Submission ID: 910618

A 49 YEAR OLD FEMALE WITH ACUTE HYPOXIC RESPIRATORY FAILURE AND TRACHEAL DEBRIS

KAREN VOLPE, M.D.; KATIE WHITE, M.D., Ph.D.
Vanderbilt University Medical Center, Nashville, TN

Karen Volpe, M.D. | karen.e.volpe@vumc.org

VANDERBILT UNIVERSITY MEDICAL CENTER

HISTORY OF PRESENT ILLNESS

This is a 49-year-old female with a history of Ehlers-Danlos, Chiari malformation, hypertension, tobacco use (15 pack year smoking history), and recurrent nephrolithiasis who was admitted on January 27, 2020 as a transfer from an outside hospital for management of acute hypoxic respiratory failure.

1 week prior: fevers, chills, malaise, fatigue

1 day prior: productive cough

Admitted to outside hospital: CT chest with possible subglottic mass

Rapid flu test negative

Day of admission: confusion, labored breathing

Transferred to VUMC

EXAM

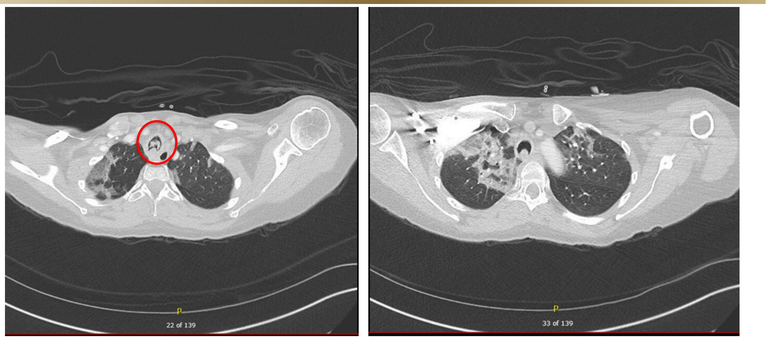
Temperature: 96.8ºF (36ºC)
Heart rate: 129 beats per minute
Blood pressure: 171/141 mmHg
Respiratory rate: 32 breaths per minute
Oxygen saturation: 95% on BiPAP with a fraction of inspired oxygen (FiO2) of 40%, inspiratory positive airway pressure (IPAP) 10 cmH_20, expiratory positive airway pressure (EPAP) 5 cmH_20.
General: Awake and alert, but ill-appearing and very anxious. Has a weak voice but still able to speak in complete sentences.
Head and Neck: Dry mucous membranes. Clear oropharynx, no mass.
Cardiovascular: Tachycardic. Regular rhythm. No murmur.
Pulmonary: Tachypneic. Anterior lung sounds are coarse with diffuse expiratory wheezing.

INITIAL LABS AND DIAGNOSTICS

WBC: 4.3 $x10^3/\mu L$
  Absolute neutrophil count: 3.80 $x10^3/\mu L$
  Absolute lymphocyte count: 0.37 $x10^3/\mu L$
Platelet: 111 $x10^3/\mu L$
Sodium: 135 mmol/L
Potassium: 3.2 mmol/L
Chloride: 115 mmol/L
Bicarbonate: 10 mmol/L

HIV Antigen/Antibody assay: non-reactive
PCR Respiratory Pathogen Panel: positive for Influenza A H1N1-2009

IMAGING



Figures 1-2. CT Angiography Chest: patchy bilateral collections of airspace and groundglass opacities; extensive airway debris with likely mucous in the upper trachea (**red circle**); and partially calcified right mediastinal lymph nodes.

HOSPITAL COURSE

Hospital Day 1
- Started on PO oseltamivir, IV vancomycin, and IV levofloxacin (has a reported penicillin allergy).
- Flexible fiberoptic endoscopic exam without airway obstruction or mass.

Hospital Day 3
- Developed progressive hypoxemia with tripoding, encephalopathy, and acidosis requiring intubation.
- Post-intubation bronchoscopy revealed **large, whitish, exudative pseudomembranous lesions throughout the large airways distorting the carina** (**Figure 3**).
  - Cytopathology: **acute angle-branching hyphae**, consistent with *Aspergillus* (**Figure 4**)
  - Fungal culture: ***Aspergillus fumigatus***
  - IV ambisome started

Hospital Day 7
- Continued to have refractory hypoxemia, persistent acidosis, and oliguric renal failure.
- Family changed goals to comfort care, and patient passed away.

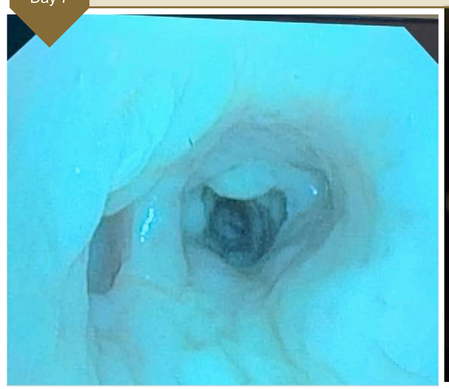


Figure 3. Endoscopic photograph obtained during post-intubation bronchoscopy. Note the distorted carina with presence of pseudomembranous lesions.

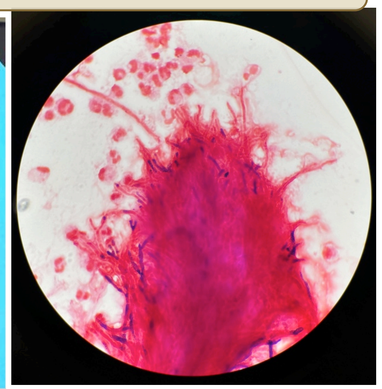


Figure 4. H&E stain from our patient's bronchial washing showing acute angle branching septate hyphae.

FINAL DIAGNOSIS

Aspergillus tracheobronchitis in the setting of influenza A infection

DISCUSSION

Aspergillus tracheobronchitis is a rare form of invasive pulmonary aspergillosis which is characterized by isolated invasion of the tracheobronchial tree by *Aspergillus* species. Infection can lead to thick mucous plugging, pseudomembrane formation, and ulceration with transmural bronchial necrosis, which can rarely result in tracheal perforation.[2,3] It primarily occurs in immunocompromised individuals, and risk factors include neutropenia, hematopoietic and solid-organ transplantation, prolonged corticosteroid use, malignancy and acquired immunodeficiency syndrome.[2] The incidence is low (<7% out of all pulmonary Aspergillosis cases)[1] although mortality is high, with case fatality rates approaching 78% despite anti-fungal therapy.[3] The pathogenesis is thought to be multifactorial, and includes viral disruption of the respiratory epithelium, disruption of ciliary clearance, impaired local immunity, viral-induced changes in T-helper cells, and lymphopenia.[4]

Diagnosis can be challenging for multiple reasons. Oftentimes, the affected patients are healthy with few co-morbidities and no history of immunosuppression. Symptoms and radiographic features are non-specific.[4] The gold standard for diagnosis is the combination of histopathological examination of lung tissue with findings of septate, acute branching hyphae invading the lung tissue, and a culture positive for *Aspergillus* from the same site.

CONCLUSIONS

- Aspergillus tracheobronchitis is a rare form of invasive pulmonary aspergillosis characterized by invasion of the tracheobronchial tree by *Aspergillus* species.
- Infection can lead to obstruction with mucous plugging, pseudomembrane formation, and even ulceration with transmural bronchial necrosis.
- Immunosuppression is the most common risk factor for infection. However, cases have been reported in immunocompetent individuals.
- Mortality is high and was reported in up to 78% of cases despite anti-fungal treatment.

REFERENCES

1. Cho B, Oh Y, Kang E, Hong Y, Jeong H, Lee O, Change Y, Choe K, Lee K, An J. *Aspergillus* Tracheobronchitis in a Mild Immunocompromised Host. *Tuberc Respir Dis (Seoul)*. 2014 Nov; 77 (5): 223-226. PubMed PMID: 25473411
2. Argüder E, Şentürk A, Hasanoğlu A, Hasanoğlu I, Kanbay A, Doğan H. Unique Case of Pseudomembranous Aspergillus Tracheobronchitis: Tracheal Perforation and Horner's Syndrome. Myc*opathologia*. 2016 June; 181: 885-889. PubMed PMID: 27255521
3. Kousha M, Tadi R, Soubani O. Pulmonary aspergillosis: a clinical review. *Eur Respir Rev.* 2011 Sep; 20(121): 156-74. PubMed PMID: 21881144
4. Crum-Cianflone N. Invasive Aspergillosis Associated with Severe Influenza Infections. *Open Forum Infect Dis.* 2016 Sep; 3(3) :ofw171. PubMed PMID: 27704024