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CASE REPORT

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A rare case of pulmonary mucormycosis complicated by hydropneumothorax, successfully treated with non-surgical therapies

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Abstract

Pulmonary mucormycosis (PM) is a rare but rapidly progressive fungal infection associated with high mortality. A review of the literature suggests that pleural effusions and pneumothoraces are uncommon manifestations associated with distant dissemination. Combined surgical interventions and prolonged antifungal therapy constitute the standard first-line management, with significantly poorer outcomes seen in patients managed with medical therapy alone. Here, we report an unusual case of PM complicated by hydropneumothorax in an immunocompromised patient, in whom comorbidities and disease burden precluded surgical debridement. His disease was ultimately treated with intravenous amphotericin B and maintenance posaconazole after adjunctive drainage. This clinical experience highlights the efficacy of antifungal therapy alone in the treatment of potentially fatal cases of PM unsuitable for surgery.

KEYWORDS
amphotericin B, hydropneumothorax, posaconazole, pulmonary mucormycosis

INTRODUCTION

Pulmonary mucormycosis (PM) is a rare angioinvasive infection predominantly found in immunocompromised patients. Uncommon occurrences of pneumothorax and pleural effusion are ominous findings associated with distal spread, which can rapidly prove fatal. Combined early surgery and prolonged antifungal therapy have been shown to improve outcomes. Here, we report an unusual case of PM complicated by a large hydropneumothorax. The patient was successfully treated with liposomal amphotericin B and posaconazole following adjunctive drainage without surgical intervention, which has been seldom reported in the literature.

CASE REPORT

A 61-year-old male presented with fever and progressive left-sided chest pain associated with a tender chest wall nodule over 12 hours. Past medical history included poorly controlled diabetes with end-stage nephropathy on haemodialysis, and sarcoidosis-related pan-uveitis on maintenance prednisone 20 mg/day. He had no fevers, eye pain or headache. The patient was a never-smoker and lived in a multigenerational household with possible mould exposure.

Chest computed tomography (CT) on admission revealed left upper lobe consolidation and multiple new right-sided pulmonary nodules initially favoured to represent satellite foci of infection (Figure 1A). Sputum for acid-fast bacilli

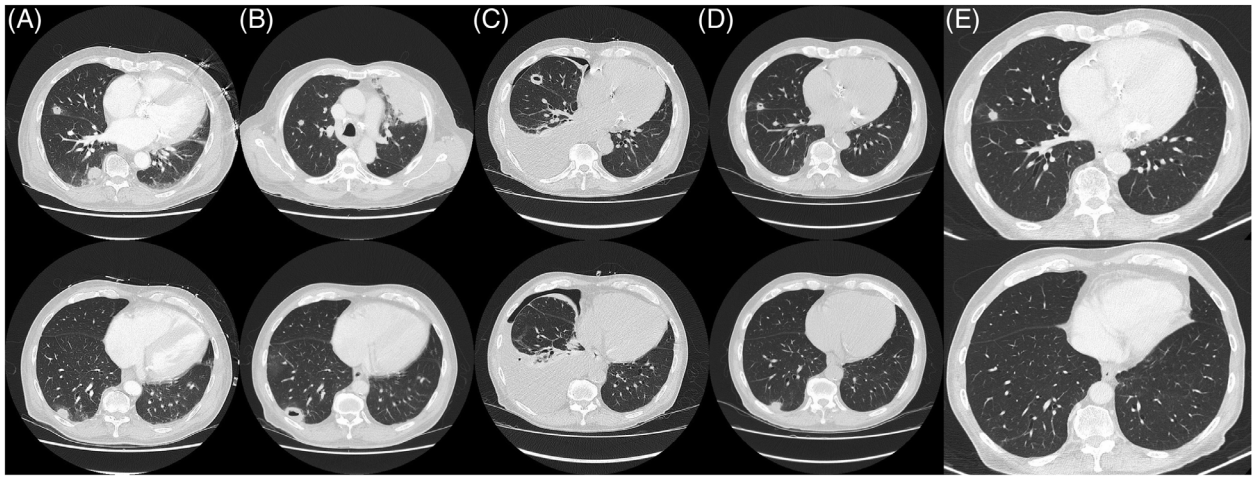

FIGURE 1 Serial chest imaging. (A) Day 1: Chest computed tomography (CT) suggested pulmonary infection with multiple right-sided pulmonary nodules. (B) Day 8: Left upper lobe consolidation along with apparent thick-walled cavitary nodules with surrounding ground-glass opacity in the right middle and lower lobes suggesting fungal invasion. (C) Day 31: High-resolution CT demonstrating large right-sided pleural effusion with pneumothorax. (D) Two months following antifungal therapy and drainage: Significant interval improvement with reduction in size of cavitary nodules and no residual hydropneumothorax. (E) Four months following antifungal therapy and drainage: Significant improvements seen with full resolution of pleural effusion and near-resolution of residual right middle and lower lobe cyst.

and *Mycobacterium tuberculosis* polymerase chain reaction was negative. Multiple blood cultures were negative. Other laboratory findings are shown in Table 1. Despite broad-spectrum antibiotics including azithromycin, meropenem and vancomycin, the patient had unremitting fevers and developed new haemoptysis on day 8. Repeat CT showed multiple thick-walled cavitating nodules in the right upper, middle and lower lobes and progressive left upper lobe consolidation (Figure 1B). Subsequent bronchoscopy demonstrated mucoid secretions from the left upper lobe but normal endobronchial mucosa. Bronchoalveolar lavage (BAL) from RB9 demonstrated heavy fungal growth. Washing from LB3 additionally grew *Aspergillus fumigatus* complex. Serum and BAL galactomannan levels were raised (Table 1). Due to inaccessibility of the right lower lobe nodule via bronchoscopy, CT-guided fine-needle aspiration (FNA) biopsy was done on day 17. Histological examination of the specimen demonstrated large numbers of inflammatory cells, predominantly neutrophils, with small numbers of non-septate hyphae with no clear evidence of angioinvasion. Culture of the biopsy specimen subsequently yielded growth consistent with *Rhizopus* microspores, confirming the diagnosis of PM.

The patient was deemed unsuitable for thoracic surgical intervention due to extensive lung involvement and significant comorbidities. Voriconazole was commenced from day 17 and switched to intravenous liposomal amphotericin B at 5 mg/kg/day on day 20 after the identification of *Rhizopus* microspores from tissue biopsy. As supportive measures, blood glucose was aggressively optimized and prednisone dose tapered. Following initial improvement, the patient developed further pleurisy and dyspnoea on day 31. High-resolution CT revealed a large right-sided hydropneumothorax, potentially as a consequence of rupture from a cavitary nodule (Figure 1C). A 12-French chest tube was inserted, which drained 1.8 L of hazy-orange fluid and reduced the pneumothorax over 48 hours. Pleural fluid analysis demonstrated an exudative, eosinophilic process with no fungal growth. The patient subsequently improved and was discharged on day 39. Intravenous amphotericin B was continued for 4 weeks and then switched to posaconazole modified-release 300 mg/day lifelong. On follow-up at 5 months, serial chest CTs demonstrated resolution of previous thick-walled cavitary nodules and upper lobe consolidation (Figure 1D,E). Interestingly, full resolution of his chest wall nodule suggested this being of the same aetiology as his lung pathology and the patient had no residual respiratory symptoms.

DISCUSSION

To the best of our knowledge, this case appears to represent the first survival of PM complicated by hydropneumothorax, successfully treated with antifungals and drainage therapy without surgical intervention. The vasotropic nature of *Rhizopus* is a hallmark feature of *Mucorales* species, with resultant parenchymal necrosis and angioinvasion. A review of literature showed that pleural effusions are relatively uncommon and only affected 8% of patients.[1] Likewise, only five cases of non-iatrogenic, spontaneous pneumothoraces in PM were reported in the literature arising from likely ruptured necrotizing cysts. Outcomes of the latter group were devastating with 100% mortality.[2–6]

Although the survival rate of PM has improved in recent years, a large difference remains between 31.2%

TABLE 1 Summary of investigations during admission

Full blood count	
White blood cells	13.1 × 10^9 cells/L
Neutrophils	11.0 × 10^9 cells/L
Lymphocytes	0.8 × 10^9 cells/L
Monocytes	1.0 × 10^9 cells/L
Eosinophils	0.2 × 10^9 cells/L
Haemoglobin	92 g/L
Haematocrit	0.29
Platelets	174 g/L
Serum chemistry	
C-reactive protein	131 mg/L
Sodium	136 mEq/L
Potassium	5.3 mEq/L
Creatinine	450 μmol/L
Albumin	30 g/L
Total protein	73 g/L
Lactate	1.5 mmol/L
Infectious disease screen	
Pneumococcal antigen test	Negative
Urinary *Legionella* antigen test	Negative
Sputum acid-fast bacilli	Negative
SARS-CoV-2 PCR	Negative
HIV screen	Negative
Serum immunoglobulins	Normal
Sputum fungal culture	*Aspergillus fumigatus* complex isolated MIC Amphotericin B: 2 mg/L (wild-type) Voriconazole: 0.25 mg/L (susceptible) Itraconazole: 0.25 mg/L (wild-type) Posaconazole: 0.12 mg/L
Aspergillus-specific IgG	173 mgA/L
Specific IgE antibody to *Aspergillus*	<0.05 KIU(A)/L
Serum galactomannan	1.43 (normal range 0–0.5)
BAL galactomannan (from RB9)	8.93 (normal range 0–1.5)
BAL	Right lower lobe: One colony of fungus isolated *Mycobacterium tuberculosis* complex DNA not detected Left upper lobe: *Pneumocystis jirovecii* detected (PCR) *M. tuberculosis* complex DNA not detected
FNA of the right lower lobe nodule	*Rhizopus microsporus* isolated MIC Amphotericin B: 1 mg/L Voriconazole: >8 mg/L Itraconazole: 1 mg/L Posaconazole: 1 mg/L
Pleural fluid analysis	Appearance: hazy orange Supernatant: clear, pale yellow LDH 390 Glucose 9.2 mmol/L Total protein 40.5 g/L Eosinophils 42% Monocytes 35% Lymphocytes 22% Polymorphs 1% No organisms or fungal elements seen

Abbreviations: BAL, bronchoalveolar lavage; FNA, fine-needle aspiration; LDH lactate dehydrogenase; MIC, minimal inhibitory concentration; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

survival in patients receiving medical therapy alone versus up to 100% survival with combined medical and surgical therapy.[7] Liposomal amphotericin B at 5–10 mg/kg/day is the first-line agent with dose-dependent efficacy but can be limited by reversible nephrotoxicity. Posaconazole in delayed-release formulations has increased bioavailability and is recommended as salvage therapy.[8] The first case of successfully treated PM without surgical intervention was reported in 1972 and was attributed to amphotericin B sensitivity testing enabling rationalized antifungal dosing.[9] In subsequent years, there have been few similar reports, with most patients either immunocompetent, lacked comorbidities or received intrabronchial antifungal therapy.[1] A previously reported case of *Cunninghamella bertholletiae* PM complicated by pneumothorax bares similarities to our case, receiving haemodialysis plus long-term steroid therapy, and survived following chest tube drainage and amphotericin B. Of note, however, this case had not been complicated by pleural effusion or diabetes, and the amphotericin dosing was somewhat unusual at 1–40 mg/day.[3]

Our patient had several negative prognostic factors, namely poorly controlled diabetes, renal failure, corticosteroid use, extensive pulmonary involvement, haemoptysis implying significant angioinvasion and high operative risk precluding surgery. The additional concomitant diagnosis of invasive aspergillosis further added to his risk of a poor outcome. Of note, *Rhizopus* also displays variable resistance to triazoles but fortunately this has not manifested in our patient to date.[10] His survival without surgical intervention may be explained by the active management of his underlying health issues including aggressive diabetes management and steroid tapering. Our clinical experience highlights the viability of antifungal therapy in successfully treating PM where surgery was prohibited, even following major structural compromise which increased the risks of distant dissemination.

AUTHOR CONTRIBUTION

Case identification: Paul Griffiths and William Good. Case management: Andrew Salmon, Nicholas Gow, William Good and Paul Griffiths. Literature search and data analysis: Qiliang Liu, Nicholas Gow and Paul Griffiths. Draft manuscript preparation: Qiliang Liu and Paul Griffiths. All

authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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