

Ulcerative Tracheobronchitis Due to *Aspergillus*

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Summary: *Aspergillus* ulcerative tracheobronchitis is a life-threatening form of invasive aspergillosis and is seldom seen in patients without underlying an immunocompromised state. Bronchoscopists must be familiar with this entity and consider *Aspergillus* ulcerative tracheobronchitis whenever mucosal erosions are seen, especially when unconventional risk factors such as intensive care unit admission and short-term glucocorticoid therapy are present. We present a case of invasive *Aspergillus* causing widespread ulcerative tracheobronchitis in a 39-year-old man with an asthma exacerbation requiring intensive care unit admission.

Key Words: ulcerative tracheobronchitis, invasive *Aspergillus*, glucocorticoids

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Aspergillus species are ubiquitous molds found in decaying organic matter throughout the globe.¹ *Aspergillus* are responsible for a spectrum of human pathologies including invasive, saprophytic, and allergic diseases.^{2,3} Invasive aspergillosis (IA) is an often fatal form well described in patients with underlying immunosuppression, such as transplant recipients, human immune deficiency virus infection (HIV), congenital immunodeficiency syndromes, and long-term corticosteroid therapy.^{2–11} IA can have several distinct pulmonary manifestations including bronchopneumonia, tracheobronchitis, and chronic necrotizing or cavitating pneumonia. Furthermore, *Aspergillus* tracheobronchitis (ATB) can be divided into 3 distinct histopathologic patterns: obstructive, pseudomembranous, and ulcerative.¹² Ulcerative ATB is seen as deep mucosal ulceration upon direct visualization. Most commonly, *Aspergillus fumigatus* is the predominant species representing 75% of the cases.¹³ We report a unique case

of ulcerative ATB found incidentally on bronchoscopy in a 39-year-old asthmatic man admitted to our intensive care unit (ICU) with a severe asthma exacerbation requiring mechanical ventilator support and intravenous glucocorticoid therapy.

CASE REPORT

The 39-year-old known asthmatic man presented with a several-day history of shortness of breath and productive cough. He had a long-standing history of asthma and was maintained on salbutamol, tiotropium, and salmeterol-fluticasone inhalers. His medical history was significant for end-stage renal disease because of primary focal segmental glomerulosclerosis, for which he received thrice-weekly hemodialysis. He was a remote intravenous drug user, but his HIV and hepatitis panels were negative. He was an active smoker, with a 15-pack-year history, and was only intermittently compliant with his asthma medications.

Initial examination demonstrated a nontoxic-looking man with significant bilateral expiratory wheeze. His chest x-ray revealed an ill-defined opacity over the left mid-lung zone (Fig. 1A). He was diagnosed with an asthma exacerbation because of community-acquired pneumonia and was discharged home on a prescription of moxifloxacin and prednisone taper. He returned 3 days later with worsening respiratory distress. Chest x-ray revealed no interval change; however, arterial blood gas demonstrated significant respiratory acidosis: pH 7.11, PaCO₂ 78 torr, PaO₂ 111 torr, HCO₃ 24 torr on high-flow oxygen by a face mask. He was referred to the ICU and ultimately intubated after failing to respond to aggressive asthma-directed therapy. Airway pressures peaked at 70 cm of H₂O, consistent with a severe asthma exacerbation. Our patient was treated with intravenous piperacillin/tazobactam, vancomycin, and 50 mg of methylprednisolone given every 6 hours intravenously. Despite this, his bronchospasm continued to be difficult to manage and he failed to improve with sedation, paralysis, isoflurane, and a trial of heliox. Ultimately, he was placed on extracorporeal membrane ventilation support to manage his hypercapnia and to reduce mechanical ventilatory parameters. Bronchoscopy was performed on day 8 because of the appearance to multiple bilateral consolidations (Fig. 1B). Bronchoscopy revealed no visible mucosal lesions; however, bronchoscopy

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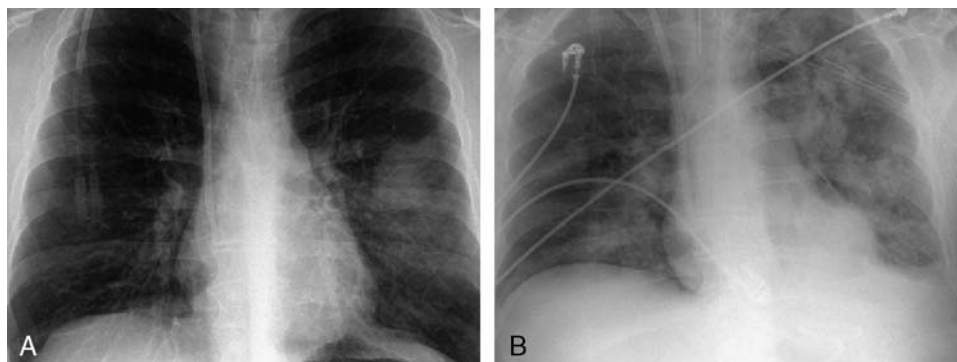


FIGURE 1. A, Posteroanterior chest film from admission. B, Portable film from day 7.

cultures grew *A. fumigatus*. Intravenous amphotericin B and oral voriconazole were added to his therapeutic regime. Owing to prolonged ventilation, our patient underwent a percutaneous tracheostomy, with bronchoscopic assistance, 6 days after the initial bronchoscopy. During the procedure, multiple punctuate bronchial ulcerations were visualized (Fig. 2). These involved the posterior tracheal wall, bilateral mainstem bronchi, and the left lower lobe bronchus. Endobronchial biopsy of the lesions was performed as well as protected brush specimen and bronchial washings were obtained. Fungal cultures from washings once again grew *A. fumigatus*. Pathology of the biopsied lesions showed squamous mucosa with IA (Fig. 3). Stains for herpes simplex virus were negative. Ultimately, the patient was diagnosed with invasive pulmonary aspergillosis and ulcerative ATB. He recovered well. Oral voriconazole was continued for a total period of 3 months. Repeat bronchoscopy showed healed ulcers and normal bronchial mucosa (Fig. 4).

DISCUSSION

ATB is a rare form of pulmonary aspergillosis, accounting for 8% to 20% of the cases.^{1,3,6}

ATB can be further subdivided into 3 categories on the basis of its clinical presentation and histopathologic appearance: ulcerative, pseudomembranous, and obstructive.¹² Ulcerative ATB is present when there is focal *Aspergillus* invasion of the mucosa, which can extend into the cartilage. It represents approximately 10% to 23% of the ATB cases.^{1,13}

Clinically, ATB can present with a range of respiratory complaints such as cough, hemoptysis, wheezing, and dyspnea. Moreover, the severity of the disease can range from fulminate respiratory failure to an asymptomatic individual.^{1,13} Endobronchially, ulcerative ATB appears as inflamed and possibly necrotic or ulcerated mucosa.¹ Several other diseases can have similar bronchoscopic appearance. A practical differential would include other fungal infections, viral, mycobacterium, endotracheal tube cuff trauma, and extraintestinal manifestations of ulcerative colitis.¹⁴ Radiographic appearance of the tracheal or bronchial wall thickening, airway narrowing or plaques, and patchy centrilobular nodules may direct

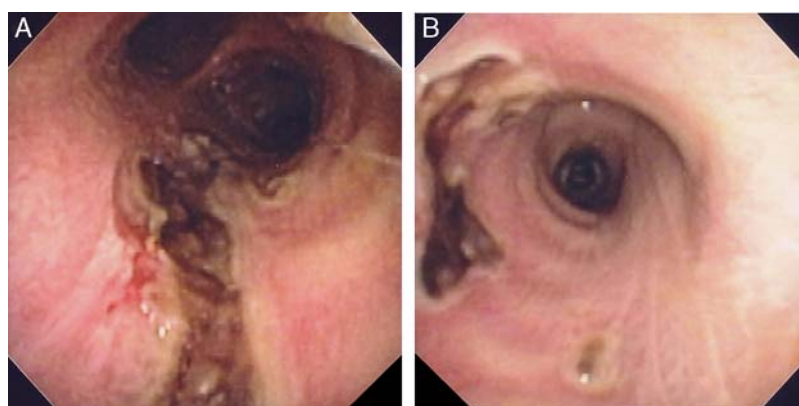


FIGURE 2. Bronchoscopic images revealing diffuse ulcerations. A, Trachea. B, Right main bronchus.

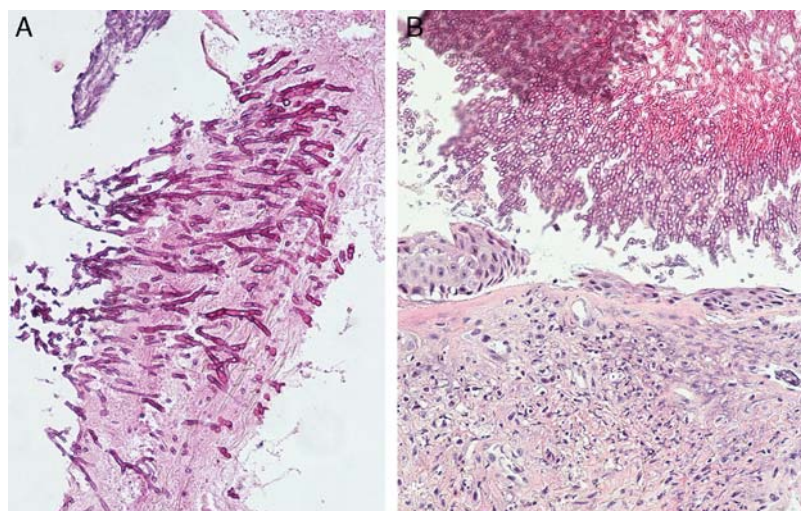


FIGURE 3. Microscopic examination of the ulcerations in the left mainstem bronchus. A, *Aspergillus* invasion of a sloughed ulcer. B, *Aspergillus* in the ulcer exudate and disruption of the squamous mucosa.

physicians to consider ulcerative ATB, but are by no means pathognomonic and are often not found until late in the disease course.^{1,13}

Direct visualization is not sufficient for the diagnosis of ulcerative ATB.¹ Diagnosis of ulcerative ATB requires histopathology to demonstrate IA with focal fungal invasion of the mucosa and/or the bronchial cartilage.¹² In contrast, pseudomembranous ATB has pseudomembranes of necrotic debris and *Aspergillus* overlying the mucosa. Finally, the third category

of ATB, obstructive ATB, shows thick mucus plugs of *Aspergillus*, without mucosal invasion. In addition, cultures must be positive for *Aspergillus* as several other fungi can mimic *Aspergillus*' morphologic appearance.

Classic high-risk factors for ATB have been well described in the literature and typically involve neutropenic, chronic steroid use (defined as >3 wk),¹⁵ inherited immunodeficiency, advanced HIV, and solid organ or hematopoietic stem cell transplant patients.^{2,3,5-9,11,13,16} However, nontraditional risk factors including short-term glucocorticoid therapy in obstructive airway disease patients and ICU admission are being described with increased frequency.^{4,7,9-11,13,17,18} Although increased risk for IA in chronic dialysis patients has not been described, one could infer that it would be based on their increased prevalence of fungal diseases.¹⁹ No studies have examined the risk factors for the subtypes of ATB separately. Much like the other forms of IA, ATB carries an ominous prognosis. Recent reviews found that ATB not stratified by an underlying cause carried 40% mortality.¹³ Moreover, ulcerative tracheobronchitis can progress to form fistulas or erode the surrounding structures often requiring surgical intervention or causing potentially fatal hemoptysis.^{20,21}

Therapy for ATB is outlined in the most recent guidelines from IDSA, with no distinction between subtypes.⁸ First-line therapy is voriconazole, as it has been shown to be superior in mortality, response, and safety when compared with amphotericin.²² Second-line therapy is



FIGURE 4. Repeat bronchoscopy revealed healed tracheal mucosa.

liposomal amphotericin.⁸ Currently, evidence does not support the combination therapy with these 2 agents and may actually have an antagonistic interaction.²³ Case studies propose the use of topical amphotericin, but its role in therapy has not been clearly delineated.²¹ Moreover, although the role of nebulized amphotericin has been studied in a prophylactic manner in several settings, no evidence for its role as an add-on therapy could be found in our literature search.

In summary, *Aspergillus* ulcerative tracheobronchitis is an infrequently encountered entity readily identifiable on bronchoscopy. Bronchoscopists are required to have a high index of suspicion and be aware of contributing risk factors to recognize and aggressively treat IA to potentially prevent significant morbidity and mortality.²⁴

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