CASE REPORT

Mucormycosis pulmonary abscess, containment in a patient with uncontrolled diabetes mellitus

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SUMMARY

A 56-year-old Hispanic male with solo risk factor of uncontrolled diabetes mellitus presented with recurrent haemoptysis. Initial concern was for malignancy with postobstructive pneumonia; however, invasive testing and biopsy confirmed infectious mass of fungal aetiology requiring surgical resection followed by a prolonged course of anti-fungal therapy. Discussion centred on approach to, progression of and course of action in the management of pulmonary abscess due to mucormycosis.

BACKGROUND

Literature images of invasive zygomycetes within necrotic sinuses are predominant in the minds of healthcare practitioners. Mucor, the most common of zygomycetes, is introduced through inhalation of spores with rapid progression of disease leading to mortality. Pulmonary mucormycosis (PM) is rare but chronicled in specific immunocompromised host with morbid results. Here, we describe a chronic course and complex management of PM in a host with diabetes mellitus.

CASE PRESENTATION

A 56-year-old Hispanic male with 10-year history of diabetes mellitus presents with 2 days of shortness of breath associated with productive cough up to two cups a day of blood with clots. Despite recent completion of 4 weeks of intravenous antibiotic therapy for pneumonia, he continues to experience fatigue, shortness of breath, dyspnoea on exertion, night sweats and weight loss. He denies lifetime steroid use, travel to endemic areas, sick contacts, iron chelation therapy, organ transplant, history of sexually transmitted infection, or family history of malignancy or autoimmune diseases. Positive occupational exposure was to dust as an electrician providing service to homes and agriculture industries in rural Southern Arizona. On physical examination, his vital signs were stable with normal oxygen saturation on room air; lung examination was remarkable for diminished breath sounds and dullness to percussion over the right middle lobe with positive aegophony. Serum studies are remarkable for neutrophil predominant leucocytosis 13.2 mg/dL, hyperglycaemia with serum glucose of 648 mg/dL, and elevated creatinine to 1.9 mg/dL. Blood gas analysis shows a mixed respiratory alkalosis and anion gap acidosis secondary to elevated lactic acid. HIV serology was non-reactive. His urine revealed the presence of ketonuria with an elevated glycated haemoglobin

of 13%. A plain chest X-ray film (figure 1A) identified a right-sided pathology that lateralised over the right middle lobe area (figure 1B). Further characterisation with CT of chest without contrast in axial configuration (figure 2A) demonstrated findings concerning malignancy with obstructive endobronchial lesions in the right middle lobe and right lower lobe causing partial collapse and superimposed necrotic postobstructive pneumonia with inflammatory changes with atelectasis (figure 2B).

Figure 1 (A) Frontal chest X-ray silhouetting the right heart border with associated volume loss with right hemidiaphragm elevation. No pleural effusion or pneumothorax. (B) Lateral chest X-ray showing dense opacification over the right middle lobe. Multilevel degenerative disc disease is seen in the visualised spine.

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Figure 2 (A) Axial CT Chest without IV contrast. Partial collapse of the right middle lobe with abrupt termination of the lateral bronchus of the right middle lobe. Interstitial septal thickening within aerated portions. Branches of the right lower lobe bronchial tree demonstrate abrupt cut-offs including a 1.8×1.7 cm endobronchial nodule and an additional elongated tubular opacity extending from peripheral lower lobe bronchus measuring 4.4×1.7 cm with extension to pleural surface. Multiple pulmonary nodules, largest measuring 0.9×0.5 cm in right lower lobe. (B) Coronal CT Chest without IV contrast. Scattered foci of necrosis present within regions of collapsed right middle lobe.

The patient was diagnosed with haemoptysis secondary to post-obstructive pneumonia and admitted for broad spectrum antibiotics including antifungal coverage with fluconazole. Specialist consultation was obtained for further investigation.

INVESTIGATIONS

A pulmonologist was consulted and a bronchoscopy with alveolar lavage and lymph node sampling was performed. At the take-off an endobronchial lesion was immediately noted in the right middle lobe. Endobronchial brushing, bronchoalveolar lavage (BAL), and ultrasound-guided fine-needle aspiration of multiple ipsilateral and contralateral lymph nodes were successful. Histological analysis of the biopsy samples were negative for any evidence of malignancy but extensive necrosis (figure 3A) and abundant fungal elements (figure 3B) were visualised. BAL galactomannan was not conducted; however, a sample of BAL aspirate tested positive for *Rhizopus oryzae* recombinant DNA via 28s and internal transcribed spacer primer sequences.

Figure 3 (A) Inflamed tissue and respiratory epithelium at 100× magnification. (B) Large, non-septa hyphae with 90° angle branching and non-parallel walls visualised at 400× magnification.

In light of the bronchoscopy findings immediate cardiothoracic surgical and infectious diseases consult were requested. The patient was started on oral posaconazole 300 mg daily. A CT scan of sinus demonstrated minimal paranasal mucous thickening and no evidence of rhinocerebral mucormycosis. Further blood cultures were negative for aerobic, anaerobic and fungal growth. Beta galactomannan serum titres were also negative. Cardiothoracic surgery recommends surgical intervention for complete source control. A right middle lobe lobectomy, adhesiolysis, and muscle flap mobilisation for buttress of the right middle lobe bronchus was performed.

Pathological evaluation of right middle lobectomy confirms acute necrotising bronchitis of proximal lobar bronchus, postobstructive bronchopneumonia, and organising fibrinous pleuritis with scattered fungal elements (evaluated with Grocott-Gomori's Methamine Silver stain) morphologically consistent with a diagnosis of PM. No angioinvasion of these fungal elements were noted histologically.

OUTCOME AND FOLLOW-UP

The patient tolerated all interventions well and was discharged home with aggressive insulin therapy for diabetes mellitus. His future plan was to follow-up with his primary care physician and salvage therapy with posaconazole 400 mg daily for at least 6-month duration with close infectious diseases follow-up.

DISCUSSION

PM transpires after *Mucorales* fungal sporangiospores are inhaled and settle in bronchioles and or alveoli.¹ *Rhizopus*,

Lichtheimia, and *Mucor* are the most common disease causing genera. They are ubiquitously found in nature, present in soil and decaying matter. Given their ubiquitous nature, most healthy individuals who are exposed remain asymptomatic. In general, risk factors for developing mucormycosis include uncontrolled diabetes mellitus, ketoacidosis, neutropenia, haematological malignancies, immunosuppression, solid organ transplant, and penetrating traumatic events.^{2–4} As with our patient, uncontrolled diabetes mellitus and ketoacidosis is the most common risk factor in those who develop mucormycosis. The particular worry with these fungi that cause PM are their angioinvasive potential. Angioinvasion can lead to pulmonary infarction, haemoptysis, and life-threatening haemorrhaging when large mediastinal vessels become involved.⁵ PM clinically present with non-specific symptoms that are generally related to a non-resolving pneumonia. These include fevers, worsening productive cough, chest discomfort, and dyspnoea. Haemoptysis should be recognised as a possible life-threatening symptom when PM is suspected.⁶ Airway occlusion is rare but can also develop from an endobronchial lesion. Other associated symptoms that have been reported with PM include Pancoast syndrome, Horner's syndrome, subcutaneous emphysema, mediastinitis, and collapsed lung.⁶

The radiological manifestations of PM are often non-specific and broad. Chest radiographs are abnormal in >80% of cases with reported abnormalities that include focal consolidations, solitary or multiple pulmonary nodules (often peripherally located), cavitating lesions, pleural effusion(s), and mediastinal or hilar lymphadenopathy.⁷ High-resolution CT is the recommended image modality and carries the highest sensitivity in the detection of atypical pulmonary fungal infections like PM.⁸ Sequenced imaging of maxillofacial sinuses without contrast in high-risk patients with suspicion can assist in diagnosis of discrete lesions. Histopathological analysis remains the gold standard for a definitive diagnosis of PM. Pathological diagnosis are defined by the presence of broad (6–16 µm) non-septate hyphal elements branching at right-angles.⁹ Fungal elements are usually detected with routine H&E preparations and typically do not require special fungal stains. Further tissue analysis with PCR-based techniques can also be utilised in the detection of fungi responsible for PM.

Prompt antifungal therapy with surgical resection along with aggressive management of any comorbid condition is the mainstay of therapy.⁸ Intravenous liposomal amphotericin B (1–1.5 mg/kg/day) is still the recommended initial antifungal therapy but oral posaconazole has gained favourable acceptance.⁸ Voriconazole is not effective against *Mucorales* fungi and is not recommended.⁶ Without surgical intervention antifungal therapy will likely fail to control the infection.⁸ Depending on the extent of PM, wedge resection, lobectomy, and/or pneumonectomy may be required. An urgent consultation with cardiothoracic surgery and or interventional pulmonology should be pursued as soon as PM is suspected and or confirmed.

PM is a rapidly fatal illness that carries an overall mortality rate of 76%, increasing to a staggering 95% in the setting of extrathoracic dissemination.^{2 8 10} Unfortunately, PM has not seen a significant improvement in mortality in recent years. The postulated reason for this fact is the overall lack of effective antifungal therapy against *Mucorales* fungi and a delay in diagnosis

of PM.^{7 8} Failure to detect infection early may lead to fatal fungal septicaemia, respiratory failure, and massive haemoptysis.^{6–8 10} When clinically suspected, clinicians should promptly initiate empirical antifungals that covers *Mucorales* fungi (along with surgical consultations) to discuss possible excisional biopsy and/or resection of suspected lung tissue.

Learning points

- ▶ Pulmonary mucormycosis (PM) transpires after ubiquitous *Mucorales* fungi sporangiospores are inhaled and settle in bronchioles.
- ▶ Angioinvasion can lead to infarction, haemoptysis, and massive haemorrhaging when large mediastinal vessels become involved.
- ▶ High-resolution CT is the recommended image modality and carries the highest sensitivity in the detection of atypical pulmonary fungal infections.
- ▶ Histopathological analysis remains the gold standard for a definitive diagnosis of PM. Pathological diagnosis is defined by the presence of broad (6–16 µm) non-septate hyphal elements branching at right-angles.
- ▶ Prompt antifungal therapy with surgical resection along with aggressive management of any comorbid condition is the mainstay of therapy.

Contributors FJ was responsible for obtaining the history, acquiring the images, patient consent for publication and generation of the original manuscript. NB was responsible for literature search and reviewing discussion points. KA was responsible for making revisions to the original manuscript.

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