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Case report

Pulmonary mucormycosis: A case report

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ABSTRACT

Mucormycosis is a rare fungal infection caused by Mucorales order fungi. The rhino-cerebral form of mucormycosis is most commonly seen in patients with diabetes mellitus, whereas, pulmonary mucormycosis is a rare manifestation in patients with haematological malignancy and transplant recipients. We report a case of pulmonary mucormycosis presenting with a late acute onset diabetes on a patient immunosuppressed with a low dose of steroids.

We aim to illustrate the need for a high clinical suspicion for the diagnosis of mucormycosis and to report the importance of early and aggressive inhiation of antifungal therapy.

Introduction

Mucormycosis is a rare fungal infection caused by Mucorales order fungi [1]. It is an angio-invasive fungal infection, which despite early diagnosis and aggressive therapy, is associated with high morbidity and mortality [2–4]. The rhino-cerebral form of mucormycosis is most commonly seen in patients with diabetes mellitus, whereas, pulmonary mucormycosis is a rare manifestation in patients with haematological malignancy and transplant recipients [3]. Diagnosis relies upon the identification of non-septate hyphae in tissue by histopathology with culture confirmation [5]. Treatment involves a combination of aggressive surgical debridement of involved tissues and antifungal therapy [3,6].

Case report

43-year-old, HIV negative man, with ocular myasthenia gravis (OMG) diagnosed in the previous year and treated with pyridostigmine (90 mg/day) and oral prednisolone (50 mg/day). He presented in the emergency department complaining of cough and shortness of breath, chest x-ray excluded pneumonia. He was discharged with the diagnosis of acute bacterial bronchitis, with antibiotic prescription (amoxicillin and clavulanate acid plus azithromycin). Three days later he returned with fever, hoarseness, productive cough and hemoptysis.

At the admission, the patient had new onset diabetes with diabetic ketoacidosis (glycated haemoglobin of 14.9 %), severe hypoxemic respiratory failure, laboratory exams with leukocytosis and elevation of C-reactive protein. Chest x-ray showed roughly rounded pneumonia located in the upper lobe of the left lung (Fig. 1). He was admitted in intermediate care unit under broad spectrum antibiotics. Sputum and blood cultures were drawn; urinary antigens for Legionella and Pneumococcus were negative.

On the fourth day, despite being hemodynamically stable and good glycemic control, the patient continued to be feverish, with hoarseness and still needing oxygen. Laryngeal direct observation showed left paralysis but no adjacent masses. OMG was stable and under treatment. Repeated chest x-ray, showed pneumonia progression and associated left upper lobe atelectasis. Flexible bronchoscopy revealed left bronchial necrosis and mucosal infiltration (Fig. 2); endobronchial biopsies and bronchial secretion were taken for histological and cultural examination. Neck and thoracic CT scan (Fig. 3) revealed lung consolidation in the left upper lobe, small bilateral pleural effusion and excluded abscesses, solid masses or apparent laryngeal recurrent nerve involvement.

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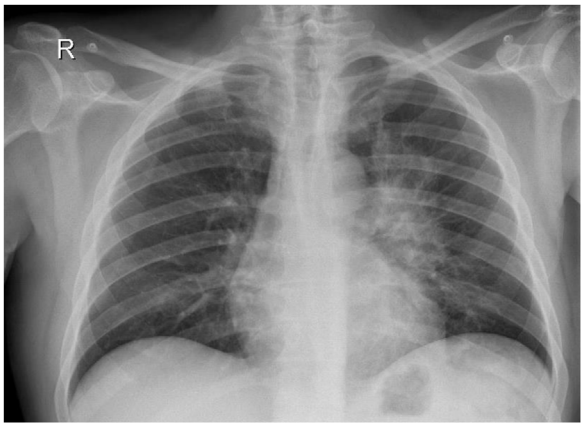

Fig. 1. Chest x-ray showed roughly rounded pneumonia located in the upper lobe of the left lung.

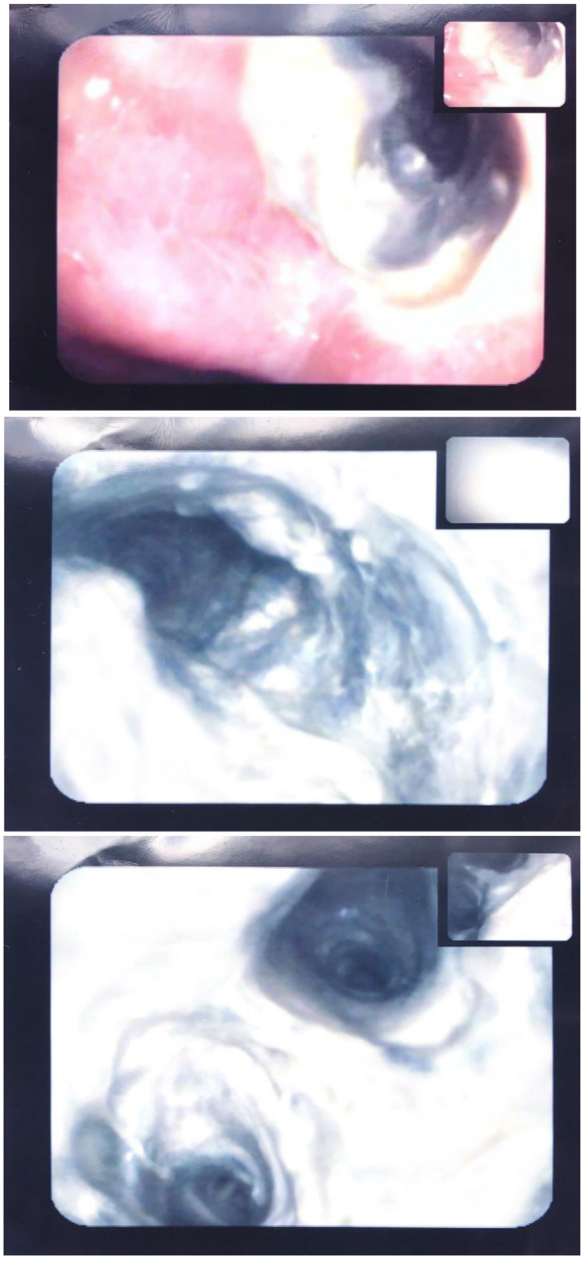

Fig. 2. Flexible bronchoscopy revealed left bronchial necrosis and mucosal infiltration.

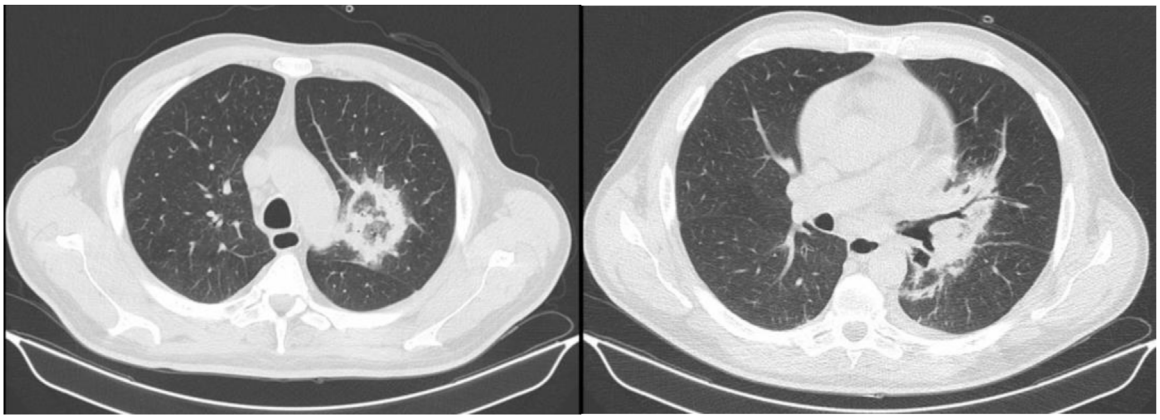

Fig. 3. Lung consolidation in the left upper lobe.

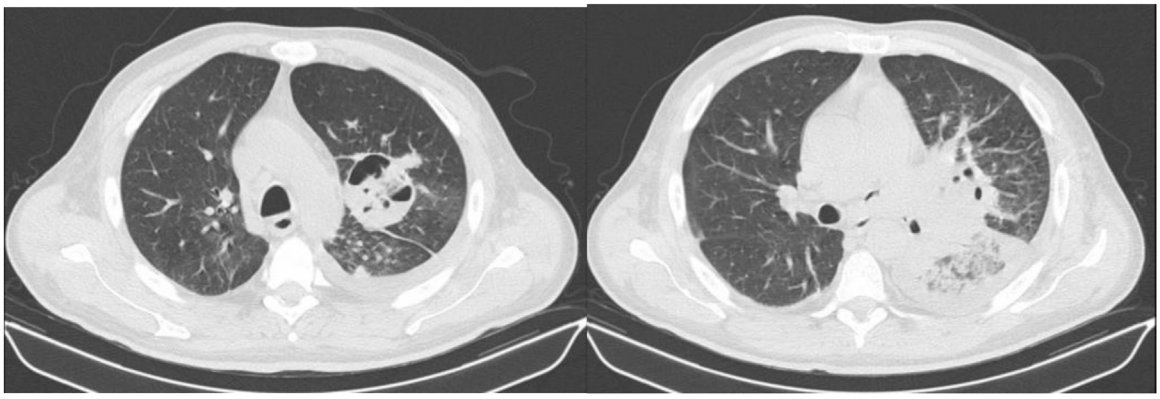

Fig. 4. Large abscess in the left upper lobe and extension to the inferior lobe, as well as laryngeal recurrent nerve compression.

There was no bacterial or fungi growth in sputum, bronchial secretions, bronchoalveolar lavage fluid or blood cultures. Pulmonary biopsy identified fungal hyphae but no further characterization was possible in that laboratory. Pulmonary fungi infection, namely lung aspergillosis, were considered, and high dose amphotericin B treatment was immediately started (5 mg/kg/day). A second flexible bronchoscopy with pulmonary biopsies was performed so that a conclusive diagnosis could be made.

After day five of antifungal therapy, the patient had sudden and progressive clinical worsening with persistent fever and hoarseness and *increasing* oxygen demands. Repeated neck and thoracic CT scan (Fig. 4) revealed a large abscess in the left upper lobe and extension to the inferior lobe, as well as laryngeal recurrent nerve compression. Vancomycin and meropenem were added to amphotericin B admitting possible nosocomial bacterial lung infection. Pan-fungal quantitative RT-PCR of the second pulmonary biopsy identified *Rhyzomucor* species from the *Mucor* genus, allowing the diagnosis of pulmonary mucormycosis. Antibacterials were suspended and Amphotericin B treatment was adjusted to the maximum daily recommended dose (10 mg/kg/day) due the unfavorable disease progression with the initial treatment. On the same day, the patient was transferred to a hospital with available thoracic surgery considering the need of complementary pneumectomy. In this institution, considering the quick progression of the disease and the worsening of the lung involvement, under optimized amphotericin B treatment, pneumonectomy surgery was scheduled. Head and brain MRI excluded rhinocerebral mucormycosis. Unfortunately, the patient died of massive hemoptysis seven days after the definitive microbiological diagnosis, while awaiting the surgery.

Conclusion/Learning points

This case report reveals the diagnostic challenge of pulmonary mucormycosis. The diagnosis was difficult not only because the clinical presentation did not differ from non-resolving community-acquired pneumonia, but also because the identification of the microbiologic agent was only possible after two invasive bronchial/lung biopsies and the use of non-widely available molecular biology methods.

Patients with haematologic malignancy appear more likely to develop invasive fungal pulmonary infection, when compared to those with diabetes, in whom rhino-orbito-cerebral disease is the most common presentation of invasive mold disease. As seen in other case series, pulmonary mucormycosis is rare in patients with diabetes mellitus [1,2,7,4].

Current guidelines recommend a combined medical and surgical approach to management, as anti-fungal agents may have poor penetration at the site of the infection and the disease is rapidly progressive and associated with a bad prognosis [7]. The main reasons for delaying or refusing lung surgery with pulmonary mucormycosis are the severity of underlying diseases and concerns for operative risk. Choi H., et al. concluded that overall survival rate was poor in patients with lung mucormycosis, but it was significantly higher in patients who were submitted to pulmonary resection surgery [8].

About the therapy for mucormycosis, there are subjective reports of using combination therapy with amphotericin B and either posaconazole or an echinocandin. These combination therapy may be an option according to the severity of disease [9,10]. However, there are no convincing data to support any form of combination therapy, and combination therapy is not

recommended in the major treatment guidelines [11,12]. The authors opted to keep monotherapy because of the lack of data and fear of interactions with other drugs.

This case also illustrates the rapid progression of pulmonary mucormycosis associated with fatal outcome. The infection may spread to contiguous structures, such as the mediastinum and heart, or disseminate haematogenously to other organs, leading to death within few days.

The interesting aspects of our case were the absence of malignancy cause for immunosuppression and the identification of *Rhizomucor* species.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Patient agreed with the publication of this article.

Author contribution

António Grilo Novais: Writing - original draft, Writing - review & editing, Conceptualization, Project administration. **Joana Capelo:** Writing - original draft, Conceptualization. **Marta Costa:** Investigation. **Mariana Conceição:** Investigation. **Pedro Crespo:** Writing - original draft, Conceptualization. **Luís Malheiro:** Writing - original draft. **Luísa Mocho:** Writing - original draft. **Beatriz Leão:** Writing - original draft. **Susana Silva:** Conceptualization, Investigation. **António Sarmento:** Supervision.

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