

中文題目：一個糖尿病控制不佳病人其肺部出現快速開洞病灶：一位肺白黴菌病例報告與文獻綜述

英文題目：Rapidly progressive pulmonary cavitory lesions in a poorly controlled diabetic patient: a case report of pulmonary mucormycosis and literature review

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### **Introduction:**

Mucormycosis is a rare, opportunistic but aggressive fungal disease. Among all possible infection sites, rhino-orbital-cerebral lesion is the most common, followed by pulmonary lesions. Initial radiographic findings largely include air crescent sign and halo sign; lung cavitation, on the other hand, is less observed. Cavitation, however, predominantly points to several differential diagnoses such as bacterial infection, tuberculosis, aspergillosis or malignancies. Mucormycosis challenges physicians with great difficulty in early diagnosis. Herein, we report a case of a 73-year-old woman with poorly controlled type II diabetes mellitus, who had several significant cavitations and was eventually diagnosed with pulmonary mucormycosis.

### **Case Presentation:**

This was a 73-year-old woman with underlying type II diabetes mellitus, chronic kidney disease, hypertension, dyslipidemia and transient ischemic attack under medication control. She presented with fever, productive cough and dyspnea for one week. Her diabetes was poorly controlled and the corresponding HbA1c upon admission reached 10.2%.

Initial survey revealed leukocytosis and chest X-ray reported ill-defined lesion over the right upper lung. We prescribed ampicillin-sulbactam and levofloxacin empirically for community acquired pneumonia. The follow-up chest X-ray revealed bilateral alveolar opacities with formation of cavities. The chest computerized tomography (CT) reported multiple solid cavitory lesions over bilateral lungs. We arranged CT-guided biopsy for the cavitory lesion over the left upper lung. Empirical anti-tuberculosis treatments were initiated immediately after the biopsy. The pathology of lung biopsy reported mucormycosis. Liposomal amphotericin B was prescribed for pulmonary mucormycosis. The follow-up chest CT two weeks later showed partial response. She was discharged with oral posaconazole as the continuing treatment of pulmonary mucormycosis. She received anti-fungal treatment for a total of six weeks. The chest x-ray showed nearly total resolution three months after the end of treatment.

### **Discussion:**

Mucorales are ubiquitous, they can be found on decaying vegetables, feces, in the soil, etc. We may inevitably breathe in the air containing abundant Mucorales spores. However, under most circumstances, our robust immune system is capable of defending the Mucorales, preventing them from thriving. On the contrary, in patients with a flawed immune system, the spores may overgrow. Mucorales may consequently devastate tissues and vessels, causing a wide variety of clinical symptoms, such as hemoptysis and impaired eyesight. Listed from high to low incidence, the infection of mucorales, or mucormycosis, may present in the rhino-orbital-cerebral, pulmonary, cutaneous or subcutaneous, gastrointestinal or disseminated form.

Pulmonary mucormycosis is a rapidly progressive infection that occurs after inhalation of spores in to the bronchioles and alveoli. The majority of patients have fever, accompanied with mild to severe hemoptysis. It may be challenging to differentiate its clinical presentations from other common bacterial pulmonary infections. Differential diagnosis is further clouded due to its often negative finding in sputum cultures. Physicians are advised to be aware of mucormycosis infection in high-risk patients with new signs and symptoms of pulmonary infection after having received empiric antibiotics but in vain. Diagnosis relies on histopathologic identification of an organism with a structure typical of Mucorales, for which transbronchial biopsy is used most frequently. Surgical extirpation or open lung biopsy may be performed alternatively if transbronchial biopsy is unavailable. Histology may facilitate the distinguishing of mucormycosis from aspergillosis, as both of which share similar clinical symptoms and presentations. More novel detection of circulating Mucorales DNA in blood and next-generation sequencing of microbial cell-free DNA both appear to be a fair and fast diagnostic test that may precede diagnosis by culture or histopathology.

Alongside deadly symptoms, mucormycosis is resistant to many antifungal agents, giving rise to high mortality rates. Individuals having diabetic ketoacidosis, having experienced major trauma, or those taking deferoxamine for iron overload, or immunocompromised patients with hematological malignancy (e.g., leukemia, lymphoma) are among high-risk patients to infect mucormycosis.

Choice of first-line therapy for mucormycosis should be based on localization, renal function, etc. Liposomal amphotericin B remains the most optimal drug of choice for those with normal renal function; alternatively, for those with renal impairment, posaconazole or isavuconazole is recommended. Oral forms of the aforementioned triazoles can also be used as step-down therapy. It should be noted that metabolism of some medications (e.g., cyclosporine, tacrolimus) may be interfered with by triazoles; thus, therapeutic drug monitoring may be indicated.

Other than antifungal treatment of mucormycosis, comprehensive management should also include, if possible, surgical debridement of the lesion and reduction of immunosuppressants, iron-chelating agents, correction of ketoacidosis, and control of hyperglycemia, etc.

**Conclusion:**

Mucormycosis is a rare but aggressive infectious disease which poses a challenge for physicians to diagnose. Physicians should consider Mucormycosis in differential diagnosis if their patients have lung cavitary lesions, especially with underlying disease of type II diabetes or hematologic malignancy.

**References:**

1. Binder U, et al. Mucormycosis--from the pathogens to the disease. *Clin Microbiol Infect.* 2014 Jun;20 Suppl 6:60-6.
2. Marty FM, et al. *Lancet Infect Dis.* 2016;16(7):828 – 37
3. Kauffman CA, et al. Zygomycosis: an emerging fungal infection with new options for management. *Curr Infect Dis Rep.* 2007 Nov;9(6):435-40.
4. Afroze SN, et al. Mucormycosis in a Diabetic Patient: A Case Report with an Insight into Its Pathophysiology. *Contemp Clin Dent.* 2017 Oct-Dec;8(4):662-666.
5. Roden MM, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis.* 2005 Sep 1;41(5):634-53.
6. Skiada A, et al. Challenges in the diagnosis and treatment of mucormycosis. *Med Mycol.* 2018 Apr 1;56(suppl\_1):93-101.
7. Spellberg B, et al. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev.* 2005 Jul;18(3):556-69.
8. Mercier T, et al. A Mortality Prediction Rule for Hematology Patients with Invasive Aspergillosis Based on Serum Galactomannan Kinetics. *J Clin Med.* 2020 Feb 24;9(2):610.