CASE REPORT

Aspergillus and mucormycosis presenting with normal chest X-ray in an immunocompromised host

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SUMMARY

Invasive aspergillus and mucormycosis infection are not uncommon in immunocompromised individuals. Endobronchial fungal infections have been reported in the literature, especially in patient's with diabetes complicated by diabetic ketoacidosis, but end bronchial coinfection with aspergillus and mucormycosis without pulmonary involvement has not been described in the literature. We report the case of a woman with diabetes who presented with gastrointestinal symptoms, ketoacidosis and respiratory distress, with an apparently normal chest X-ray. Investigations revealed a cavitary lesion in the left lower lobe of the lungs on CT scan. Bronchoscopy revealed intense mucosal oedema and whitish plaques at the lower end of the trachea and right main stem bronchus with a normal left bronchial tree. Microbiological and pathological results confirmed aspergillus and mucormycosis. Despite aggressive medical management, the patient deteriorated and died of respiratory failure. Strong suspicion of invasive fungal infections in immunocompromised patients with respiratory failure and minimal chest infiltrates, early fiberoptic bronchoscopy and early aggressive treatment is crucial for the patient's survival.

BACKGROUND

Invasive fungal infections such as aspergillus and mucormycosis affecting the respiratory system are not uncommon in immunocompromised patients. The usual presentation of these invasive fungal infections is solitary or multiple consolidations and cavitary lesions in the lungs. Endobronchial fungal infections have been reported in the literature, especially in patient's with diabetes complicated by diabetic ketoacidosis. These usually present with cough and haemoptysis and radiologically by either focal consolidation or atelectasis. Endobronchial lesions also cause shortness of breath secondary to stenosis of the main airway. Endobronchial mucormycosis without any chest X-ray findings has not been reported in the literature. We report the case of a patient who presented with diabetic ketoacidosis with predominant gastrointestinal symptoms who also had endobronchial mucormycosis with no major respiratory symptoms and, interestingly, a normal chest X-ray.

CASE PRESENTATION

A 53-year-old lady with a long history of poorly controlled type 2 diabetes mellitus, hypothyroidism on replacement thyroid, adrenocortical insufficiency on replacement steroids and ischaemic heart disease presented with abdominal pain, vomiting

and diarrhoea of 4 days duration. She was found to be in severe diabetic ketoacidosis and was clinically severely hypovolaemic with a blood pressure of 80/60 mm Hg and a heart rate of 130/min. She was in severe respiratory distress with a respiratory rate of 36/min. She was unable to articulate with pulse oximetry showing sPO₂ of 80%. She was emergently intubated and placed on a mechanical ventilator. She was fluid resuscitated and started on norepinephrine to keep mean arterial pressure >65 mm Hg. Blood cultures, urine culture and respiratory secretions were sent for appropriate bacterial cultures.

INVESTIGATIONS

Initial investigations carried out are shown in [table 1](#).

TREATMENT

The patient was started on piperacillin-tazobactam for broad-spectrum coverage for intra-abdominal infection. Chest X-ray showed no evidence of infiltrate, consolidation, cavity, pleural effusion or features of congestive heart failure ([figure 1A](#)). A CT scan of the abdomen was ordered which showed a diffuse large bowel wall thickening with increased mucosal enhancement. A small area splenic infarct was also noted. A small thin-walled cavity was detected in the left lower lobe in the upper abdominal cuts of the CT abdomen ([figure 1B](#)).

Table 1 Initial investigations

Investigations	Day 1
Haemoglobin	8.6 g/dL
Platelets	60 000/mm ³
Total white cell count	3.5/mm ³
Differential count	Neutrophils—91.1%, lymphocytes—5.3%, monocytes—3.0%, eosinophils—0.5%, basophils—0.1%
Urine glucose	Negative
Urine ketone bodies	Trace
Serum creatinine	2.0 mg/dL
Serum electrolytes	Sodium—141 mmol/L, potassium—2.3 mmol/L, chloride—105 mmol/L
Liver function tests	Protein—1.6 g/dL
Brain natriuretic peptide	2550 pg/mL
Lactic acid	1.8 mmol/L
Serum amylase	128
Serum lipase	1316
Random serum cortisol	>75.00 µg/dL
Procalcitonin	18.40

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Figure 1 (A) Chest radiograph showing apparently normal lungs. (B) CT chest showing a cavitary lesion in the left lower lobe.

Essentially, the latter finding prompted further investigations pertaining to the chest. Fiberoptic bronchoscopy revealed intense mucosal oedema and whitish plaques at the lower end of the trachea and right main stem bronchus (figure 2A,B). All

the orifices to the upper lobe could be identified. There was minimal mucosal oedema of the right upper lobe and bronchus intermedius. The right lower lobe was not involved and the left bronchial tree was also unaffected (figure 2C). Biopsies were taken from the abnormal mucosa without any major complications.

The patient was started on liposomal amphotericin after bronchoscopy because of a strong suspicion of either mucormycosis or aspergillosis. Her condition started to deteriorate requiring higher doses of inotropes/vasopressor support to maintain the hemodynamics. Meropenem and linezolid were added.

Bronchial cultures grew *Klebsiella pneumoniae* sensitive to carbapenams. The fungal stain showed budding yeasts with pseudo-hyphae. There were multiple septate filamentous fungi with acute angle branching suggestive of aspergillus (figure 3A, B). There were also non-septate broad filamentous fungi with infrequent branching at 90°, suggestive of mucormycosis (figure 3C). Fungal culture showed the growth of aspergillus (figure 3D).

OUTCOME AND FOLLOW-UP

After reviewing the fungal stains, the patient was also started on voriconazole to cover aspergillus. Despite all these measures, the patient went into severe septic shock from which she could not be resuscitated.

DISCUSSION

Mucormycoses are a group of fungal diseases caused by fungi of class Zygomycetes and order Mucorales.¹ Pulmonary mucormycosis can be regarded as an opportunistic infection affecting mainly immunocompromised hosts.² Patient's with diabetes with diabetic ketoacidosis are particularly vulnerable to this fungal infection.³ Furbinger⁴ described the first case of pulmonary mucormycosis in 1876.

Two forms of pulmonary mucormycosis have been recognised. The more common form affects pulmonary parenchyma and results in rapidly progressive respiratory failure.⁵ This form of disease is seen mainly in patients with haematological malignancies and those being treated with immunosuppressive medications.³ Endobronchial mucormycosis has been reported in the literature and is seen mainly in poorly controlled diabetes. Patients affected by this form of disease present with a history of cough and haemoptysis. Radiologically localised areas of atelectasis or consolidation are usually seen in these patients. Before the advent of bronchoscopy and CT scans, endobronchial mucormycosis was often a postmortem diagnosis.⁶

Figure 2 Bronchoscopic image showing (A) main carina with mucosal oedema in the right main bronchus, (B) mucosal oedema and whitish plaques in the right main bronchus and (C) the left main bronchus which is apparently normal.

Figure 3 (A) Microscopic image showing (A) aspergillus with multiple septate filaments, (B) aspergillus in Gomori's methanamine silver (GMS) stain, (C) mucor on GMS stain and (D) macroscopic image of aspergillus in the culture bottle.

Aspergillus species are ubiquitous fungi. Humans commonly inhale its conidia. Alveolar macrophages and circulating neutrophils prevent inhaled spores from establishing pulmonary infection. In patients with impaired immunity, typically those with prolonged neutropenia or transplant recipients, the spores germinate into hyphae and a life-threatening fungal infection develops.⁷ Pseudomembranous Aspergillus tracheobronchitis is one form of invasive tracheobronchial aspergillosis, which is a rare manifestation of pulmonary aspergillosis. It is more common in immunocompromised hosts.⁸

Most patients with mucormycosis have been treated with lipid preparations of amphotericin (predominantly liposomal) with few reactions or adverse events.⁹ The Infectious Diseases Society of America guidelines recommend voriconazole for primary treatment of invasive Aspergillus tracheobronchitis.¹⁰

Coinfection with mucormycosis and aspergillus has been described in the literature. We have reported a patient with a cavitary lesion in the lung caused by a combination of these two fungi.¹¹ Endobronchial fungal disease without any major pulmonary involvement caused by both these fungi has not been described previously. In our patient, we suspect that the yeast and pseudohyphae representing candida could be merely colonising and less likely to be contributing to the endobronchial disease. Microbiological and fungal cultures taken from the left lower lobe were negative. We suspect that the small cavity may represent a bacterial or fungal abscess resulting from aspiration.

Treatment of this combined infection can often be challenging. While the drug of choice for aspergillus infection is voriconazole, treatment of mucormycosis requires amphotericin. Even though there is no report of failure of treatment when these two drugs are combined, there is an apparent theoretical

conflict. Voriconazole interferes with ergosterol synthesis, which is an essential component of fungal cell membrane, whereas amphotericin binds with ergosterol.

We did attempt to treat this patient with a combination of voriconazole and amphotericin without success.

Learning points

- ▶ Aspergillosis and mucormycosis coinfection affecting the airway can present with a normal chest X-ray in patients with diabetes presenting with diabetic ketoacidosis.
- ▶ Fiberoptic bronchoscopy should be performed early in patients with diabetes presenting with respiratory failure even in the presence of a normal chest X-ray if no other source of infection is obvious.
- ▶ As treatment of combined infection with mucormycosis and aspergillosis can have a high treatment failure, perhaps multimodality treatment consisting of intravenous and nebulised antifungals could be considered.

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