and fibrosclerotic tissue invaded by abundant broad aseptate fungal hyphae, some showing branching at  $90^\circ$  angles.

Management of mucormycosis involves multimodal approach, including reversal of predisposing factors, early administration of active antifungal agents at the optimal dose and surgical debridement. Good glycemic control is mandatory in a patient with diabetes and mucormycosis. Amphotericin B is the drug of choice for pulmonary mucormycosis.(5) Posaconazole and isavuconazole are used as second line drugs or in patients who are intolerant to amphotericin. The duration of treatment with active antifungal agents has not been determined. Active agents that have oral formulations such as posaconazole and isavuconazole are preferred because they can be administered for several months, if needed.(3)

Only medical therapy may be sufficient if the patient shows rapid and continued response. Surgical intervention plays a role in a patient with isolated pulmonary mucormycosis and involves the removal of infected tissue as much as possible.(4) Our patient was treated with liposomal amphotericin B 200 mg IV

daily for 11 days and 40 mg daily for 6 days with good response. Hence surgical intervention was not warranted.

## Conclusion

Pulmonary mucormycosis is rare and life-threatening, unless diagnosed early and managed aggressively. The management of the patient requires a multidisciplinary approach.

## Declarations

### Author contributions

Dr Dikshaladevi Pathmanathan initiated this case report along with Dr Nisanthan Selvaratnam as the first contact medical officer under supervision of Dr Nalayini Jegetheesan and Dr Thambipillai Peranantharajah who helped in arranging necessary investigations and guided the management.

### Conflicts of interest

The authors declare that they have no conflicts of interest to be addressed regarding this case report.

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