Bronchoscopic instillation of liposomal amphotericin B in management of nonresponding endobronchial mucormycosis

Sir,

Mucormycosis is an invasive fungal infection usually seen in the setting of underlying immunosuppression, hematologic malignancies, or poorly controlled diabetes. It can present either as localized or as disseminated disease. Rarely, the disease occurs in immunocompetent individuals. Thoracic involvement usually presents as a non-resolving consolidation. Endobronchial mucormycosis is rare, under-recognized, and presentation can often mimic an endobronchial tumor.[1]

A 40-year-old gentleman, never smoker with no previous comorbid illness presented with a history of fever, cough, and streaky hemoptysis of 20 days duration. Chest radiograph showed a left lower zone opacity [Figure 1a]. Hemogram (Hb-14.2 mg/dl, total leukocyte count - 5500/mm³, platelet count - 174,000/mm³), blood glucose - (76 mg/dl) and glycated hemoglobin (HbA1C) levels - (4.5%), renal (blood urea - 21 mg/dl and serum creatinine - 0.7 mg/dl) and liver function tests (total bilirubin - 0.7 mg/dl, serum glutamic-oxaloacetic transaminase - 21 IU/L, serum glutamate pyruvate transaminase - 25 IU/L, alkaline phosphatase - 90 U/L) were normal. Sputum smear examination for acid-fast Bacilli (three occasions), bacterial cultures, fungal culture, and cytological examination were negative. HIV serology was negative. The patient was not receiving corticosteroids, and an effort was made to exclude idiopathic CD4 lymphopenia. Following a lack of clinico-radiological improvement with broad spectrum antibiotics, the patient underwent a computed tomography (CT) scan of the thorax which demonstrated a dense left lower lobe consolidation [Figure 1b]. Flexible bronchoscopy revealed a smooth glistening, polypoidal endobronchial growth occluding the anterior and lateral basal segmental bronchi of the left lower lobe [Figure 1c]. Histopathological examination of the endobronchial biopsy showed numerous broad, right-angle branching, aseptate hyphae consistent with invasive endobronchial mucormycosis. CT examination of the head and paranasal sinuses was normal.

The patient received intravenous liposomal amphotericin B (L-AMB) (6 g cumulative dose) over 1 month. There was no radiological improvement and cough persisted. Follow-up bronchoscopy showed no reduction in the size of the endobronchial growth and bronchial biopsy again demonstrated mucormycosis. The patient refused any surgical intervention. In view of nonresponding course with systemic amphotericin, bronchoscopic instillation of L-AMB was discussed and performed. The patient underwent weekly sessions of endobronchial L-AMB (25 mg diluted in 20 cc of saline and administered under visualization over the left lower lobe endobronchial growth) instillation. After the 3rd week, there was a significant reduction of endobronchial growth and the following five sessions, no endobronchial growth was visible [Figure 2a]. The patient received oral posaconazole (400 mg twice daily) for the next 8 weeks.

Follow-up bronchoscopy examination showed no...
recurrence, the patient remained asymptomatic, and CT thorax 3 months later showed resolution of left lower lobe consolidation [Figure 2b].

Mucormycosis is a life-threatening invasive fungal infection primarily affecting immunosuppressed hosts, especially postsolid organ transplant and patients with poorly controlled diabetes. It has the propensity to cause vascular invasion resulting in thrombosis and tissue infarction. Delay in diagnosis is associated with high morbidity and mortality. Even though, the predominant mode of infection is through inhalational route, mucormycosis presenting as endobronchial mass is uncommon.[3]

Treatment of mucormycosis includes a combination of surgical debridement and antifungal treatment.[6] L-AMB is the antifungal of choice for initial therapy. Oral posaconazole is utilized as step-down treatment following response to AMB. Control of the predisposing factors is essential.[1] Treatment of endobronchial mucormycosis is based on similar principles as stated above. Other described treatment options for the endobronchial disease in nonresponding patients include nebulized AMB, endobronchial instillation of AMB and endobronchial laser therapy.[3]

Alfageme et al. demonstrated the safety of endobronchial AMB instillation in a patient with pulmonary mucormycosis, unresponsive to systemic and inhaled AMB.[4] Hinerman et al. reported successful management of persistent endobronchial mucormycosis (despite systemic and nebulized AMB) in a post renal transplant diabetic patient with endobronchial instillation of AMB (daily 25 mg AMB mixed with 20 ml sterile saline administered for 35 days) along with systemic and nebulization therapy.[3]

There are no data regarding the exact dosage and duration for endobronchial AMB treatment as the data are limited. Our patient had no immediate or delayed adverse effects with the endobronchial administration. We hypothesize that the initial lack of response to systemic AMB in our patient occurred due to the failure of therapeutic local concentration at the site of involvement. The bronchoscopic administration allowed targeted high local drug concentration which led to a dramatic clinical response. Although, our patient had initially failed to respond with systemic AMB, we believe that endobronchial AMB can evolve into a promising primary therapeutic modality in endobronchial mucormycosis. It can potentially decrease the total cumulative antifungal dose required and the total duration of therapy.[9] This may especially be important in patients who develop side effects with systemic antifungals or fail to respond or are poor surgical candidates with/without nonresectable lesions and patients refusing surgery/absence of surgical expertise. Our patient had rapid clinical, radiological, and bronchoscopic response without any complications.

Our case highlights that mucormycosis can affect even immunocompetent hosts and can present as an endobronchial growth resembling malignancy. Endobronchially administered AMB requires greater evaluation as a therapeutic modality for endobronchial mucormycosis.

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Conflicts of interest
There are no conflicts of interest.

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REFERENCES
1. Mahajan R, Paul G, Chopra P, Suri P. Mucormycosis masquerading as an endobronchial tumor. Lung India 2014;31:308-10.
2. McCarthy M, Rosengart A, Schuetz AN, Kontoyiannis DP, Walsh TJ. Mold infections of the central nervous system. N Engl J Med 2014;371:150-60.
3. Husari AW, Jensen WA, Kirsch CM, Campagna AC, Kagawa FT, Hamed KA, et al. Pulmonary mucormycosis presenting as an endobronchial lesion. Chest 1994;106:1889-91.
4. Alfageme I, Reina A, Gallego J, Reyes N, Torres A. Endobronchial instillations of amphotericin B: Complementary treatment for pulmonary mucormycosis. J Bronchology Interv Pulmonol 2009;16:214-5.
5. Hinerman R, Alvarez F, Singh A, Keller C. Treatment of endobronchial mucormycosis with amphotericin B via flexible bronchoscopy. J Bronchology 2002;9:294-7.

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