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CASE REPORT

Fatal Tracheal and Bronchial Destruction Due to Pulmonary Mucormycosis in a 20-Year-Old with Diabetic Ketoacidosis

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Abstract: Pulmonary mucormycosis is a rare and aggressive invasive fungal infection that predominantly affects immunocompromised individuals, such as those with diabetes mellitus or those undergoing immunosuppressive therapy. This case describes a severe instance of pulmonary mucormycosis resulting in progressive tracheal wall destruction in a young, previously healthy male. A 20-year-old male with a denied history of diabetes mellitus was admitted to a local hospital with abdominal pain for 9 days and diagnosed with acute pancreatitis and diabetic ketoacidosis (DKA). During his stay at the local hospital the patient developed respiratory distress and was transferred to our hospital. Although initially given non-invasive respiratory support and broad-spectrum antibiotics, the patient's condition deteriorated and invasive mechanical ventilation and VV-ECMO were given. Bronchoalveolar lavage fluid (BALF) next-generation sequencing (mNGS) identified Rhizopus species, confirming pulmonary mucormycosis. Aggressive antifungal therapy with amphotericin B was administered, followed by the addition of isavuconazole, but the patient's lesions continued to expand, ultimately leading to fatal tracheal and bronchial wall disruption and subsequent haemorrhage. This case emphasizes the rapid progression and extensive tissue destruction characteristics of pulmonary mucormycosis. Early diagnosis and treatment, especially simultaneous antifungal therapy and appropriate surgical intervention, are crucial for improving the prognosis of such severe cases.

Keywords: pulmonary mucormycosis, bronchus, necrosis, treatment, fiberoptic bronchoscopy

Introduction

Pulmonary mucormycosis is a rare but severe invasive fungal infection predominantly caused by fungi of the order Mucorales. This condition primarily affects immunocompromised individuals, including those with diabetes mellitus, hematologic malignancies, or those undergoing immunosuppressive therapy.[1] The clinical presentation of pulmonary mucormycosis can be highly variable, often manifesting with nonspecific symptoms such as fever, cough, dyspnea, and hemoptysis, which can complicate early diagnosis.[2] Diagnostic challenges are further compounded by the need for invasive procedures like bronchoalveolar lavage or tissue biopsy to confirm the presence of fungal elements.[3] Despite advances in antifungal therapy, the prognosis for pulmonary mucormycosis remains poor. Especially, delaying the use of antifungal drugs is associated with increase in 90-day mortality related to mucormycosis,[4] while combined antifungal treatment and surgical resection can overall reduce mortality.[5] Here we report a case of short-term fatal tracheal and bronchial destruction and eventual death from haemorrhage due to pulmonary mucormycosis.

Case Presentation

A 20-year-old male university student, who denied a history of diabetes and other illnesses, was admitted to a local hospital with abdominal pain for nine days and diagnosed with acute pancreatitis and diabetic ketoacidosis (DKA). During his stay at the local hospital, he gradually developed dyspnoea with cough and blood in sputum. A Chest CT scan performed at the local hospital

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showed that the left main bronchus was narrowed, partially occluded (Figure 1). He was transferred to our hospital because of his critical condition. On admission to our hospital, the patient presented as conscious, with shortness of breath, cyanosis of the lips, and no respiratory sounds could be heard from the left lung on examination. With brief non-invasive ventilator assistance, he was still in respiratory distress and hypoxia, so tracheal intubation and invasive ventilation, prone ventilation, piperacillin tazobactam for anti-infection, fibreoptic bronchoscopy and alveolar lavage sent for pathogenic microorganisms and mNGS were immediately performed. The patient's oxygenation still did not improve, so VV-ECMO treatment was performed immediately on the same day. Enhanced CT on the second day showed thickening of the wall of the left main bronchus, occlusion of the middle and distal segments of the left main bronchus and the left bronchial branches, and complete atelectasis of the left lung (Figure 2).

On the 3rd day of admission, the patient's immunofluorescence staining of the lavage fluid showed fungal hyphae (Mucor) and fibrilloscopic lavage fluid mNGS showed Rhizopus microsporus (Figure 3). The patient was diagnosed with pulmonary mucormycosis and began receiving intravenous infusion of amphotericin B 400mg qd and 5mg nebulized inhalation for anti-mucormycosis treatment. On the 11th day of admission, repeat CT showed severe stenosis in the middle and distal segments of the left main bronchus, mild-to-moderate stenosis in the segmental left main bronchus, left lung reopening compared with the previous one, and the occlusion of the left main bronchus was slightly improved. Scattered inflammation in both lungs (Figure 4). The VV-ECMO was running well during the course of the disease, the respiratory cycle was stable, and the breath sounds of the left lung were audible, so the VV-ECMO was withdrawn on the tenth day.

However, repeated fibrilloscopies during the course of the disease revealed progressive destruction of the tracheal wall, erosion of the tracheal mucosa, and airway collapse, including a large amount of mycobacteria and necrotic material adhering to the surface of the left main bronchus, and destruction of the airway wall up to the bifurcation of the upper and lower lobes of the left lung, and congestion and oedema of the right airway (Figures 5 and 6). The patient's trachea and bronchial destruction was severe, and another CT examination was performed on the 15th day after admission, which showed discontinuity of the airway wall, severe stenosis of the middle and distal segments of the left main bronchus and its branches, and occlusion of most of the lumen, which was aggravated compared with the previous one. The left lung atelectasis was worse than before. There was extensive pneumoperitoneum in the cervical root, anterior chest wall and mediastinum bilaterally (Figure 7). Due to severe damage and destruction of the tracheal and bronchial walls extending to the mediastinum, and considering that pulmonary mucormycosis was not well controlled, an infusion of isavuconazole

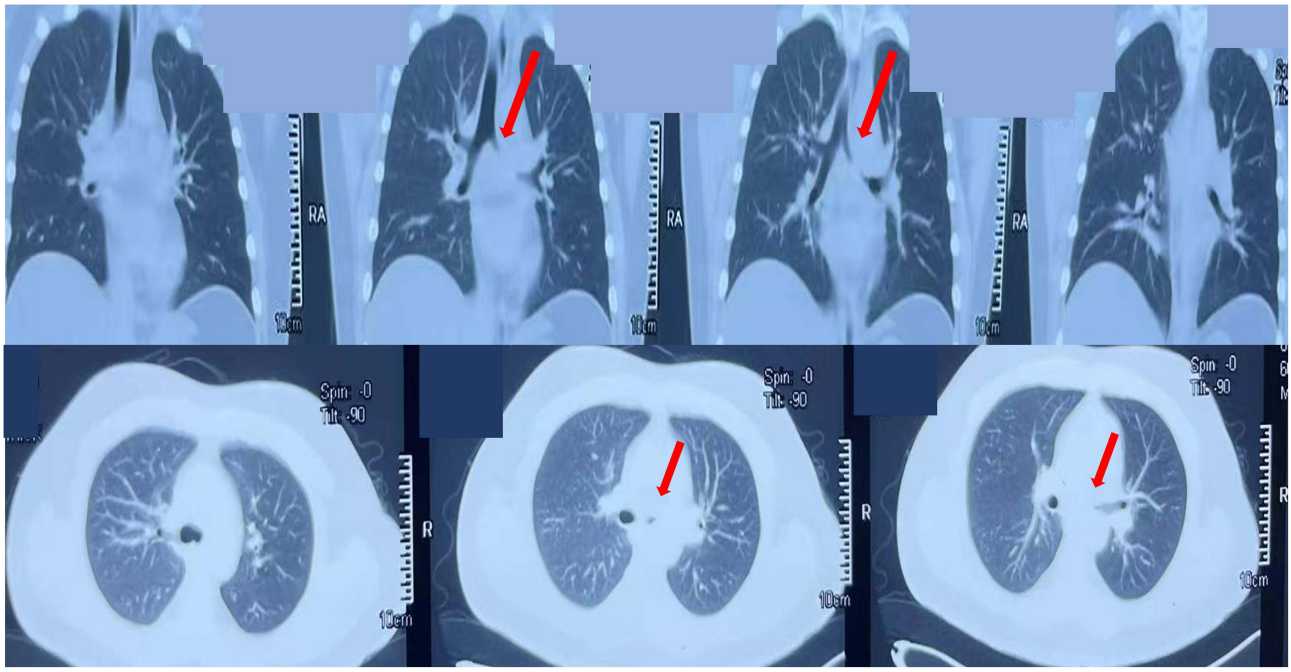

Figure 1 Patient's outpatient chest CT showing left bronchial stenosis (red arrow).

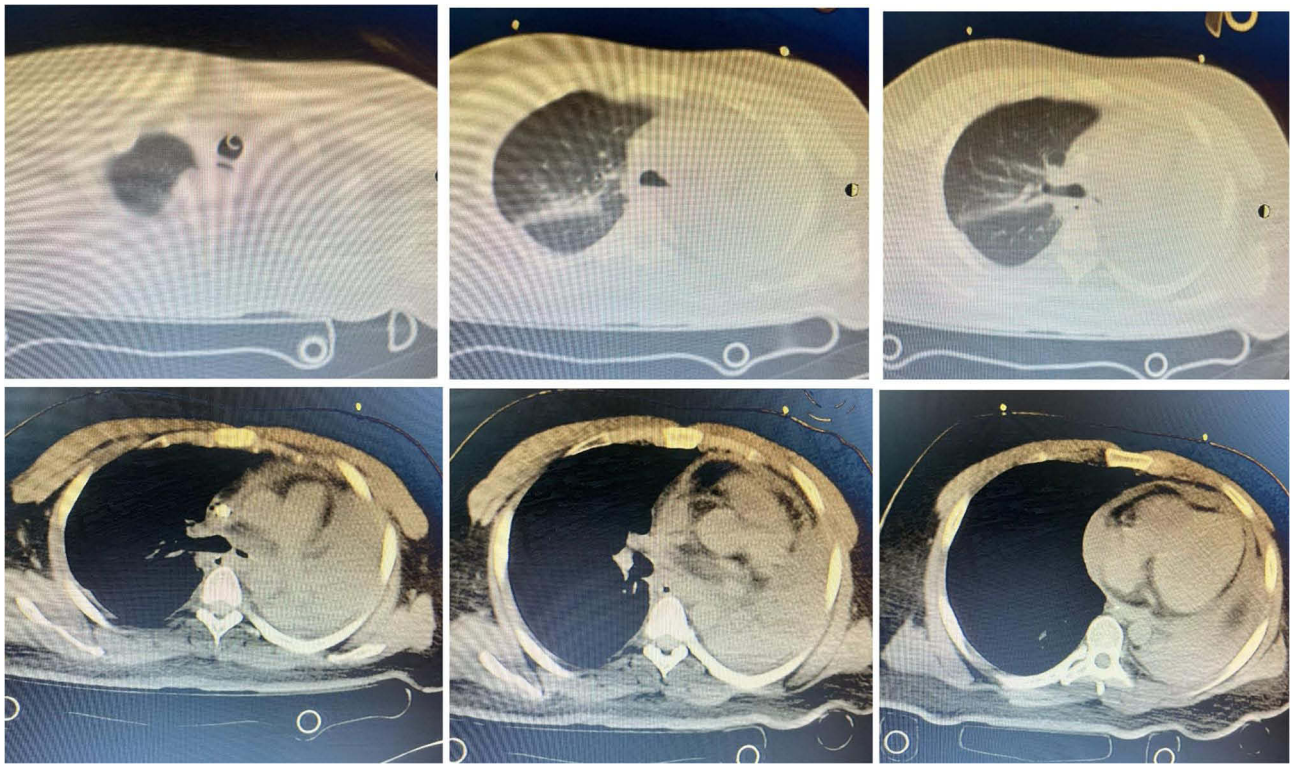

Figure 2 Chest CT on the second day of admission suggested left bronchial stenosis and left lung atelectasis.

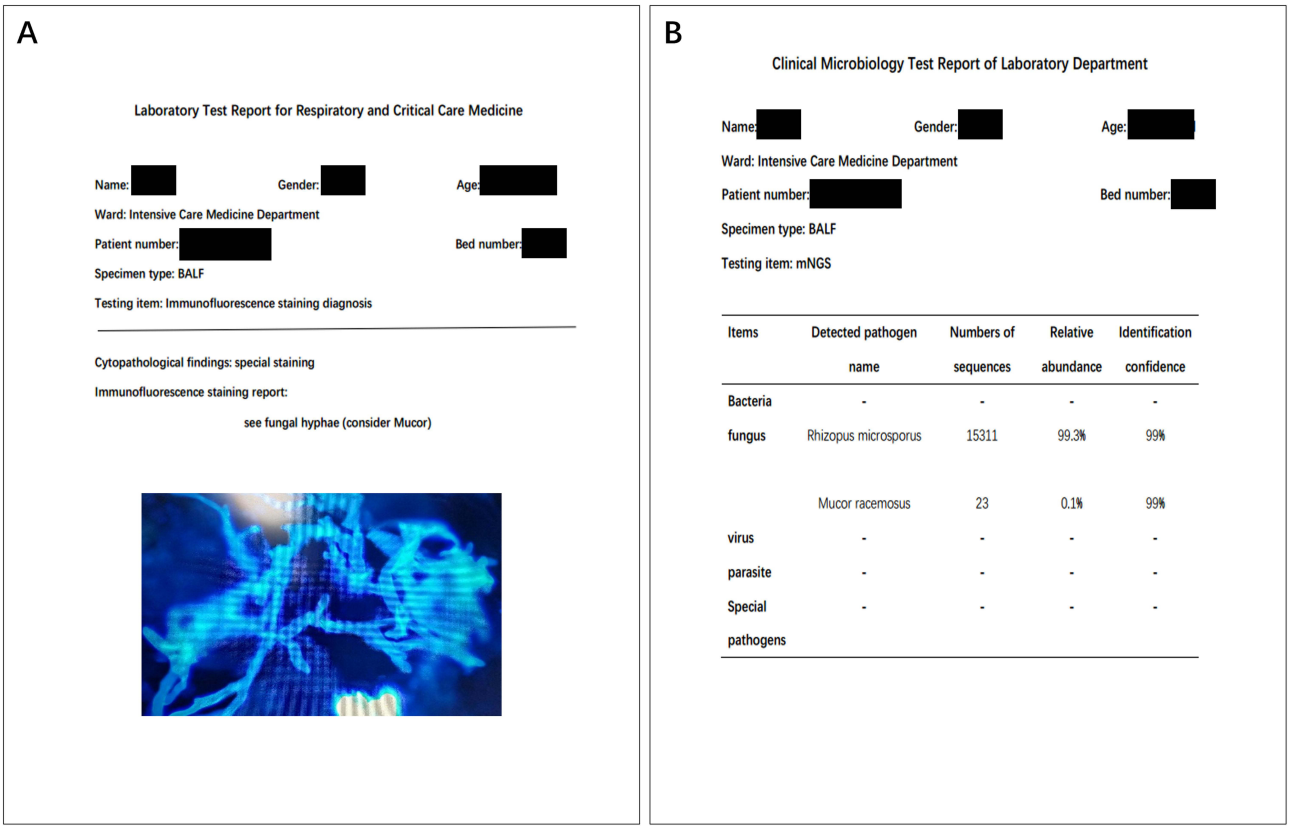

Figure 3 (**A**) The results of immunofluorescence staining. (**B**) The results of mNGS.

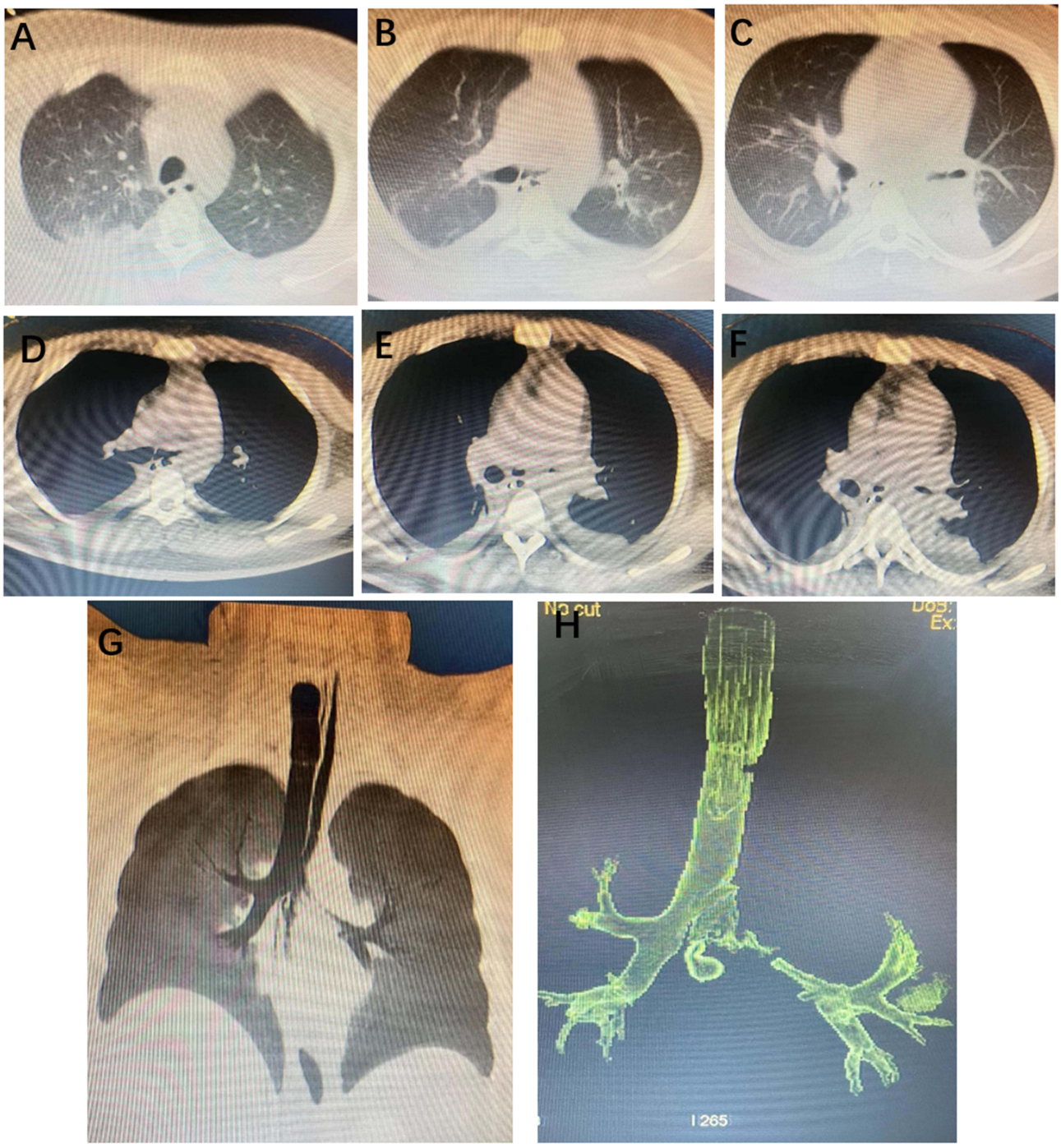

Figure 4 Chest CT on the 11th day of admission suggested stenosis and partial necrosis of the left main bronchus, with the left lung reopened compared to the previous one.
Notes: (**A-G**) The results of Chest CT examination. (**H**) Three dimensional reconstruction results of trachea.

was added on the 16th day after admission, in addition to the ongoing treatment with amphotericin B. On the 20th day after admission, the patient suddenly coughed up a large amount of blood from the tracheal intubation, accompanied by a gradual decline in heart rate and blood pressure, ultimately resulting in unsuccessful resuscitation and death. The cause of death was determined to be massive hemorrhage due to the involvement of the mediastinum and arteries by pulmonary mucormycosis.

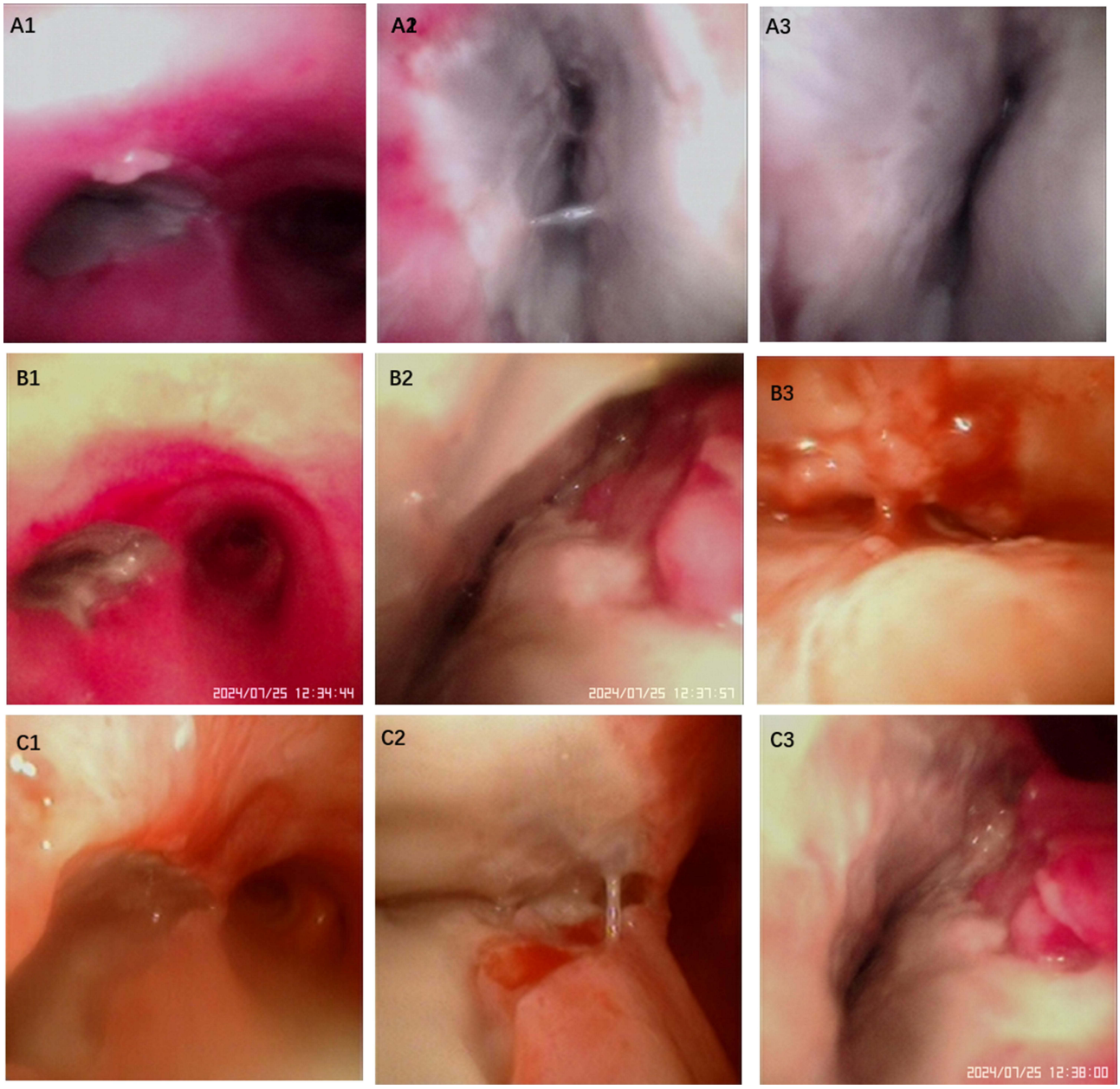

Figure 5 Fibrobronchoscopy showed disruption and stenosis of the left main bronchus, with necrotic material and white mucormycosis attached. **(A1-A3)** Day 2 of admission. **(B1-B3)** Day 4 of admission. **(C1-C3)** Day 9 of admission).

Discussion

Most mucormycosis infections are caused by Rhizopus, Mucor, and Rhizomucor, which are common fungi and typically present in soil, decaying organic matter, compost, and contaminated food. Pulmonary mucormycosis is a rare but highly aggressive fungal infection predominantly affecting immunocompromised individuals, such as those with diabetes mellitus, hematological malignancies, or undergoing immunosuppressive therapy.[1] In particular, mucormycosis are more commonly seen in patients with diabetic ketoacidosis (DKA) and are associated with the following causes: persistent hyperglycemia impairs the chemotaxis and phagocytosis of neutrophils and reduces the body's resistance, acidic environment increases serum free iron concentration and promotes fungal proliferation, as well as ketone bodies act as a source of nutrients for Mucorales, increasing the susceptibility of the host to the fungus.[6] In this case, a 20-year-old male admitted with a diagnosis of acute pancreatitis and DKA presented with rapidly progressing pulmonary

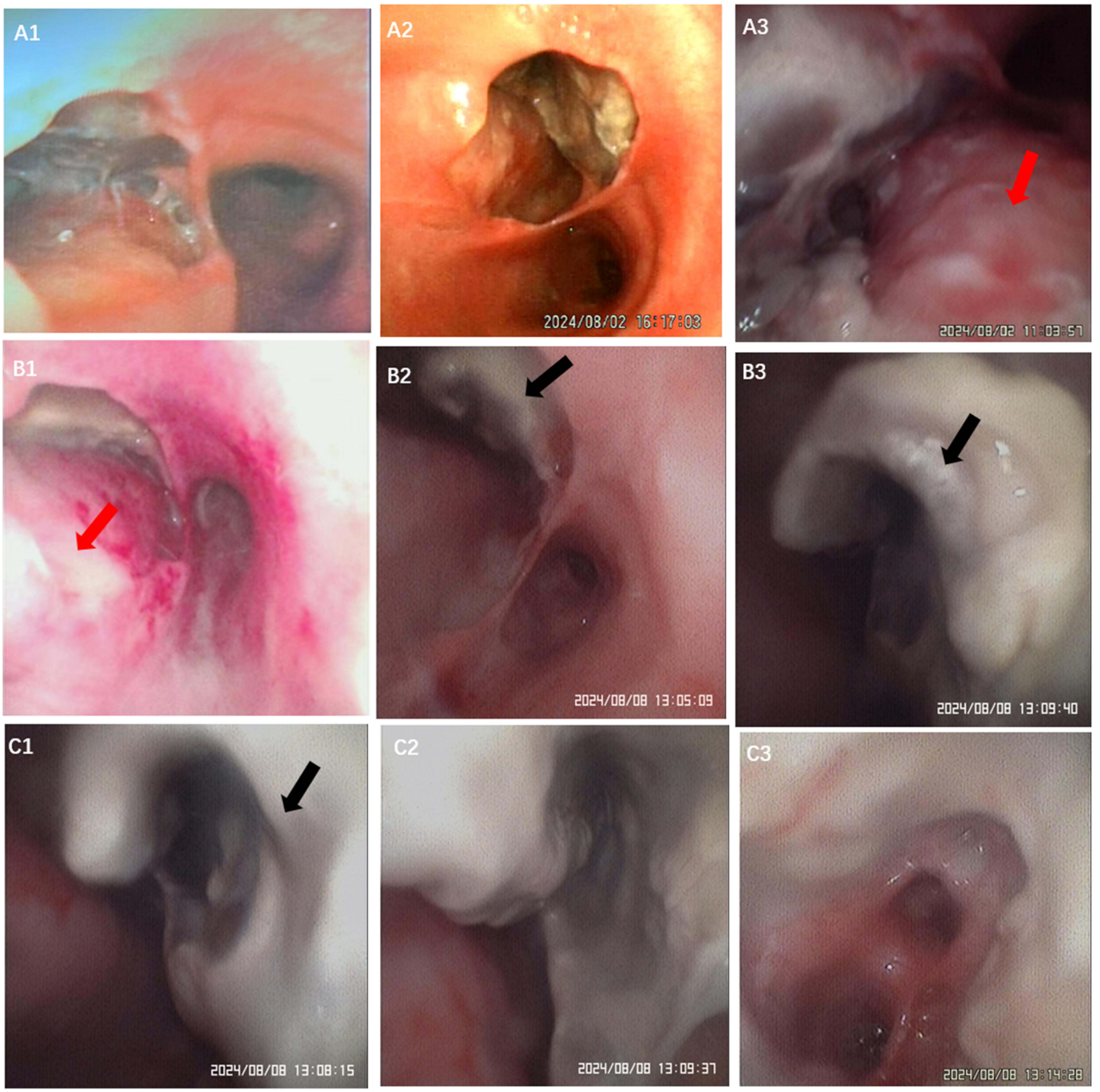

Figure 6 Fibrobronchoscopy showed severe destruction of the distal trachea, rongeur and left main bronchus, with the stump of the left main bronchus exposed (black arrow), a large amount of necrotic material and white hairy moulds attached, and the mediastinum exposed (red arrow). **(A1-A3)** Day 12 of admission. **(B1-C3)** Day 18 of admission.

mucormycosis leading to severe tracheobronchial destruction and ultimately fatal hemorrhage. The rapid progression and severe tissue destruction observed in this case are consistent with the angioinvasive nature of mucormycosis, which leads to vascular invasion, thrombosis, and tissue necrosis.[7]

To our knowledge, this case of fatal bleeding caused by mucormycosis in a very short period of time is rare worldwide.

Pulmonary mucormycosis often presents with nonspecific symptoms such as fever, cough, hemoptysis, and chest pain, which can delay diagnosis and treatment.[2] Imaging studies, such as CT scans, typically reveal lung nodules, consolidation, and pleural effusion, but these findings are not pathognomonic.[5] In this case, the patient's initial early imaging suggested the possible presence of a low-risk pulmonary nodule as well as subsequent imaging visualising left-

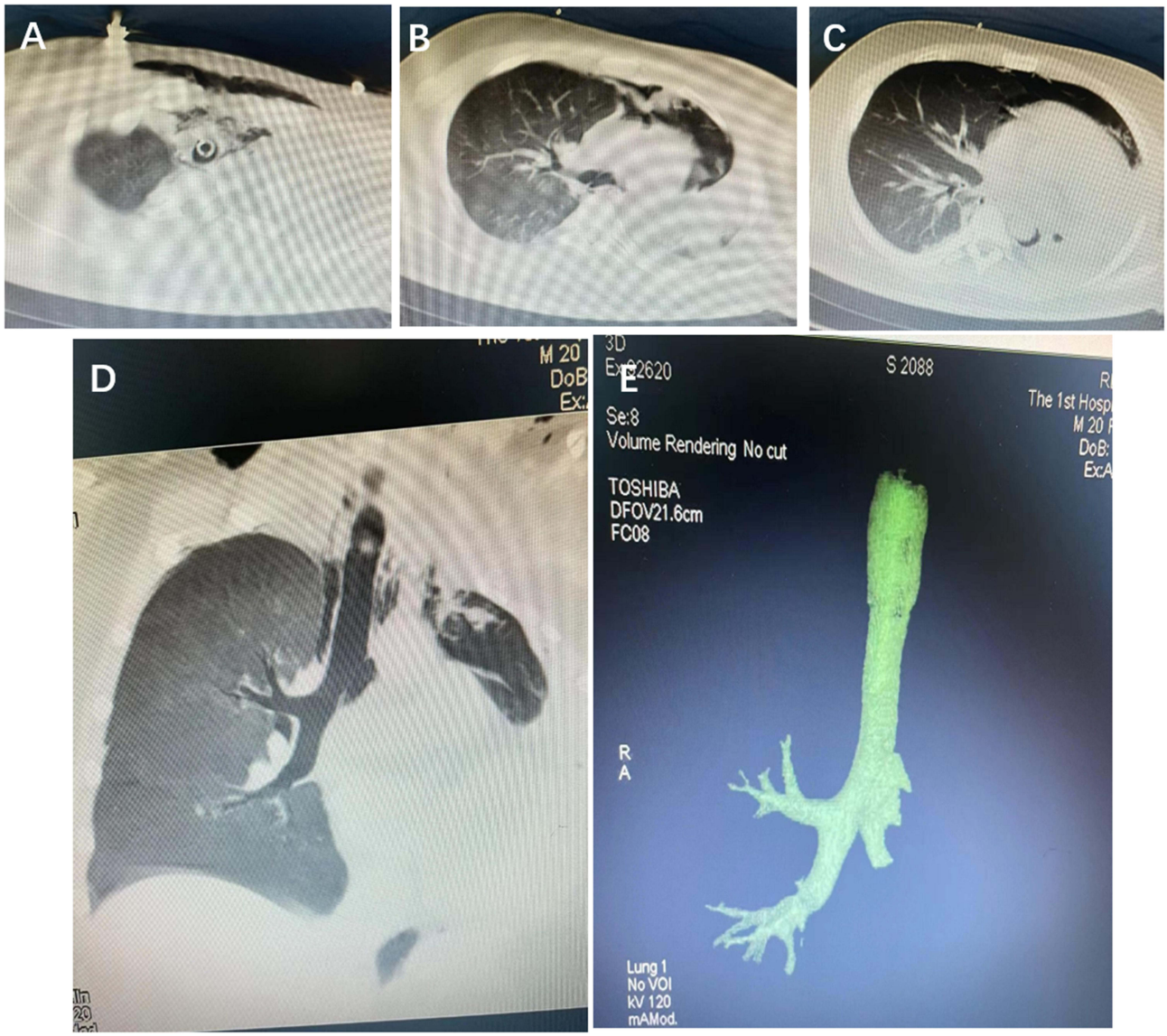

Figure 7 Chest CT on the 15th day of admission showed stenosis and necrosis of the left main bronchus and left lung atelectasis. Mediastinal emphysema formation.
Notes: (**A-D**) The results of Chest CT examination. (**E**) Three dimensional reconstruction results of trachea.

sided bronchial obstruction, but this did not immediately indicate the presence of a serious fungal infection. Prompt antifungal therapy was therefore not initiated.

The diagnosis of pulmonary mucormycosis in this case was confirmed via bronchoalveolar lavage (BAL) and next-generation sequencing (mNGS), which identified Rhizopus species. This diagnostic approach aligns with current recommendations that emphasize the importance of invasive procedures like BAL and tissue biopsy for definitive diagnosis.[3] Once the diagnosis was confirmed, the patient began receiving antifungal treatment with amphotericin B. However, the infection progressed rapidly, leading to extensive tracheobronchial damage and fatal bleeding.

Management of pulmonary mucormycosis requires a multifaceted approach, including prompt antifungal therapy and, when feasible, surgical intervention to remove necrotic tissue.[8] A case of pulmonary mucormycosis in which a necrotic mass almost completely occluded the airway has been successfully rescued by adjunctive rigid bronchoscopy to dilate the airway and remove the necrotic mass, as well as by performing a lesion pneumonectomy, has been reported.[9] Another case of pulmonary mucormycosis was reported to have achieved good therapeutic effects by implanting a covered metallic stent and transbronchoscopic microtube drip of amphotericin B through bronchoscopy outside the metallic stent (gap between the stent and the airway wall).[10] In this case, the patient received a combination of amphotericin B and

isavuconazole intravenously, which are recommended as first- and second-line treatments, respectively,[11] but surgical debridement of the necrotic tissue was not performed. However, it may be due to insufficient drug penetration into the lesion, and the drug concentration in the necrotic tissue is much lower than the blood drug concentration, leading to worsening of the patient's condition, worsening of infection, and expansion of tissue necrosis. Therefore, we need to be aware that when intravenous use of antifungal drugs is ineffective, assisting in the clearance of necrotic substances and topical application of antifungal drugs may be of great help in treating severe pulmonary mucormycosis.

The high mortality rate associated with pulmonary mucormycosis, particularly in cases with delayed diagnosis and extensive tissue involvement, emphasizes the need for heightened clinical suspicion and early aggressive intervention.[12] A delay in the administration of antifungal therapy beyond 6 days is associated with a twofold increase in the 90-day mortality rate related to mucormycosis.[4] Indeed, the difficulty in early diagnosis and initiating treatment may lead to a high mortality rate of this disease.[13] Additionally, surgical intervention combined with antifungal therapy can reduce mortality from mucormycosis compared to medication alone.[14] Reports have indicated that a combined surgical and medical approach is associated with better outcomes in pulmonary mucormycosis patients.[15–17] Particularly, combination surgery is recommended for patients with mucormycosis who do not respond well to medication.[18]

Conclusion

This case of fatal tracheal and bronchial destruction due to pulmonary mucormycosis in a 20-Year-Old with DKA highlights the aggressive nature of the infection and the challenges in timely diagnosis and effective management. Future clinical practice should focus on multidisciplinary treatment, involving critical care, infectious disease specialists, pulmonologist and thoracic surgeons, while early identification and timely antifungal treatment, especially necessary surgical intervention, may be crucial for treating this severe pulmonary mucormycosis.

Ethics Approval

The study has received ethical exemption from the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. The Ethics Committee of the First Affiliated Hospital of Chongqing Medical University has granted permission for the publication of case details.

Consent for Publication

Written informed consent was obtained from the patient's relatives for publication of this article and any accompanying images.

Disclosure

The authors declare no competing interests.

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