The Expert Clinician

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An Uncommon Cause of Bronchial Obstruction

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Case Vignette

A 72-year-old woman presented to our institution with fevers and cough. Her history was remarkable for stage IA adenocarcinoma of the right lung for which she had undergone wedge resection of the right lower lobe and right middle lobe 4 years before presentation. She subsequently had recurrence in the right infrahilar region for which she was treated with stereotactic body radiation therapy for a total of 50 Gy over five fractions, after being deemed a poor surgical candidate. Following radiation therapy, she was diagnosed with *Mycobacterium avium* complex (MAC), isolated via bronchial wash from the right bronchus intermedius (BI). She was actively being treated with rifampin, azithromycin, and ethambutol for 6 months at the time of presentation, with follow-up sputum cultures that were negative for growth.

At presentation, the patient's vital signs were grossly normal with an oxygen saturation of 96% on room air. Physical exam was remarkable for decreased breath sounds on the right. Admission labs included a normal complete blood count and comprehensive metabolic panel. A computed tomographic angiography of the chest demonstrated increased right perihilar and infrahilar tissue fullness with occlusion of the BI in close proximity to the right pulmonary artery as well as patchy nodular opacities in the right lower lobe (Figures 1A

Figure 1. (A and B) Computed tomographic angiography of the chest demonstrating increased right perihilar and infrahilar tissue fullness with occlusion of the bronchus intermedius (BI) in close proximity to the right pulmonary artery as well as patchy nodular opacities in the right lower lobe. Bronchoscopic images showing (C) orifice of BI with fibropurulent material before debridement and (D) debrided BI orifice with pulsatile mass as outlined in yellow. The arrow is indicating the pulmonary artery.

and 1B). Empiric treatment for pneumonia was initiated, including piperacillin-tazobactam and levofloxacin. Bronchoscopy was subsequently performed. Upon entering the right mainstem bronchus, there was extensive fibropurulent material obstructing

the orifice of the BI (Figure 1C). After debridement with forceps, the area was traversed. The pulmonary artery was then observed protruding through the medial wall of the BI (Figure 1D; see Video 1, showing pulsatile mass in BI).

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(Received in original form February 17, 2020; accepted in final form July 20, 2020)

Supported in part by a National Institutes of Health Clinical and Translational Science Award (TL1TR002368) to the University of Kansas.

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Ann Am Thorac Soc Vol 17, No 11, pp 1476–1479, Nov 2020

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DOI: 10.1513/AnnalsATS.202002-140CC

Internet address: www.atsjournals.org

Video 1. Bronchoscopy demonstrating evidence of the pulmonary artery protruding through the medial wall of the bronchus intermedius.

Questions

1. *What is your differential diagnosis for this patient?*
2. *What are the next steps in management of this patient?*

[Continue onto next page for answers]

Clinical Reasoning and Diagnosis

The patient presented for fever and cough and was found to have an occluded BI on imaging. Given her history of lung cancer, radiation therapy, and MAC infection, we proceeded with bronchoscopy for further evaluation and found an area of bronchus that was eroded. Our main differential diagnosis for this finding included malignancy (primary vs. metastatic); radiation necrosis; and infectious pathogens including bacteria such as *Staphylococcus* and *Klebsiella* and fungi such as *Aspergillus*. Other, uncommon etiologies we considered less likely included autoimmune disorders such as relapsing polychondritis, sarcoidosis, granulomatosis with polyangiitis, and extraintestinal manifestation of inflammatory bowel disease.

Given the concern for erosion of the bronchus leading to herniation of the pulmonary artery, thoracic surgery consultation was obtained. The patient subsequently underwent right pneumonectomy with associated laparotomy for mobilization of omentum flap to cover the bronchial stump and hilum. Pathologic analysis of specimens from the pneumonectomy demonstrated necrotizing granulomas and the presence of fungal hyphae within the necrotic bronchial walls without evidence for tumor recurrence (Figures 2A–2C). Cultures demonstrated *Aspergillus fumigatus*. The patient was diagnosed with necrotizing pseudomembranous *Aspergillus*

tracheobronchitis. Subsequent long-term treatment included micafungin followed by isavuconazole.

Discussion

Invasive pulmonary aspergillosis can have a wide array of presentations including aspergilloma, angioinvasive disease, chronic necrotizing aspergillosis, and *Aspergillus* tracheobronchitis (ATB). ATB is an uncommon variant that accounts for approximately 7% of cases (1).

There are multiple risk factors for the development of ATB, many of which were present in this case. Malignancy and conditions related to immune compromise such as neutropenia, acquired immunodeficiency syndrome, and hematopoietic and solid organ transplant are common underlying conditions in ATB. Additionally, treatment with chronic corticosteroids, chemotherapy, radiation therapy, anatomic structural defects, and prior infection, including MAC, have all been reported as predisposing factors (2, 3).

Clinically, ATB can present with a wide range of symptoms such as cough, hemoptysis, wheezing, and shortness of breath, but patients may be asymptomatic (4). Imaging findings seen in ATB include thickening of the tracheobronchial wall as well as multifocal, irregular plaques. However, these findings are only observed in approximately 25% of cases (4). Because of nonspecific symptoms and

imaging, bronchoscopy is required for the diagnosis of ATB.

Three subtypes of ATB have been described: pseudomembranous, ulcerative, and obstructive (5). Pseudomembranous tracheobronchitis is characterized by the formation of a pseudomembrane composed of hyphae, fibrin, and necrotic debris that fills the airway. In ulcerative tracheobronchitis, erosive lesions are seen in the cartilaginous tracheal rings. Obstructive tracheobronchitis is a noninvasive form characterized by growth of *Aspergillus* in the airways leading to endobronchial obstruction. More recently, a staging system has been proposed that includes the following: type I, superficial cartilage infiltrate; type II, erosion into the cartilage with airway destruction; type III, obstructive (pseudomembrane occluding >50% of airway); and type IV, mixed form (2). The prognosis of ATB depends on the type or stage and the patient's immune status. Overall, ATB is fatal in approximately 40% of cases, and the rate is even higher when necrosis and pseudomembranes are present (6).

Once diagnosis of ATB is confirmed, pharmacologic therapy is typically the mainstay of treatment. The Infectious Diseases Society of America guidelines recommend treatment with voriconazole as first-line therapy (7). Alternate primary therapy options include isavuconazole and amphotericin B. In immunocompromised patients, the combination of voriconazole with an echinocandin may be beneficial. Minimum duration of therapy is typically

Figure 2. Pathologic analysis of pneumonectomy specimen. (A) Grocott stain demonstrating hyphae with acute angle branching characteristic of *Aspergillus*. Hematoxylin and eosin stain demonstrating (B) parenchymal necrotizing granulomas and (C) necrotizing inflammation within the airway wall.

6–12 weeks, but extended treatment is often needed in the immunocompromised population. In some situations, depending on the location and extent of disease, surgery may be required, as it was in our case.

Historically, patients were not treated for central tumors (within 2 cm of the proximal bronchial tree) owing to grade 5 toxicity (8). Fatal hemorrhage from radiotherapy to the more central airway has been well described in the literature. Because this concept has been challenged by more recent reports, some patients, including ours, are offered stereotactic body radiation therapy to an area traditionally not felt to be suitable for radiotherapy. Unfortunately, our patient subsequently developed ATB in the radiation field with significant complications. Given the high risk of fatal hemorrhage related to exposure of the pulmonary artery in this situation, pneumonectomy was performed. Right pneumonectomy carries substantial risk of excess morbidity and mortality after neoadjuvant chemotherapy and conventional radiotherapy at 45 Gy (9). Unlike the left mainstem bronchus, which is buried within the mediastinum under the aortic arch, the right mainstem bronchus is exposed to a large pneumonectomy space, making it more prone to devascularization-related dehiscence. In our patient, risk for poor outcome due to the prior radiation was

increased by the history of underlying infection. Soft tissue coverage has been described to mitigate these risks, and therefore, the omentum was chosen as the most robust choice to protect the right hilum from wound complications (10).

In summary, ATB is an infrequently encountered disease that is diagnosed by bronchoscopy. It is important to be aware of risk factors for development of ATB, several of which were present in our patient, and to aggressively treat when ATB is diagnosed, given the associated high mortality.

Answers

1. What is your differential diagnosis for this patient?

Malignancy (primary vs. metastatic); radiation necrosis; bacterial infection including *Staphylococcus*, *Klebsiella*, and MAC; and fungal infection such as *Aspergillus*. Other rarer etiologies to consider include autoimmune disorders such as relapsing polychondritis, sarcoidosis, granulomatosis with polyangiitis, and extraintestinal manifestations of inflammatory bowel disease.

2. What are the next steps in management of this patient?

Given the risk for fatal hemorrhage, thoracic surgery should be consulted for evaluation for

pneumonectomy. Treatment with antifungal agents such as voriconazole, isavuconazole, or amphotericin B should be initiated.

Follow-Up

The patient underwent successful complex right pneumonectomy and was treated for 6 months with isavuconazole.

Insights

- ATB can have a wide array of clinical presentations and imaging studies are usually nonspecific. Consequently, bronchoscopy is necessary to establish the diagnosis.
- Following diagnosis, most cases of ATB can be managed medically with antifungal therapy, but surgical intervention may be necessary depending on the location and extent of disease. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

Acknowledgment: We thank Dr. Rashna Madan for generously providing the pathologic specimen slides.

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