Pseudomembranous Tracheitis Caused by Aspergillus Fumigatus in the Setting of High Grade T-Cell Lymphoma

Prashant Malhotra
Karan Singh
Paul Gill
Sonu Sahni
*Touro College of Osteopathic Medicine (New York)*, sonu.sahni@touro.edu

Mina Makaryus

*See next page for additional authors*

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Authors
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Case report

Pseudomembranous tracheitis caused by *Aspergillus fumigatus* in the setting of high grade T-cell lymphoma

Prashant Malhotra, M.D. a, Karan Singh, MBBS b, Paul Gill, B.S. b, Sonu Sahni, M.D. b, Mina Makaryus, M.D. b, Arunabh Talwar, M.D., FCCP b, *

a Northwell Health, Department of Infectious Diseases, 400 Community Drive, Manhasset, NY 11030, United States
b Northwell Health, Department of Pulmonary, Critical Care and Sleep Medicine, 410 Lakeville Rd., New Hyde Park, NY 11040, United States

1. Introduction

Pseudomembranous tracheitis (PMT) is a rare condition most commonly caused by fungal or bacterial infection that is characterized by a pseudomembrane that partially or completely covers the tracheobronchial tree. PMT is most often found in immunocompromised patient populations, such as post-chemotherapy, AIDS, post-transplant, and hematological malignancies. Fungal infections of the trachea can cause this rare phenomenon which may potentially lead to necrosis [3]. The pathogens known to cause this pseudomembranous infection are: *Aspergillus*, *Candida*, *Cryptococcus*, *Rhizopus*, and *Mucorales* [4,5]. In more rare cases, pseudomembranous tracheitis may be caused by invasive bacterial pathogens such as *Bacillus cereus* [6]. PMT should be considered in the differential diagnosis of refractory cough in the immunocompromised population. However, it has been described in patients with nonspecific respiratory symptoms such as dyspnea, cough, and other airway issues [7]. Herein, we present a case of pseudomembrane tracheitis in the setting of high grade T-cell lymphoma.

2. Case report

A 65 year old male with a past medical history of non-obstructive coronary artery disease, urothelial cancer (status post resection), abdominal aortic aneurysm (status post repair), hypothyroidism, and 50 pack-year history of smoking, was admitted presenting with recurring fevers and a 30-pound weight loss over the past several months. A Chest x-ray (CXR) revealed a right mid-lung consolidation. Computer tomography (CT) showed a left supraclavicular/lower cervical mass, hilar lymphadenopathy as well as enlargement of the subcarinal and mediastinal lymph nodes. Subsequent lymph node biopsy revealed high grade T-cell lymphoma.

The patient was started up on empiric antibiotic therapy but continued to be febrile. He subsequently underwent bronchoscopy which revealed a pseudomembrane extending from the bronchus intermedius down to the right lower lobe (Fig. 1). Bronchoscopy was negative for any masses, abscesses, erosions or areas of bleeding.

Both an endobronchial biopsy as well as culture of the bronchoalveolar lavage revealed *Aspergillus fumigatus* (Fig. 2).
Patient was initiated on Voriconazole. Repeat bone marrow biopsy was negative for Aspergillus. The patient was discharged on Voriconazole and oxygen. Despite treatment the patient died of progressive pulmonary infiltrates and respiratory failure.

3. Discussion

Pseudomembranous tracheitis (PMT) is commonly caused by fungal or bacterial infection that is characterized by pseudomembrane formation in the large airways [1,2]. Here we described a case of a 65-year-old male with undiagnosed malignancy that had developed Aspergillus-related PMT. PMT is a rare condition that manifests with different symptoms and etiologic microorganisms. Previously reported cases of PMT have been outlined in Table 1.

Invasive pulmonary aspergillosis (IPA) is the most common form of disease caused by Aspergillus species infection. In addition, a rare form of IPA is an infection of the tracheobronchial tree, called Aspergillus Tracheobronchitis (AT) [17]. Four types of AT: ulcerative tracheobronchitis, obstructive bronchial aspergillosis, aspergillus bronchitis, and pseudomembranous necrotizing bronchial aspergillosis, or PMT have been described [1,2]. The pseudomembrane is thought to be derived from fibrin, hyphae, and necrotic tissue [12]. Other fungi such as Rhizopus, Cryptococcus and Candida can also form a pseudomembrane via similar mechanisms [4,5]. Rarely viruses may be implicated in PMT. Known causes of PMT have been outlined in Table 2.

Patients with pseudomembranous tracheitis typically present symptoms of dyspnea, fever, non-resolving cough, and chest pain. Dyspnea, as one of the presenting symptoms, is usually caused by the pseudomembrane obstructing the airways to the lungs [11]. Colonies of fungi create plaques that line the bronchi which leads to a necrotizing bronchitis. Most common signs and symptoms of PMT are outlined in Table 3.

PMT is a rare condition, therefore a strong clinical suspicion is
needed to diagnose this condition. Bronchoscopy is essential to discover pseudomembrane in the airways. A pseudomembrane has the potential to form and constrict the airways, thus causing the symptoms that are associated with PMT [7]. Based on pathological tissue, brush smear, and fluid from bronchial that are obtained by a bronchoscopy, the results can lead to a diagnosis of airway aspergillus infection and the type of Aspergillus as well [11]. In our case non-resolution of infiltrates despite adequate antibiotic therapy prompted us to perform a bronchoscopy.

Since pseudomembranous tracheitis is mostly caused by fungal infection, a range of antifungal treatments would deemed most effective towards the condition. Table 1 suggests that amongst health care providers intravenous Amphotericin B is the initial treatment of choice [11]. Other treatments such as voriconazole, itraconazole, and echinocandins (caspofungin) [5,12] However recently, Voriconazole has been administered to patients with PMT due to its better prognosis, as shown in Table 1.

PMT has a high morbidity and mortality in immunosuppressed patients. This in itself lends to a high morbidity and mortality that is associated with opportunistic infections. It has been reported that

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Table 1
Cases of PMT.

<table>
<thead>
<tr>
<th>Author</th>
<th>Primary disease</th>
<th>Causes</th>
<th>Organism</th>
<th>Signs/Symptoms</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al. [5]</td>
<td>Leukemia</td>
<td>Stem cell transplantation secondary to pancytopenia</td>
<td>Aspergillus</td>
<td>Progressive cough, nausea</td>
<td>Amphotericin B (IV), Amphotericin B (inhaled), caspofungin (IV)</td>
<td>Deceased</td>
</tr>
<tr>
<td>Strauss et al. [6]</td>
<td>Unknown</td>
<td>Aplastic Anemia</td>
<td>Bacillus cereus</td>
<td>Petechiae, weakness, dyspnea</td>
<td>Broad-spectrum antibiotic, anti-viral, anti fungal therapy</td>
<td>Deceased (multiple organ failure)</td>
</tr>
<tr>
<td>Chang et al. [8]</td>
<td>Diabetes mellitus</td>
<td>Diabetic ketoacidosis</td>
<td>Aspergillus</td>
<td>Chest pain, cough, dyspnea, wheezing</td>
<td>Parenteral amphotericin B</td>
<td>Deceased (septic shock)</td>
</tr>
<tr>
<td>Tait et al. [7]</td>
<td>Tuberculosis</td>
<td>Neutropenia</td>
<td>Aspergillus</td>
<td>Weight loss, anorexia, non-productive cough, right side chest pain, fever</td>
<td>Amphotericin B intravenous amphotericin B (1 mg/kg/day), fluconazole (120 mg/kg/day), and oral itraconazole (600 mg/day) commenced,</td>
<td>Deceased (respiratory failure)</td>
</tr>
<tr>
<td>Hines et al. [9]</td>
<td>COPD</td>
<td>Respiratory arrest</td>
<td>Aspergillus</td>
<td>Fever, wheezing, Fever, hypotension Epigastic and lower back pain</td>
<td>Vancomycin, Clindamycin, Amikacin</td>
<td>Deceased (progressive respiratory insufficiency)</td>
</tr>
<tr>
<td>Pornsuriyasak et al. [10]</td>
<td>Tuberculosis Tracheal Stenosis</td>
<td>Tuberculous tracheal stenosis 62.5% (10/16)</td>
<td>Aspergillus</td>
<td>Fever, Dyspnea, Chest pain 87.5% (14/16) Progressive dyspnea 75.0% (12/16) Irritable cough</td>
<td>Oral voriconazole Nebulized amphotericin B</td>
<td>68.8% (11/16) Deceased</td>
</tr>
<tr>
<td>Huang et al. [11]</td>
<td>Pulmonary</td>
<td>Pulmonary malignancies 56.3% (9/16)</td>
<td>Aspergillus</td>
<td>Weight loss, anorexia, non-productive cough, right side chest pain, fever</td>
<td>Amphotericin B intravenous amphotericin B</td>
<td>Deceased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bronchial involvement secondary to non-pulmonary tumor 12.5% (2/16)</td>
<td>Aspergillus</td>
<td>Weight loss, anorexia, non-productive cough, right side chest pain, fever</td>
<td>Amphotericin B intravenous amphotericin B</td>
<td>Deceased</td>
</tr>
<tr>
<td>Putnam et al. [3]</td>
<td>Lung transplant</td>
<td>Bone marrow transplantation secondary to aplastic anemia</td>
<td>Aspergillus</td>
<td>Weakness, fatique, dyspnea</td>
<td>Amphotericin B (IV)</td>
<td>Deceased</td>
</tr>
<tr>
<td>Patel et al. [12]</td>
<td>Leukemia</td>
<td>Pancytopenia</td>
<td>Aspergillus</td>
<td>Shortness of breath, cough, pleuritic chest pain</td>
<td>Amphotericin B (IV)</td>
<td>Deceased (progressive leukemia and sepsis)</td>
</tr>
<tr>
<td>Williams et al. [5]</td>
<td>Type 2 Diabetes</td>
<td>Allogeneic stem cell transplantation</td>
<td>Aspergillus</td>
<td>Progressive cough, dyspnea, nausea and emesis</td>
<td>Intravenous liposomal amphotericin B, intravenous caspofungin</td>
<td>Deceased (respiratory failure)</td>
</tr>
<tr>
<td>Le et al. [13]</td>
<td>Acute lymphoblastic leukemia.</td>
<td>chemotherapy</td>
<td>Aspergillus</td>
<td>Cough, fever, and hoarseness</td>
<td>Intravenous voriconazole G-CSF liposomal amphotericin B</td>
<td>Improved</td>
</tr>
<tr>
<td>Argüder et al. [14]</td>
<td>Diabetes</td>
<td>Inconsistent use of insulin</td>
<td>Aspergillus</td>
<td>Cough, chest pain, hoarseness, fever, dyspnea</td>
<td>Deceased</td>
<td></td>
</tr>
<tr>
<td>Ramos et al. [15]</td>
<td>Cardiac amyloidosis</td>
<td>Heart transplant</td>
<td>Aspergillus</td>
<td>Fever, dyspnea, wheezing, and a cough</td>
<td>IV voriconazole IV caspofungin</td>
<td>Improved</td>
</tr>
<tr>
<td>Shah et al. [16]</td>
<td>Stillbirth</td>
<td>Pulmonary edema</td>
<td>Aspergillus</td>
<td>Fever, dyspnea, stridor</td>
<td>Voriconazole</td>
<td>Improved, then lost to follow up</td>
</tr>
</tbody>
</table>
4. Conclusion

PMT is a rare condition that is mostly caused by fungal, and sometimes, bacterial infection. It usually requires a high index of suspicion for diagnosis. The prognosis depends on timely diagnosis and initiation of antifungal therapy.

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