CASE REPORT

Rare cause of pulmonary cavitation in a 75-year-old man

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SUMMARY

A 75-year-old man of Asian descent presented to the acute medical unit with signs and symptoms suggestive of a community-acquired pneumonia. He had multiple comorbidities and was relatively immunocompromised as a result. Initial investigations supported the diagnosis of community-acquired pneumonia complicated by a cavitating lung lesion, and the patient was treated as per hospital guidelines. He continued to deteriorate despite appropriate therapy and developed a hydropneumothorax, requiring the insertion of a chest drain. A diagnosis of pulmonary mucormycosis (*Rhizopus microsporus*) was made based on microbiology results from pleural aspirate, and patient was treated with intravenous antifungals. The patient was referred to the thoracic team for consideration of surgical intervention but was not suitable due to his multiple comorbidities. This case highlighted the importance of early consideration of fungal infection in patients with multiple risk factors and the need for aggressive therapy to ensure the best outcome.

BACKGROUND

Cavitating lung disease is an important presentation in the acute medical care that is infrequently encountered by many physicians. Due to a wide range of differential diagnoses, these patients can represent both a diagnostic and treatment challenge, even to the most experienced doctors. Here we discuss a case where a man presented with acute infective symptoms and a cavitating lung lesion on his chest X-ray, in the hope that this will improve our understanding of how best to manage these complex patients.

CASE PRESENTATION

A 75-year-old man with a medical history of Janus kinase 2 positive prefibrotic myelofibrosis with chronic neutrophilia, Addison's disease, chronic kidney disease stage 4, type 2 diabetes mellitus, hypertension, myocardial infarction and previous tuberculosis (TB) adenitis (treated with a 6-month course of antituberculosis medications), presented to our hospital with a 1-week history of increasing shortness of breath and reduced exercise tolerance. This was associated with a dry cough, generalised weakness and reduced appetite. On further questioning, the patient reported significant weight loss over the previous 6 months, but denied any further symptoms. His medication on admission included aspirin, cholecalciferol, fludrocortisone, hydrocortisone,

lansoprazole, linagliptin, pregabalin, sodium bicarbonate, modified release tamsulosin and verapamil.

On initial assessment in the medical admissions unit, the patient had normal observations including oxygen saturation of 96% on room air, a respiratory rate of 16 breaths per minute, a heart rate of 76 and a blood pressure of 136/82. Respiratory examination demonstrated coarse crackles in the right lower zone, with dullness to percussion and increased vocal resonance. He was clinically dehydrated and appeared very malnourished. The cardiovascular and abdominal examinations were both unremarkable, and there were no peripheral stigmata of systemic disease.

Investigations showed a white cell count of $63.3 \times 10^9/L$ (relatively stable compared with his old full blood count), C-reactive protein (CRP) 177 mg/dL and haemoglobin of 93 g/dL. His kidney function was at baseline (sodium 131 mmol/L, potassium 4.5 mmol/L, urea 16.8 mmol/L, creatinine 216 $\mu\text{mol/L}$ and estimated glomerular filtration rate of 26) and his liver function tests were relatively normal apart from an alkaline phosphatase of 216 u/L (bilirubin 12 $\mu\text{mol/L}$, alanine aminotransferase 20 u/L and albumin of 37 g/L). His chest X-ray showed a cavitating lesion in his right middle zone with surrounding consolidation (figure 1).

Patient was initially treated for a severe community-acquired pneumonia (with a CURB score of 2) with a course of intravenous antibiotics as per local antimicrobial guidelines (intravenous benzylpenicillin 1.2g four times daily and intravenous clarithromycin 500mg twice daily). His dose of hydrocortisone was doubled (total daily dose of 40mg in two divided doses of 30mg in the morning and 10mg in the afternoon) and he was referred to the diabetes team to ensure good glycaemic control during this acute illness. A plan was put in place to switch to oral antibiotics once clinically improved and to follow-up in outpatient clinic for further assessment of his X-ray changes with cross-sectional imaging.

On day 6 of admission, the patient started to complain of worsening cough and pleuritic chest pain. He was noted to have an increased work of breathing and oxygen requirements. He was seen by the on-call medical team and a repeat set of bloods and chest X-ray was requested. His blood test results showed worsening of his inflammatory markers (white cell count $73.3 \times 10^9/L$) and a second rise in CRP (126 mg/dL) after initial improvement) and a chest X-ray demonstrated a hydropneumothorax (figure 2).

Patient was referred to interventional radiology for urgent insertion of a chest drain under

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Figure 1 Initial chest X-ray showing cavitation in the right middle zone with surrounding consolidation. PA; Posterior-Anterior

ultrasound guidance. A sample of pleural fluid was obtained and sent for pleural pH, protein, gram stain, MC&S, acid fast bacilli, TB PCR and cytology. After discussion with the on-call microbiologist, he was switched to intravenous piperacillin–tazobactam (dose of 4.5 g every 8 hours), while awaiting further microbiology results.

The following day (day 7 of admission) he remained breathless despite the insertion of his chest drain and continued to require high flow oxygen to maintain his saturation. A post-insertion chest X-ray showed only mild improvement in the size of the pneumothorax. Therefore, a CT thorax was requested to further assess the nature of the air leak. Images obtained are shown in [figure 3](#). The patient had a brisk air leak from a 5 mm hole in the right lung. Due to the brisk nature of the air leak,

Figure 3 Cross-sectional image showing a cavitation with a 5 mm hole and a large pneumothorax.

Figure 2 Chest X-ray showing a hydropneumothorax. PA; Posterior-Anterior

a blunt dissection was performed, and a larger chest drain was inserted under local anaesthetic, which resulted in a significant improvement in his shortness of breath and oxygen requirement.

The patient was managed on the respiratory ward with two chest drains in situ. He was kept on intravenous piperacillin–tazobactam (4.5 g three times a day), while awaiting further microbiology results from the pleural aspirate.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for a cavitating lung lesion is wide and diverse. It includes both infectious and non-infectious causes.¹ The diagnostic approach would need to consider patient risk factors and symptoms at presentation. Our patient was a lifelong non-smoker with no significant occupational exposure. He was born overseas in the Indian subcontinent, had multiple comorbidities, including previous treatment for TB and was relatively immunocompromised secondary to his prefibrotic myelofibrosis, treatment for Addison's disease and history of diabetes.

The most common and important cause to consider in this man taking his medical history into account, would be *Mycobacterium tuberculosis* infection. This can commonly cause cavitating lung disease and is an important diagnosis to consider in the initial stages, as the patient will require appropriate isolation until it is ruled out.¹ Although the incidence in the UK was 10.5 per 100 000 in 2015, the patient had multiple risk factors including previous exposure and being born in the Indian subcontinent. Therefore, this remained high on our list of differential diagnoses. Infections caused by common gram positive or negative organisms can occasionally cause cavitation in the lung.¹ This can occur because of haematogenous spread through septic emboli or a necrotising pneumonia caused by entry of the organism through the upper airways.¹ Common causative organisms for community-acquired pneumonia, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, do not usually cause cavitation, but cases can be frequently encountered due to their high incidence.^{1–3} Less common organisms such as *Klebsiella pneumoniae* and *Staphylococcus aureus* are more likely to be associated with a severe necrotising pneumonia causing cavitation and should be considered in this case.¹

Fungal infections can also cause cavitation in the lung. Perhaps, the most common cause will be infections with *Aspergillus* species, which can cause a spectrum of pulmonary diseases including invasive and cavitating lung disease.⁴ This tends to affect the relatively immunocompromised elderly patient with chronic lung disease and other comorbidities such as diabetes.¹ Other important fungal organisms include *Mucorales*, *Cryptococcus*, *Blastomyces* and *Histoplasmosis* in endemic areas.¹ *Pneumocystis jirovecii* is an important cause in immunocompromised patients infected with the HIV.⁵

The distinction between infectious and non-infectious causes needs to be established earlier on in the diagnostic process, as it will alter the management route that the patient will go into.¹ Primary lung cancer has an incidence of 46 403 cases in the UK in 2014, making it a relatively common diagnosis.⁶ Cavitation has been identified in 22% of cases of lung cancer on CT scan, and this has been associated with a worse prognosis.¹⁷ Metastatic disease may also cause cavitation, but this occurs less frequently than primary lung cancers.¹

The final category to consider in our differential is rheumatological disease. Although pulmonary involvement is relatively common in autoimmune disease, this rarely results in cavitation.¹ Cavitation can occur in antineutrophil cytoplasmic antibodies-associated vasculitis, but this is a rare disease with an annual incidence of 24–157 per million.¹⁸ The patient's diagnosis of Addison's disease suggests that he may have a predisposition to autoimmune disease, and therefore one should briefly consider this as a possible diagnosis despite its low incidence.

TREATMENT

A formal diagnosis was made on day 10 of admission, when the microbiology results from the pleural aspirate became available. This showed growth of *Rhizopus microsporus* in the pleural fluid. The pleural aspirate samples were processed at the mycology reference lab in Bristol, and species identification was done phenotypically under microscopy. The samples were reported as sensitive to amphotericin B (minimum inhibitory concentration (MIC) of 0.25) and resistant to echinocandin (MIC of >8), itraconazole (MIC of >16) and voriconazole (MIC of >16). Intermediate sensitivities were reported for posaconazole and isavuconazole, with MICs of 1 and 2, respectively. The patient's TB PCR, acid fast bacilli and atypical pneumonia screen were all negative.

After discussion with the infectious diseases team, the patient was switched from his intravenous piperacillin–tazobactam to intravenous AmBisome (amphotericin B liposomal at a dose of 305 mg (5 mg/kg)) on day 10 of his admission, with close monitoring of his renal and liver function. Despite having two chest drains in situ, the patient's lung failed to inflate. He was therefore referred to the regional thoracic surgery team for further intervention. The patient was transferred to the regional thoracic surgery team for further management.

OUTCOME AND FOLLOW-UP

The patient was reviewed by the thoracic surgical team and was deemed not to be fit enough to undergo any surgical intervention. He sadly deteriorated within 48 hours of being transferred and passed away.

DISCUSSION

Rhizopus is a genus of mostly saprobic species of filamentous fungi in the family *Rhizopodaceae*, in the order *mucorales*. Many *Rhizopus* species are responsible for diseases in both animals

and plants. Mucormycosis is the term used to describe infections caused by *Rhizopus* species and other *Mucorales* (*Mucor*, *Rhizomucor*, *Lichtheimia*, *Apophysomyces*, *Cunninghamella* and *Saksenaea*). Six clinical syndromes are recognised: rhino-orbital-cerebral, pulmonary, cutaneous, disseminated, gastrointestinal and miscellaneous forms.⁹

Several underlying conditions predispose patients to infection, this includes haematological malignancies, solid malignancies, solid organ transplant and diabetes mellitus.¹⁰ In a report of 230 cases of mucormycosis, it was noted that 46% patient received corticosteroids and 44% received other immunosuppressive medication.^{11 12}

Pulmonary disease is one of the most common sites of infection.^{13 14} In a recent analysis of 230 cases from the registry of the European confederation of medical mycology, it was noted that pulmonary disease accounted for 30% of all cases and was associated with a 56% mortality.¹¹

The management of mucormycosis involves the use of anti-fungal agents, surgical intervention and management of comorbidities. Amphotericin B is the first-line antifungal, usually given at a dose of 5 mg/kg/day for a duration of 6–8 weeks.¹⁴ Aggressive surgical debridement of necrotic tissue also plays a significant role in the management of these patients, due to the difficulty in eradication with medical therapy alone.¹⁴ This should therefore be done without delay. Patients also benefit from good glycaemic control, in the setting of diabetic ketoacidosis, and discontinuation (or dose reduction) of any immunosuppressive medication.¹⁴

In our literature review, we identified a small number of cases of pneumothorax occurring in the context of pulmonary mucormycosis are noted with iatrogenic causes (mechanical ventilation and bronchoscopy),¹⁵ pneumothorax occurring spontaneously in the presence of mucormycosis and methicillin-resistant *Staphylococcus aureus* (MRSA) in an immunocompromised patient,¹⁶ and in combination with *Aspergillus* in a patient on dialysis.¹⁷ However, only one other case is noted to have occurred with a spontaneous pneumothorax of a non-iatrogenic aetiology in the absence of proven co-infection.¹⁸

This case highlights the importance of considering pulmonary mucormycosis as a differential diagnosis when encountering a patient with pulmonary cavitation and risk factors for invasive fungal infection. The rapidly progressive nature of this condition and poor morbidity and mortality outcomes in the absence of optimal therapy it is important that these cases are recognised and treated correctly to maximise the potential for a better clinical outcome.

Learning points

- ▶ Early consideration of pulmonary mucormycosis is important when encountering a patient with pulmonary cavitation and risk factors for invasive fungal infection.
- ▶ Conditions predisposing patients to infection include haematological malignancies, solid malignancies, solid organ transplant, diabetes mellitus, corticosteroids and other immunosuppressive medication.
- ▶ Optimal management relies on early initiation of appropriate antifungal therapy, aggressive surgical debridement and treatment of predisposing conditions.
- ▶ A good clinical outcome for these patients relies on early recognition and initiation of aggressive therapy, due to the rapidly progressive and aggressive nature of disease.

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