Pediatric pulmonary mucormycosis in a diabetic patient treated with extended pleurectomy and Clagett procedure

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Abstract

Mucor is a ubiquitous fungus that is non-pathogenic in healthy people. In immunocompromised hosts, non-functional or absent neutrophils and macrophages result in fungal invasion and infection [1]. Invasive mucor (mucormycosis) most commonly involves the sinuses, brain, or lungs. Pulmonary mucormycosis typically presents in patients with a history of organ transplantation or hematologic malignancy [2], and is rare in patients with diabetes alone. The epidemiology and management of pediatric pulmonary mucormycosis is poorly described. We report an unusual occurrence of this disease, complicated by segmental pulmonary artery thrombus in a 15-year-old with poorly controlled diabetes. His severe, medication-resistant infection was ultimately treated successfully with antifungal medication combined with aggressive surgical debridement. The pulmonary artery segmental thrombus resolved after treatment of the underlying infection without anticoagulation.

Keywords

Mucormycosis; Pulmonary mucormycosis; Diabetes; Pneumonectomy; Clagett procedure; Pediatric thoracic surgery

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Patient consent
Consent to publish this case report was obtained from the patient and his guardian.

Authorship
All authors attest that they meet the current ICMJE criteria for Authorship.
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Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.epsc.2019.101210.
1. Introduction

Pulmonary mucormycosis is a form of mucormycosis that affects the lungs. Fungal entry into the body occurs by inhalation, and once in the respiratory tract, fungal hyphae may enter lymphatics, arteries, and veins, resulting in disseminated disease and infarct [2]. Typical presentation resembles that of community-acquired pneumonia and includes productive cough, fever, and pleuritic pain [3]. Diagnosis is made by transbronchial biopsy, bronchoalveolar lavage, or thoracic fluid sampling with visualization of fungal hyphae [2,3]. Treatment includes antifungal therapy, aggressive surgical debridement or excision of necrotic tissue and stabilization of underlying comorbidities [6]. Mortality is estimated to be 50–80%, with the severity of comorbidities positively correlating with death rate [1]. Incidence and management of pulmonary mucormycosis in children is poorly described. One review article described 44 definitive cases identified by registry, of which 63% were associated with malignancy or bone marrow transplant, and 48% of all patients were treated with a combination of antifungal medication and surgery [4]. Combination therapy was associated with lower mortality; however, additional details, such as underlying etiology and surgical intervention, were not reported [4].

1.1. Case report

A 15-year-old boy with insulin-dependent type two diabetes (HbA1C 13.3) and obesity presented to the emergency department with one week of worsening dyspnea, orthopnea, and four weeks of a productive cough. Vital signs were normal and decreased right-sided breath sounds were present on physical examination. Laboratory workup was significant for white blood count (WBC) of $12.1 \times 10^3/\mu L$ with 40% eosinophils, blood glucose of 220 mg/dL, elevated erythrocyte sedimentation rate, and normal venous blood gas. Initial blood and sputum cultures with gram stain were negative. Computed tomography (CT) of the chest without contrast showed a large right-sided hydropneumothorax (Fig. 1). Despite initial treatment with a pigtail catheter that improved lung expansion and reduced the hydrothorax, the patient developed respiratory distress requiring placement of a second pigtail and transfer to the intensive care unit. Pleural fluid evaluation showed negative gram stain and acid-fast bacilli, and cytology showed 3499 WBC with 87% eosinophils and lactate dehydrogenase of 249 u/L, consistent with an exudative process. Since the blood and pleural fluid eosinophilia raised suspicion for an atypical infectious etiology, ceftriaxone and doxycycline were started.

One week after admission, a causative organism had still not been identified, necessitating video-assisted thoracoscopic surgery (VATS) to obtain tissue for diagnosis. We performed a VATS wedge resection of the markedly inflamed lung and sampled the fibrotic visceral and parietal pleura. Histologic examination and culture of the pulmonary segment revealed Rhizopus fungal hyphae; therefore, we switched the antibiotics to a two-month course of ambisome. Possible predisposing conditions including HIV, systemic lupus erythematosus, and hematologic malignancy were ruled out by serologic testing. After two weeks with slow clinical improvement and persistent hydropneumothorax, the patient underwent repeated VATS with mechanical and doxycycline pleurodesis, wherein we resected a segment of pulmonary parenchyma because of air leak.
Four weeks later, we evaluated for interval change with CT of the chest. Imaging revealed a loculated pleural effusion with lung entrapment, necessitating a third operation. The patient underwent a thoracotomy, revealing a dense pleural rind with pockets of purulence and required a parietal and visceral pleurectomy with decortication and near-total resection of the right upper, middle, and lower lobes. Care was taken to spare healthy-appearing parenchyma.

Seven weeks after admission, CT of the chest showed a large right-sided loculated hydropneumothorax with empyema (Fig. 2). A second thoracotomy revealed copious purulent fluid and necrotic debris; the lung was obscured with inflammatory rind. We irrigated the thoracic cavity with peroxide and betadine, packed, and made a Clagett window by resecting part of the sixth and seventh ribs and raised subcutaneous flaps around the chest wall defect to keep the chest open and allow continuous irrigation and drainage (see Fig. 3). After two months of daily bedside debridement until there was no visible residual infection, we closed the chest wall with latissimus dorsi advancement flaps Fig. 3.

During his recovery, the patient was also diagnosed with a right lower lobe segmental pulmonary artery thrombus, thought to be secondary to angiolymphatic-invasive mucor. Because the patient suffered no hemodynamic or respiratory compromise, anticoagulation was not given. Deep vein thrombosis and a hypercoagulable condition were ruled out as contributing factors on the basis of imaging and hematologic workup, respectively. Thrombus resolution was documented on repeat imaging.

At a follow-up visit 12 months after diagnosis, the patient was well with no evidence of infection, no respiratory complaints, and normal chest wall excursion.

2. Discussion

This case of a pediatric patient with history of type two diabetes who was successfully treated with antifungal medication and aggressive surgical therapy for pulmonary mucormycosis is unusual because of the patient’s good health and young age at the time of diagnosis, in contrast to the typical at-risk population. No underlying immunodeficiency was identified, so the reason for his sensitivity to this opportunistic infection is unclear. Pulmonary mucormycosis has been described in patients in diabetic ketoacidosis [4], and it is speculated that a combination of hyperglycemia and ketoacidosis suppresses innate immune function and promotes fungal spread [4]. However, there is no analogous mechanism in type two diabetes [5,6].

A unique characteristic of pulmonary mucormycosis is its propensity to invade surrounding structures, resulting in infarct, mediastinitis, or hematogenous spread [6]. Involved pulmonary parenchyma becomes necrotic, with cavitating lesions filled with fungal hyphae. The underlying immunologic disorder normally associated with mucormycosis makes early surgical intervention key to survival, because patients cannot mount an immune response to prevent spread of disease. Therefore, all involved tissue must be excised to prevent progression [1]. Similarly, in our patient, aggressive surgical debridement and excision was key to his survival. As the infection seemed to diffusely involve the pleura and spare
some regions of lung parenchyma, the focus of resection was to clear the pleura and infected, necrotic areas of lung and avoid pneumonectomy in this young patient. Because of persistent, severe empyema after three debridements, the patient ultimately required a Clagett procedure.

The angioinvasive and lymphatoinvasive nature of mucor was also demonstrated by the development in our patient of a segmental pulmonary artery thrombus, which, unlike hematogenous spread or infarct, has not been described. Continued antifungal therapy successfully treated the condition, as the patient had no respiratory or hemodynamic compromise.

Even in the young, healthy patient described, extensive surgical management including extended pleurectomy and Clagett procedure was required to achieve cure. Eight months after completion of treatment he has no residual respiratory symptoms.

3. Conclusion

This case illustrates the difficulty associated with diagnosis of mucormycosis, which often requires tissue sampling with visualization of fungal hyphae. Expeditious diagnosis improves prognosis and may limit the degree to which aggressive debridement is needed. The diagnosis may be considered in patients who do not have the classic predisposing conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.
CT of the chest on day of admission, showing a right-sided hydropneumothorax.
Fig. 2. 
CT of the chest 7 weeks after admission demonstrating persistent right-sided loculated hydropneumothorax.
Fig. 3.
Healing Clagett window at two days (A) and two months (B) after surgery with no evidence of infection.