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CASE REPORT

A Case of Invasive Pulmonary Mycosis (Rhizopus microspores) secondary to Hematological Disease

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SUMMARY

Background: **Pulmonary mucormycosis is most common in patients with hematologic malignancies and transplant recipients. This article describes a case of mucormycosis in the lungs secondary to a hematologic disorder with suspected lung cancer.**
Methods: **Rhizopus (Rhizopus microspores) was detected by blood NGS and bronchoalveolar lavage fluid NGS, and pulmonary mucormycosis was confirmed.**
Results: **Secondary to hematologic disease, pulmonary pneumonia, mycosis, and symptoms improved after comprehensive treatment.**
Conclusions: **Clinical data and radiologic knowledge are combined to diagnose invasive pulmonary mycoses; early empirical medicine is very important.**
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KEYWORDS

invasive pulmonary mycoses, Rhizopus, Rhizopus microspores, hematological diseases

INTRODUCTION

An uncommon fungal infection called pulmonary mucormycosis typically affects patients with impaired immune systems. Since fungal cultures have a relatively low positive rate, diagnosis is typically made using imaging in addition to pathology [1]. Clinicians are prone to trivialize the disease and misdiagnose it as a general infectious disease or a lung lesion caused by other reasons due to the lack of specificity in the patient's clinical features. Even though the disease progresses quickly, delaying treatment can worsen the condition and prolong symptoms. As a result, the prognosis greatly depends on an early, accurate diagnosis and a consistent course of treatment.

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CASE REPORT

The patient was previously diagnosed with myelodysplastic syndrome combined with type 2 diabetes mellitus. He was admitted to a local hospital for fever and treated with imipenem cilastatin sodium anti-infection therapy. The peak body temperature decreased compared to the previous. A review of the chest CT lung shows shadows increased compared to the previous CT. On December 23, 2023, he was admitted to our hospital for further treatment. After admission the following tests were done: blood routine: leukocytes 0.5 x 10^9/L, neutrophils 0.19 x 10^9/L, hemoglobin 56 g/L, platelets 67 x 10^9/L, reticulocytes 0.001; blood biochemistry: albumin 35.7 g/L, glucose 17.99 mmol/L, coagulation series: D-dimer 1,618 ng/mL, plasma fibrinogen 8.26 g/L, plasma prothrombin time 15.6 seconds; blood sedimentation: 158 mm/hour; interleukin 6: 88.248 pg/mL; C-reactive protein > 200 mg; chest + abdominal CT (Figure 1): 1. right lung hilar enlargement considered to be inflammatory lesions. 2. right lung nodules and inflammatory fibrosis. Blood NGS was suggestive of Rhizopus (Rhizopus microspores). After admission, imipenem, meropenem, tigecycline antibacterial treatment and amphotericin B antifungal treatment were given successively, but the temperature was not well controlled. The review of chest CT (Figure 2) suggested a neoplastic lesion in the right hilum. Respiratory consultation was requested several times, and it was recommended that bronchoscopy should be performed to clarify the nature of the mass. Bronchoscopy was performed under general anesthesia on January 2, 2024 with the following results: alveolar lavage fluid NGS: fungi Rhizopus Rhizopus microspores with sequence number 18382; Candida spp. Candida tropicalis with sequence number 699. He continued to be receive amphotericin B combined with Posaconazole enteric-coated tablets 300 mg 1/day orally and aerosolized amphotericin B antifungal therapy. During the course of the disease, the patient's severe anemia and platelets were markedly reduced, with a total of 10 U of red blood cells and 11 therapeutic doses of platelets infused. The review of the results suggested granulocyte deficiency, and he was given recombinant human granulocyte stimulating factor 300 µg subcutaneous injection 1/day to increase granulocytes. The patient's current diagnosis is clear, after the above combined treatment, the general symptoms improved significantly compared with the previous. Because the patient's immunity is poor, he still had intermittent fever and fungal infections for a long time. The guidelines recommend treatment with antifungal therapy for at least 6 - 12 weeks. The patient and his family asked to return to the local hospital to continue antimicrobial therapy.

DISCUSSION

This patient has malignant hematological disease, and a chest CT scan suggested lung inflammation. Blood NGS revealed Rhizopus, which is relatively uncommon. Clinicians assumed fungal pneumonia based on experience, and the patient was treated for inflammation with antifungal and antibacterial medications. The patient's temperature did not drop significantly. A review of the chest enhancing CT revealed that there might be a pulmonary hilar tumor. A bronchoscopy was conducted right away to collect tissue, and pathology revealed that Rhizopus microspores were the source of the fungal lung infection. The patient's peak temperature was lower than before, the symptoms were less severe, and the clinician continued the antifungal medication. The goal of the literature analysis about pulmonary mycoses, using this case as an example, is to make clinicians more aware of this kind of illness and to caution them against delaying diagnosis and treatment.

Ninety percent of all fungal infections are produced by the family Mucoraceae, which is mostly composed of Rhizopus and Mucor. Mucormycosis is a newly discovered and frequently deadly fungal infection. Globally, the incidence of mucormycosis has increased recently due to novel infections and susceptible populations resulting in increased morbidity [2]. With prevalence rates ranging from 38% to 62%, hematologic malignancies are the most prevalent underlying illnesses associated with mucormycosis [3]. Mucormycosis can cause disseminated disease as well as symptoms in the lungs, gastrointestinal tract, skin, nose-mouth-brain, and lungs. Patients with diabetes are more likely to develop nasal-brain types of mucormycosis, while immunocompetent hosts are more likely to develop cutaneous mucormycosis following trauma. The second most prevalent symptom, pulmonary mucormycosis, accounts for 58% of infections and is frequently seen in patients receiving transplants and hematologic malignancies. With a mortality rate of up to 80%, it is recognized for its quickly advancing clinical course [4]. HIV infection, intravenous drug use, low birth weight babies, malnourishment, persistent alcoholism, liver disease, chemotherapy, and calcineurin inhibitor use are additional risk factors linked to trichinosis [5].

The most typical clinical signs of mucormycosis include fever, neutropenia, dyspnea, and cough [6], which are not much different from lung infections brought on by other pathogenic bacteria. Typically, mucormycosis does not have any particular clinical signs. The hallmark of mucormycosis is the fungal invasion of arteries, which obstructs and stops the blood flow, resulting in tissue necrosis. The hallmark of mucormycosis is tissue necrosis. There may also be inflammatory changes that are neutrophilic, granulomatous, or nonspecific; vascular invasion or infarction is a unique pathologic alteration in mucormycosis. Necrotizing pneumonia, pulmonary artery aneurysms, fatal hemoptysis, and catastrophic aortic dissection can result from

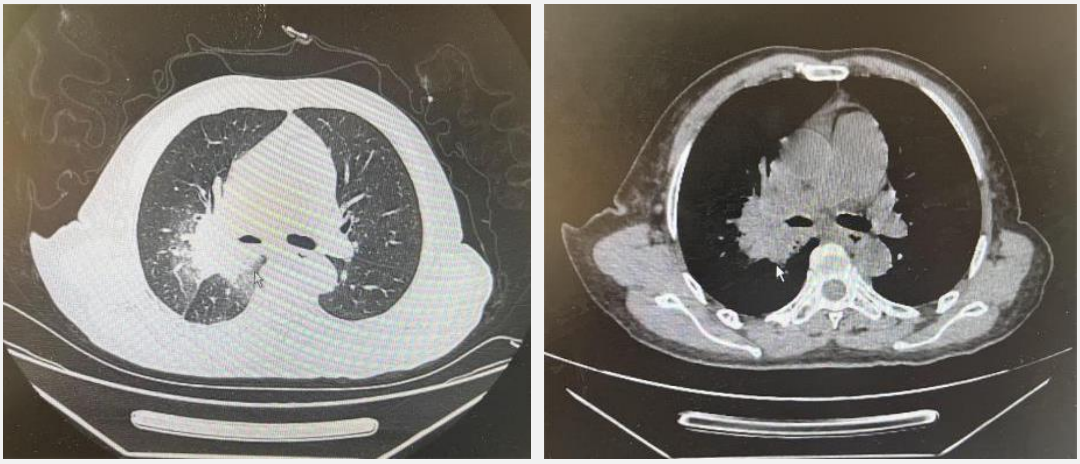

Figure 1. Enlarged right hilar, multiple hyperdense shadows in the right lung with blurred borders and some bronchial stenosis. Inflammatory lesions were considered.

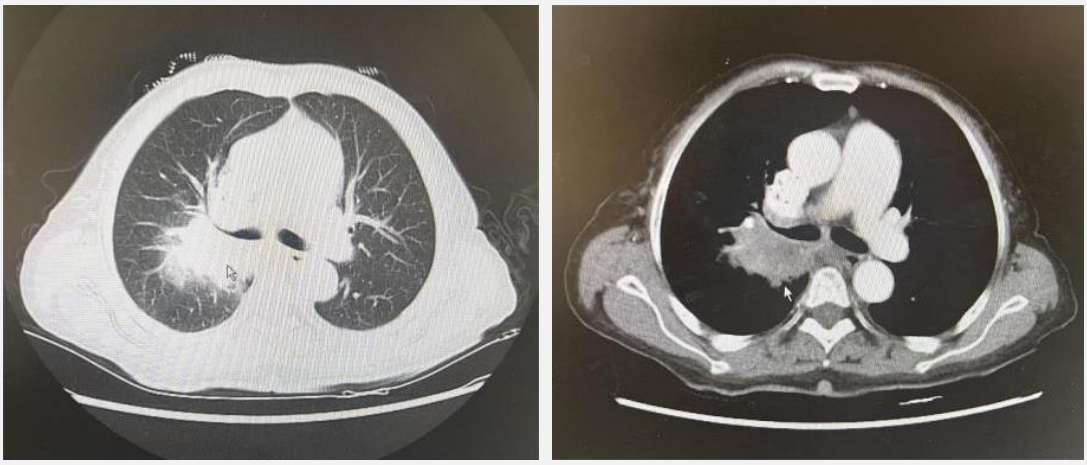

Figure 2. Enlarged right hilar with a lesion that has not improved from the previous one, and a tumor-like hilar lesion is considered.

invasion of the pulmonary vasculature [7]. Prior investigations found that most patients had imaging abnormalities, but these results were not unique to fungal infections. Before a more comprehensive imaging picture appears, the initial CT scan in cases of early lung fungal infections may only reveal perivascular gross glassy lesions. Lesions that resemble hairy glass typically develop into masses, nodules, or solid lesions. Gross glass halo lesions can be seen around nodules and masses, and a gross glassy lesion with a solid edge is known as the reverse halo sign. The reverse halo sign has been reported with a wide range of frequency, occurring in 19% - 94% of patients with trichiasis [8], despite the fact that most fungal pneumonias show nonspecific signs on imaging. This phenomenon may be related to the severity of the underlying disease and the presence

of neutropenia at the time of diagnosis. Reverse halo signs are more common in patients with neutropenia (79% vs. 31%) than in non-neutropenic patients [9]; therefore, the clinician may be prompted to diagnose based on this presentation.

For clinicians, diagnosing invasive fungal respiratory infections is still a challenging task. To save patients' lives, early diagnosis and treatment are essential. A polysaccharide called galactomannan is generated by Aspergillus and a few other fungi. By using culture, it can be found in serum and bronchoalveolar lavage fluid [10]. Culture results are often inaccurate and may be less positive in patients with non-hematologic disorders or in patients already receiving antifungal therapy. However, galactomannan in bronchoalveolar lavage fluid has better sensitivity than serum. So, bronchoscopy is an important complementary test for pulmonary mycosis [11]. In addition to imaging and pathological tissues to assist in the diagnosis of pulmonary mycosis, molecular diagnostic technology is becoming a key tool for diagnosis. Amplification of fungal DNA by PCR, followed by DNA sequencing of tissues, is another way to identify invasive pathogens [15]. A different approach to identifying invasive pathogens observed on histopathology is the amplification of fungal DNA by PCR followed by DNA sequencing of the tissue. Molecular diagnostic techniques are increasingly being used in the diagnosis of invasive fungal respiratory infections [12].

Antifungal therapy is still limited, with only three classes of antifungal drugs used for invasive infections: polyenes (amphotericin), azoles (voriconazole), and echinocandins (carbofungin). Treatments based on amphotericin B account for the majority of the therapeutic experience. The secret to curing mucormycosis is adjuvant therapy. Iron chelation, or more precisely, deironing, is one effective adjuvant treatment that has the potential to stop mucor's growth by lowering the nutrient iron availability, which is necessary for mucor's growth [13]. Moreover, research is being done on immunomodulatory treatments such granulocyte infusions and cytokine therapy to strengthen the host immune response against Trichoderma infection [14]. Even though these adjuvant therapies seem promising, more investigation and clinical testing are required to establish the best application and efficacy of these treatments.

CONCLUSION

Physicians still struggle to treat pulmonary fungal disease, which is typically treated empirically. However, in order to address the growing threat of antifungal resistance in society, we must tailor the risk assessment process to each patient, ensuring early diagnosis, early medication, early downgrading, and early discontinuation of the drug.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in the studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

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