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

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**A B S T R A C T**

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 commonly found in immunocompromised patient populations, such as post-chemotherapy, AIDS, post-transplant, and hematological malignancies. Due to its rarity, PMT is often not included in the differential diagnosis. This case describes a 65 year old male with persistent fever and refractory cough despite high dose empiric antibiotics. Subsequent bronchoscopy with biopsy revealed pseudomembranous tracheitis due to *Aspergillus fumigatus* in the setting of T-cell lymphoma. 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.

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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 [1,2]. 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 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 1.

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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 asper-
gillus 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 deem 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**

| Author          | Primary disease | Causes                                      | Organism | Signs/Symptoms | Treatment                                        | Outcomes  |
|-----------------|-----------------|---------------------------------------------|----------|----------------|-------------------------------------------------|-----------|
| Williams et al. | Leukemia        | Stem cell transplantation secondary to pancytopenia | Aspergillus | Progressive cough, nausea | Amphotericin B (IV), Amphotericin B (inhaled), caspofungin (IV) | Deceased  |
| Strauss et al.  | Unknown         | Aplastic Anemia                             | Bacillus cereus | Petechiae, weakness, dysnea | Broad-spectrum antibiotic, anti-viral, antifungal therapy               | Deceased (multiple organ failure) |
| Chang et al.    | Non-Hodgkin’s Lymphoma | Diabetes mellitus                           | Aspergillus | Chest pain, cough, dyspnea, wheeze Non-productive cough, right side chest pain, fever | Parental amphotericin B amphotericin B | Deceased (septic shock) Improved |
| Tait et al.     | Systemic lupus erythematosus-like disorder | Neutropenia	 | Aspergillus | Weight loss, anorexia, non-productive cough, and pyrexia | Amphotericin B intravenous amphotericin B (1 mg/kg/day), fluocytosine (120 mg/kg/day), and oral itraconazole (600 mg/day) commenced, | Deceased (respiratory failure) |
| Hines et al.    | COPD            | Respiratory arrest                          | Aspergillus | Fever, wheezing, Fever, hypotension Epigastric and lower back pain | Vancomycin, Clindamycin, Amikacin Anfotericin B Amphotericin B | Deceased (respiratory failure) Deceased (progressive respiratory insufficiency) Deceased |
| Huanget al.     | Myelodysplastic syndrome | Neutropenia	 | Aspergillus | Weight loss, polyarthralgia, night sweats, pyrexia | Vancomycin, Clindamycin, Amikacin Amphotericin B Amphotericin B | Deceased (respiratory failure) Deceased (progressive respiratory insufficiency) Deceased |
| Putnam et al.   | Leukemia        | Bone marrow transplantation secondary to aplastic anemia | Aspergillus | Weakness, fatigue, dyspnea | Oral voriconazole Nebulized amphotericin B | 100% Amphotericin B (inhalation and infusion) 68.8% (11/16) Deceased |
| Patel et al.    | Leukemia        | Pancytopenia	 | Aspergillus | Shortness of breath, cough, pleuritic chest pain | Amphotericin B (IV) | Deceased Deceased (progressive leukemia and sepsis) Deceased (respiratory failure) Improved Deceased |
| Williams et al. | Type 2 Diabetes and leukemia | allogeneic stem cell transplantation. | Rhizopus sp. | Progressive cough, dyspnea, nausea and emesis | intravenous liposomal amphotericin B, inhaled amphotericin B, intravenous caspofungin | Deceased |
| Le et al.       | Acute lymphoblastic leukemia, Diabetes mellitus | chemotherapy | Aspergillus | Cough, fever, and hoarseness. | Intravenous voriconazole G-CSF liposomal amphotericin B | Deceased |
| Argüder et al.  | Inconsistent use of insulin | Aspergillus | Aspergillus | Cough, chest pain, hoarseness, fever, dyspnea | IV voriconazole IV caspofungin | Deceased |
| Ramos et al.    | Heart transplant | Pulmonary edema | Aspergillus | Fever, dyspnea, wheezing, and a cough Dyspnea, stridor | Voriconazole | Improved |
| Shah et al.     | Stillbirth       | | | | | | Improved, then lost to follow up |
Table 2
Causes of Psuedomembranous tracheitis.

| Infectious Causes  | Noninfectious Causes |
|--------------------|----------------------|
| Fungal             | Smoke inhalation     |
| Aspergillus species| Endotracheal intubation|
| Candida            | Crohn disease        |
| Cryptococcus       | Stevens-Johnson syndrome |
| Rhizopus           | Agents of bioterrorism|
| Mucorales          | Ligneous conjunctivitis|
| Bacterial          | Paragquat ingestion  |
| Pseudomonas aeruginosa|                       |
| Haemophilus influenza|                        |
| Corynebacterium diphtheriae|                  |
| Staphylococcal infections|                 |
| a-hemolytic Streptococcus species|         |
| Moraxella catarrhalis|                          |
| Bacillus cereus    |                          |
| Chlamydia species  |                          |
| Mycoplasma bovis   |                          |
| Pseudomembranous croup|                       |
| Viral              |                          |
| Bovine herpes virusI|                          |
| Adenovirus         |                          |
| Influenza (co-infection) |                     |

Adapted from Patel et al. [12].

Table 3
Common symptoms of PMT.

| Symptom          |
|------------------|
| Fever            |
| Dyspnea          |
| Cough            |
| Chest pain       |
| Fatigue          |
| Unilateral wheeze|

death usually ensues between 1 and 6 weeks after diagnosis [18]. Majority of cases of PMT have resulted in demise as demonstrated in Table 1. Some causes for death include respiratory failure, septic shock, or other organ failure. Respiratory failure in PMT may result from the pseudomembrane constricting the airways and can even dislodge thus creating a ball valve that leads to obstruction [6,12].

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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Conflict of interest

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