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Pulmonary Mucormycosis Mimicking a Lung Tumor in a Patient with Advanced Retroviral Disease

İleri Retroviral Hastasında Akciğer Tümörünü Taklit Eden Pulmoner Mukormikozis

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Abstract

Pulmonary mucormycosis is a relatively rare disease that may become more common with the increasing number of immunocompromised patients. The male case presented here, with advanced retroviral disease, presented with persistent cough and acute respiratory distress. A chest radiograph and computed tomography (CT) of the thorax revealed a right apical pneumothorax and a mass in the right main bronchus. Flexible bronchoscopy revealed an endobronchial mass, occluded entirely the right main bronchus. Histopathological examinations of multiple biopsies revealed fungal bodies suggestive of mucormycosis. The patient was treated with Posaconazole, leading to a complete clinical and radiological cure.

Keywords: *Pulmonary mucormycosis, lung mass, retroviral disease, bronchoscop.*

Öz

Pulmoner mukormikozis nadir bir hastalık olmakla birlikte immunsuprese hasta sayısının artması ile birlikte görülme sıklığı beklenilenden fazla olabilmektedir. Bu olgu sunumunda, öksürük ve nefes darlığı şikayetleri ile acil servise başvuran akut solunum yetmezliği nedeniyle entübe edilen ilerlemiş retroviral hastalığı olan bir erkek olgu sunuldu. Toraks bilgisayarlı tomografisinde sağ ana bronşta total oklüzyona yol açan endobronşial lezyon ile birlikte sağ apikal pnömotoraks mevcuttu. Fleksibl bronkoskopide tomografi ile uyumlu olarak sağ ana bronşu tamamen tıkayan endobronşiyal lezyon izlendi. Bronkoskopik biyopsi histopatolojik incelemesinde mukormikozis ile uyumlu mantar cisimcikleri görüldü. Posakonazol ile tedavi edilen hastada klinik ve radyolojik olarak tam iyileşme görüldü.

Anahtar Kelimeler: *Pulmoner mukormikozis, akciğerde kitle, retroviral hastalık, bronkoskopi.*

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Mucormycosis is a rare but potentially life-threatening fungal infection that most frequently affects immunocompromised patients. Infection can progress rapidly, leading to substantial morbidity and mortality owing to the angioinvasive properties of the condition. Rhino-orbital-cerebral sites are the most common targets of mucormycosis-related infections, followed by the pulmonary system. The clinical symptoms, physical signs and radiological findings of pulmonary mucormycosis are often non-specific, and can closely mimic other respiratory conditions, including endobronchial malignancies to pulmonary infections and/or airway diseases. As a result, distinguishing pulmonary mucormycosis from other competing differentials can be challenging, and often requires a high index of clinical suspicion. We present here the case of a middle-aged male with advanced retroviral disease who was referred for a tumor-like endobronchial lesion in the right lung.

CASE

A 56-year-old male with a history of chronic obstructive pulmonary disease and advanced retroviral disease (CD4+ T-cell count of 53 cells/mm^3 and viral load of 11,615 copies/mL) presented with a 1-week history of worsening shortness of breath and productive cough. The patient, who reported no fever, night sweats, chest pain and hemoptysis, was in acute respiratory distress upon presentation to the emergency service, requiring urgent intubation and mechanical ventilation. A physical examination revealed generalized rhonchi in both lung fields, along with reduced air entry on auscultation of the entire right lung. Blood investigations produced the following results: total white cell count of 5200/uL, hemoglobin 10.6 g/dL, platelet 326x109/L, and C-reactive protein at 11.6 mg/L.

The patient's history included a diagnosis of retroviral disease in 2008 for which he was treated with antiretroviral medications (tenofovir-emtricitabine and efavirenz), however, the patient's compliance with the medications was poor and he was lost to follow-up in 2018. The patient had also undergone a 6-month course of antituberculous medications for smear-positive pulmonary tuberculosis in 2013. He is an active chronic smoker of 35 pack/years and has a history of intravenous drug abuse.

An urgent chest radiograph in the emergency department revealed a right apical pneumothorax that prompted a decision to proceed with a chest drain insertion and broad-spectrum intravenous antibiotics, and regular nebulization together with intravenous corticosteroids. The patient responded to the above treatments and was successfully extubated after 5 days of hospitalization. A repeat chest radiograph on day 6 of admission, however, revealed a persistent non-expandable right lung, raising clinical suspicion of either a trapped right lung due to a pleural pathology or an obstructing endoluminal airway lesion. His chest drain was fluctuating with respiration but was not actively bubbling, ruling out the possibility of an active pneumothorax with persistent air leak (Figure 1). The patient remained oxygen dependent with oxygen saturations of only 85–90% on nasal prong oxygen running at 3 L/min. A computed tomography (CT) of the thorax revealed an occluding endoluminal lesion in the right main bronchus (Figure 2).

Flexible bronchoscopy revealed a whitish endobronchial mass causing total occlusion of the right main bronchus, and the origin of the mass was identified as approximately 1cm distal from the main carina (Figure 3). Multiple biopsies were performed using flexible forceps, which resulted in a patent right main bronchus and, therefore, a fully expanded right lung post-procedure. A histopathological examination revealed fungal bodies with predominantly non-septate hyphae and yeasts (Figures 4A and B). Ziehl-Neelsen stain for acid-fast bacilli was negative. The overall findings were suggestive of pulmonary mucormycosis. Since the patient was deemed unfit to undergo surgery due to poor physical fitness secondary to advanced retroviral disease, he started systemic antifungal treatment with oral Posaconazole for 2 weeks. The patient was weaned off oxygen and was discharged well.

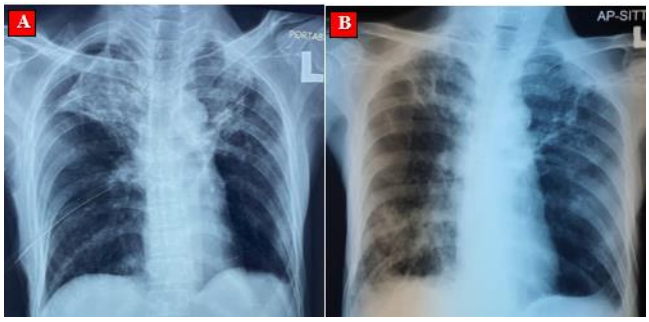

Figure 1: Persistent pneumothorax and right upper lobe consolidation after antibiotic treatment, despite chest tube insertion (A). Chest X-ray after antifungal treatment revealing resolved right upper lobe consolidation (B)

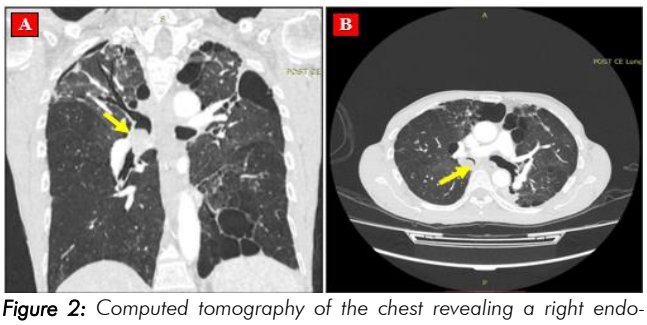

Figure 2: Computed tomography of the chest revealing a right endobronchial mass (1.3 × 1.9 cm)

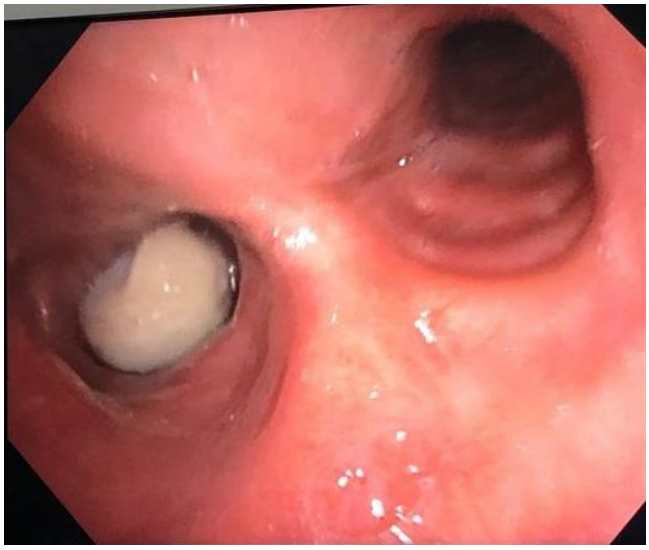

Figure 3: Fiberoptic bronchoscopy revealing an endobronchial mass in the right main bronchus

DISCUSSION

Mucormycosis is a rare and often opportunistic infection caused by fungi of the Zygomycetes class, which can be further subdivided into 3 subtypes: namely, *Mucor*, *Rhizopus* and *Lichtheimia*. Mucormycosis is prevalent among patients diagnosed with diabetes, hematological malignancies and other immunocompromised conditions. Patients may present with various clinical forms, the most common of which are rhino-cerebral and pulmonary mucormycosis, which are usually acute and fulminant, and are associated with mortality rates as high as 76% (1–3). Patients with HIV are much less likely to develop pulmonary mucormycosis than neutropenic cancer patients undergoing induction chemotherapy or recipients of hematopoietic stem cell transplants (HCST) (4), as neutrophils, as opposed to T lymphocytes, play a significant role in defense against Mucorales. In a study by Antinori et al. (5), only two patients were diagnosed with mucormycosis in a comprehensive retrospective investigation of the autopsy reports of 1,630 patients who died of AIDS from 1984 to 2002. Mucormycosis in HIV patients is usually associated with intravenous drug use and is more common in young men with lower CD4+ cell counts (6), as in our case, although iron overload and deferoxamine therapy also play a major role in the pathogenesis of mucormycosis (6,7). Rare cases of mucormycosis have also been reported among immunocompetent patients. Ng et al. (8) reported on an immunocompetent pregnant female with pulmonary mucormycosis that initially masqueraded as an endobronchial tumor who responded well to a 2-week course of intravenous amphotericin-B. The non-specific radiological and clinical attributes of pulmonary mucormycosis may make it difficult to distinguish it from other lung diseases, such as angio-invasive aspergillosis and lung cancer (2). Dyspnea, fever, chest pain and cough are some of the more common symptoms noted among those suffering from pulmonary mucormycosis (3). Pulmonary mucormycosis may rarely present as an endobronchial lesion, as in the present case (8–10). Endobronchial mucormycosis can cause airway obstruction, leading to pulmonary collapse, and has the potential to invade the hilar blood vessels, resulting in extensive hemoptysis (2). Aside from isolated masses, X-rays frequently reveal wedge-shaped consolidations, nodules, pleural effusion, halo signs and cavitation, with the upper lobe of the lungs being the most commonly affected area (11). High-resolution chest computed tomography (CT) is considered the most effective approach to the assessment of the extent of pulmonary mucormycosis, and can often detect infection before it becomes apparent on chest X-rays (4). The case presented here is a chronic smoker who suffers from COPD, which puts him at high risk of developing lung cancer and is vulnerable to opportunistic conditions such as fungal infection due to his immunodeficiency.

The diagnosis of the presented case was confirmed from histopathological findings obtained from a biopsy of the mass in the right bronchus. The culture method is important but with low sensitivity (3). Recent multi-center trials have revealed consistently low bronchoalveolar lavage (BAL) culture yields, with a sensitivity in the range of 20–50% (12). For this reason, biopsy and histological examination can be considered the optimum approach to the detection of pulmonary mucormycosis (4). A histopathological examination of biopsy material revealing non-septate hyphae is suggestive of such Zygomycete species as *mucor*, *rhizomucor* and *cunninghamela*, and degenerating *Aspergillus* is another probable mimic. In our case, a fungal PCR was ordered, although the biopsy was contaminated with a formalin solution. Our patient's predisposing condition (HIV infection), acute clinical presentation, radiographic appearance (endobronchial lesion) and histological findings of non-septated hyphae, as well as his rapid remission with posaconazole, all pointed to mucormycosis.

Factors supporting the successful treatment of pulmonary mucormycosis include the prompt administration of antifungal therapy, timely diagnosis, the early and broad surgical debridement of infected areas, and the adoption of a multidisciplinary approach. In the presented case, surgery was inappropriate due to the patient's premorbid condition, and so only medicinal therapy was prescribed. A study investigating the survival rate of pulmonary mucormycosis revealed a huge variance between the rate of 31.2% among patients undergoing only medicinal therapy and 69.1% among patients treated with both surgical and medicinal therapies (13). It is worthy of note that only a handful of reports to date have reported successful antifungal treatment in isolation (14,15).

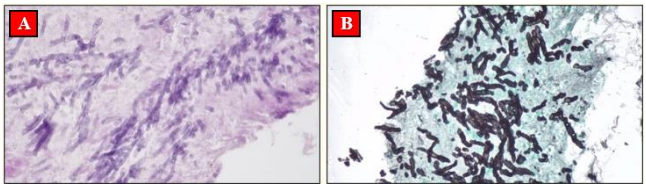

Figure 4: Non-septated hyphae (x600 PAS) (A). Non-septated hyphae (x600 GMS) (B)

Reversing the underlying risk factors that can lead to mucormycosis is also critical, aside from the administration of antifungal therapy. Interventional pulmonological procedures such as snaring, cryodebulking and laser ablations of the mass were unavailable at our center. Fortunately, the quick turnaround time of the histopathological analysis facilitated early and accurate diagnosis and treatment, preventing such devastating complications as hemoptysis and airway obstruction. Our patient responded well to the antifungal treatment, which supported an improvement in symptoms and the resolution of the pneumothorax, although no further chest CT or flexible bronchoscopy were made as the patient did not turn up for his follow-up appointments.

In conclusion, in rare cases, pulmonary mucormycosis may present as a right bronchus lesion on bronchoscopy showing a pedunculated mass mimicking a bronchial malignancy. Biopsy and histopathological examination are key to the confirmation of the diagnosis. The case presented here emphasizes the need to keep pulmonary mucormycosis firmly in mind when assessing immunocompromised patients, as early recognition and antifungal treatments are important for the avoidance of complications and mortality.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.C.C., K.L.N., N.C.H., W.F.G., D.A., K.M.N.; Planning and Design - S.C.C., K.L.N., N.C.H., W.F.G., D.A., K.M.N.; Supervision - S.C.C., K.L.N., N.C.H., W.F.G., D.A., K.M.N.; Funding - K.M.N.; Materials - D.A.; Data Collection and/or Processing - S.C.C., K.L.N.; Analysis and/or Interpretation - S.C.C., K.L.N.; Literature Review - W.F.G., N.C.H.; Writing - S.C.C., K.L.N., N.C.H.; Critical Review - S.C.C., K.L.N., N.C.H.

REFERENCES

1. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi (Basel) 2019; 5:26. [CrossRef]
2. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis 2012; 54(Suppl 1):s23-34. [CrossRef]
3. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: An update. J Fungi (Basel) 2020; 6:265. [CrossRef]
4. Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev 2005; 18:556-69. [CrossRef]
5. Antinori S, Nebuloni M, Magni C, Fasan M, Adorni F, Viola A, et al. Trends in the postmortem diagnosis of opportunistic invasive fungal infections in patients with AIDS: A retrospective study of 1,630 autopsies performed between 1984 and 2002. Am J Clin Pathol 2009; 132:221-7. [CrossRef]
6. Moreira J, Varon A, Galhardo MC, Santos F, Lyra M, Castro R, et al. The burden of mucormycosis in HIV-infected patients: A systematic review. J Infect 2016; 73:181-8. [CrossRef]
7. Alqarihi A, Kontoyiannis DP, Ibrahim AS. Mucormycosis in 2023: an update on pathogenesis and management. Front Cell Infect Microbiol 2023; 13:1254919. [CrossRef]
8. Ng KL, Huan NC, Nasaruddin MZ, Muhammad NA, Daut UN, Abdul Rahaman JA. Pulmonary mucormycosis masquerading as endobronchial tumour in an immunocompetent pregnant young lady. Respirol Case Rep 2020; 9:e00704 [CrossRef]
9. Yang J, Zhang J, Feng Y, Peng F, Fu F. A case of pulmonary mucormycosis presented as Pancoast syndrome and bone destruction in an immunocompetent adult mimicking lung carcinoma. J Mycol Med 2019; 29:80-3. [CrossRef]
10. Banimostafavi ES, Fakhar M, Zakariaei Z, Sharifpour A, Soleymani M. Pulmonary mucormycosis mimicking lung tumour in an uncontrolled diabetic patient. Vol. 10, Respirol Case Rep 2022; 10:e0917. [CrossRef]
11. Dobrilovic N, Wait MA. Pulmonary mucormycosis. Ann Thorac Surg 2005; 79:354. [CrossRef]
12. Maertens JA, Raad II, Marr KA, Patterson TF, Kontoyiannis DP, Cornely OA, et al. Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): A phase 3, randomised-controlled, non-inferiority trial. Lancet 2016; 387:760-9. [CrossRef]
13. Muthu V, Agarwal R, Dhooria S, Sehgal IS, Prasad KT, Aggarwal AN, et al. Has the mortality from pulmonary mucormycosis changed over time? A systematic review and meta-analysis. Clin Microbiol Infect 2021; 27:538-49. [CrossRef]
14. Liu Q, Good W, Salmon A, Gow N, Griffiths P. A rare case of pulmonary mucormycosis complicated by hydropneumothorax, successfully treated with non-surgical therapies. Respirol Case Rep 2022; 10:e0959. [CrossRef]

15. Qu J, Liu X, Lv X. Pulmonary mucormycosis as the leading clinical type of mucormycosis in Western China. Front Cell Infect Microbiol 2021; 11: 770551. [CrossRef]