Unusual Presentation of a Recurrent Asthmatic with Bronchiectasis on Multiple Computed Topographies

OKLAHOMA STATE UNIVERSITY
CENTER FOR HEALTH SCIENCES

OSU Internal Medicine

Dr. Reagan Livingston, PGY-2 , DO *Contributing authors: Dr. Nadim Daher, MD*

Background

Recurrent treatment resistant asthma in high risk patient populations may be the inciting factor that leads to further evaluation of other contributing etiologies of a patient's symptoms. Allergic bronchopulmonary Aspergillus, ABPA, is primarily an immunologic response that is most commonly seen in asthmatics and cystic fibrosis patients. Common presentation will include symptoms of hemoptysis, fever, weight-loss, malaise as well as transient and fleeting pulmonary opacities and bronchiectasis on imaging. ABPA is classified as an allergic respiratory mycosis against *Aspergillus fumigatus*, and has a higher incidence seen in asthmatic specialty clinics as well as those in the intensive care unit (1).

The pathogenesis of ABPA is not fully understood, but is thought to be due to difficulty with clearance of the airways in genetically predisposed patients as well as T-helper 2 cell immune response. In these genetically predisposed patients, they are unable to clear the *Aspergillus fumigatus* conida from their airways which subsequently germinates into hyphae leading to a activation of the adaptive immune response and release of both chemokines and cytokines. This ultimately leads to development of a large inflammatory response with mast cell degranulation, recruitment of eosinophils and neutrophils, and the development of the characteristic immunologic response seen in ABPA as well as progression to bronchiectasis and pulmonary fibrosis (1).

Case Presentation

52 year old male with a pertinent past medical history of asthma, sinusitis, and allergic rhinitis that initially presented to the outpatient clinic for evaluation of chronic bronchiectasis. Patient stated that he had a history of approximately 3 to 4 years of bronchiectasis noted on multiple CT scans of his chest and underwent a bronchoscopy which was unremarkablr. On follow up questioning, the patient stated that he was diagnosed with a pneumonia as a child and that he had been told this was the cause of his bronchiectasis previously. Of note, the patient stated that he never smoked and had no significant occupational related exposure on further history.

Initially patient did complain of a cough with clear and yellow mucus, but denied any fever, chills, or hemoptysis. All other review of systems were unremarkable. On physical exam, the patient did have normal respiratory effort, no distress, no wheezes, no rales, but had rhonchi in the right upper field, right middle lobe, and right lower field. The remainder of the physical exam was unremarkable.

Pt started on Symbicort 80mg BID for asthma and further work up of bronchiectasis with CBC with differential, immunoglobins, Aspergillus antibodies, Aspergillus galactomannan antigen, allergen Aspergillus fumigatus and repeat CT chest was ordered with plan for close follow up in the clinic.

Observations and Investigations

CT Chest with contrast:
Multifocal tree-in-bud nodular opacities within the right upper lobe and to a lesser extent the middle lobes with findings concerning for a possible infectious process as well as bronchiectasis bilaterally in the upper lobes with right greater than left and mucus impaction within the right upper lobe bronchi. Also noted to have a lung nodule in the RUL and transient pulmonary infiltrates.

Bronchoscopy:
Non-diagnostic with negative AFB culture with stain, bronchial culture with no growth, negative legionella culture, negative KOH prep, negative fungus culture, no isolates on viral culture, and grain stain showing only few WBC and very few GPC.

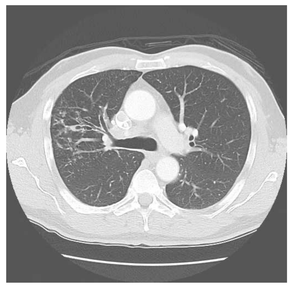

Figure 1 Bronchiectasis

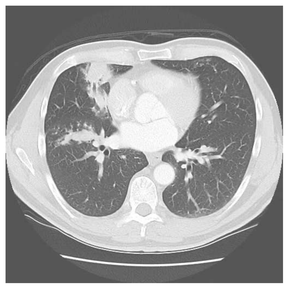

Figure 2 Bronchiectasis and mucus impaction

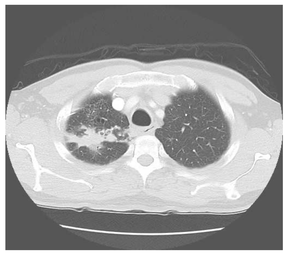

Figure 3 Mucus Impaction

Diagnosis

International Society for Human and Animal Mycology- Allergic Bronchopulmonary Aspergillus Working Group Criteria.

Predisposing condition of either asthma or cystic fibrosis
Obligatory criteria with both needing to be present
- Immediate cutaneous hyper-reactivity to Aspergillus antigens or *Aspergillus fumigatus*-IgE >0.35 kUA/l
- Total IgE >1,000 IU/ml

Other criteria (at least 2 of 3)
- Peripheral blood eosinophil count >500 cells/microliter
- Transient pulmonary infiltrates on chest radiograph
- Presence of precipitans (IgG) against *Aspergillus fumigatus*

Suggested modifications to this criteria have considered bronchiectasis on CT chest to be equivocal to transient pulmonary infiltrates on chest radiography (1).

Aspergillus Fumigatus-specific (m3) immunoglobin E – 29.7, Class 4.
Serum total IgE- initial value of 3,116
Serum total IgM- 139
Serum total IgA- 84
Peripheral blood eosinophil count- 900 cells/microliter.
Aspergillus galactomannan antigen- negative
Aspergillus antibodies- negative

Treatment

The mainstay of treatment of ABPA is with anti-inflammatory medications such as glucocorticoids, anti-fungals to decrease the fungal burden, as well as alternative medications to prevent future disease flairs and limit progression and worsening of bronchiectasis (1).

After the initial diagnosis of ABPA, this patient was started on prednisone 40mg qd for a total of 14 days followed by 40 mg qod and a 4 month course of itraconazole 200 mg BID. After 3 months, prednisone was decreased to 20 mg qod and after another 2 months, prednisone was able to be decreased to 10 mg qod. However, 3 months later the patient developed worsening shortness of breath with associated chest tightness and non-productive cough in which they were diagnosed with a flair of their ABPA. Prednisone was restarted at 40 mg qd for 14 days followed by 20 mg qd and eventual steroid taper for 4 months. Patient was able to tolerate being off of steroids for approximately 5 months, but then presented to the clinic with another flair of his ABPA with noted IgE level of 3,184. Levaquin 500 mg for 10 days was started as well as prednisone 40 mg qd for 14 days with plans for a 3 month taper. After recurrent flairs not being controlled on first-line therapy, Omalizumab was considered. However, the patient developed an allergic reaction to Omalizumab at the site of the injection and was discontinued. Patient developed another flair and prednisone 20 mg qd was restarted and later decreased to 20 mg qod. Referral was placed to allergy clinic for evaluation of starting Mepolizumab every 28 days as an alternative therapy with recurrent flairs. Prednisone was decreased to 10 mg qd and the patient tolerated their first dose of Mepolizumab without any adverse effects. At last clinic visit, prednisone was decreased to 5 mg qod and patient's symptoms were well controlled.

Discussion

Globally, there is an estimated 139 million cases of asthma with approximately 5 million of those cases involving ABPA, 2.5%, with the highest prevalence being in patients that need more specialized care. Likewise, it is imperative that patients that are high risk for this condition are appropriately screened for early diagnosis of this condition with the most accepted screening test of *Aspergillus fumigatus*-specific IgE. Ultimately, the goal of early detection can lead to starting treatment sooner and decreasing the progression of bronchiectasis or preventing it all together (1).

Also, use of alternative agents such as Mepolizumab should be used in patients like this study who continue to have flairs despite use of first-line therapy of glucocorticoids and anti-fungals. Mepolizumab's mechanism of action is an anti-Th2 agent with being a monoclonal antibody targeted against IL-5 which is one of the main cytokines produced in the pathogenesis of ABPA. Further studies are still need to better understand the utilization of Mepolizumab in the treatment of ABPA, but with its targeting of one of the main cytokines that leads to worsening outcomes in these patients, theoretically it could show promise in the treatment of future ABPA patients as well as in the life of our patient (1).

REFERENCES

"Allergic Bronchopulmonary Aspergillosis." *Indian Journal of Medical Research*, 1 Jun. 2020, journals.lww.com/ijmr/Fulltext/2020/51060/Allergic_bronchopulmonary_aspergillosis.6.aspx. Accessed 21 Dec. 2022. *1*