Allergic bronchopulmonary aspergillosis in a 56-year-old female with recently diagnosed asthma

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Introduction

- Aspergillus is an environmentally ubiquitous fungi that has mastered the art of survival, proliferating in even the most inhospitable of domains.[1,2,3]
- This survivability has enabled Aspergillus spp to overcome human immune responses and colonize: a condition known as Aspergillosis.[1,3]
- Invasive aspergillosis is an opportunistic infection occurring after inhalation of Aspergillus fumigatus fungal spores, resulting in significant morbidity and mortality in the immunocompromised as well as those with underlying pulmonary disorders.[1,4,5]
- One form of Invasive Aspergillosis that affects asthma and cystic fibrosis patients in particular through an IgE-mediated hypersensitivity reaction is known as allergic bronchopulmonary aspergillosis (ABPA).[5-7]
- ABPA can be separated into three subclassifications: ABPA-S, ABPA-CB, SAFS.[2,6]

Table 1. Variations among published diagnostic criteria [6]

1977, Rosenberg-Patterson criteria [17, 18]	2013, Truly Minimal Criteria [4]	2013, ISHAM Working Group [9]
Major Criteria	Criteria	Predisposing Conditions
		(1) Asthma, (2) CF
		Obligatory Criteria (both need to be present)
(1) Asthma, (2) Presence of fleeting or fixed pulmonary opacities on chest radiograph, (3) Immediate cutaneous hypersensitivity reaction to Af, (4) Total serum IgE elevated, more than 1000 IU/mL, (5) Precipitating antibodies against Af, (6) Peripheral blood eosinophilia, (7) Central or proximal bronchiectasis with normal tapering of distal bronchi	(1) Asthma, (2) Immediate cutaneous hypersensitivity reaction to Af, (3) Total serum IgE elevated more than 1000 ng/mL (417kU/L), (4) CB in absence of distal bronchiectasis	(1) Type 1 Aspergillus skin test positive (immediate cutaneous hypersensitivity reaction to Af) or elevated IgE levels against Af, (2) Elevated total IgE levels more than 1,000 IU/mL (unless all other criteria is met, then total IgE levels can be less than 1,000 IU/mL)
		Other criteria (two out of three at least)
Minor Criteria		(1) Presence of IgG antibodies against Af or precipitating antibodies, (2) Presence of fleeting or radiograph pulmonary opacities consistent with ABPA, (3) Eosinophil count more than 500 cells/μL in steroid naïve patient (may be a historical value)
(1) Golden brown sputum plugs in expectorant, (2) Positive sputum culture for Aspergillus species, (3) Late (arthus-type) skin reactivity to Af		

Adapted from Patel AR, Patel AR, Singh S, Singh S, Khawaja I. Treating Allergic Bronchopulmonary Aspergillosis: A Review. Cureus. 2019;11(4):e4538. Published 2019 Apr 24. doi:10.7759/cureus.4538

Fig 1. Bronchiectasis on computed tomography [6]

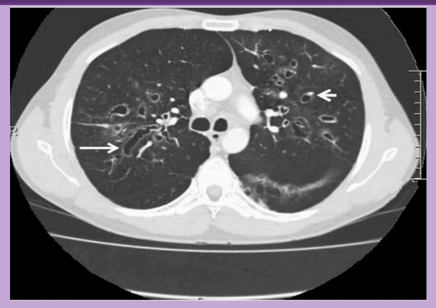


Image obtained from Patel AR, Patel AR, Singh S, Singh S, Khawaja I. Treating Allergic Bronchopulmonary Aspergillosis: A Review. Cureus. 2019;11(4):e4538. Published 2019 Apr 24. doi:10.7759/cureus.4538

Case Description

Brief History

- A 56-year-old female with recently diagnosed asthma presented to the ED with worsening shortness of breath of one week duration.
- En route oxygen saturation was 84% on room air.
- Patient was admitted to the hospital for a presumed asthma exacerbation.
- Past Medical History: Migraines, Mitral valve prolapse, recently diagnosed asthma
- Past Surgical History: Appendectomy, Tonsillectomy
- Medications:
- Family History: None
- Allergies: None
- Social History: non-smoker, no history of alcohol or drug usage
- Review of Systems: (+) dyspnea, (+) chest tightness, (+) wheezing; (-) fever, (-) chills, (-) congestion, (-) sore throat.

Physical Exam

- Gen: Ill-appearing, moderate respiratory distress
- Resp: Accessory muscle use, tripoding, tachypnea, No retractions, no stridor, decreased lung sounds globally, Inspiratory wheezing and rhonchi audible
- Cardiac: Regular rate and rhythm; Tachycardia
- Neuro: Alert & oriented x3; Anxious demeanor

Vitals

- Temp: 98.6 F
- HR: 90 beats per minute
- RR: 35 breaths per minute
- BP: 151/71 mmHg
- SpO2: 98% on 8 L/min oxygen via nebulizer

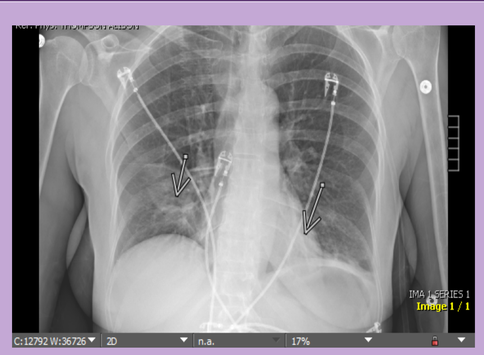
Initial Diagnostic Testing

- CBC – unremarkable
- CXR- hyperinflation; no obvious infection
- EKG- normal sinus
- COVID- negative
- Urine Culture- NGTD
- Blood Culture- NGTD

Table 2. Inpatient Diagnostic Testing

Test	Result
Chest X-Ray	▪ Bilateral lower lobe pneumonia.
CTA Chest w/ IV Contrast	▪ No pulmonary embolism. ▪ Occlusion of the right middle, right lower, and left lower lobe bronchi reflecting mucoid impaction and/or aspiration. ▪ Post obstructive atelectasis in the right middle lobe, postobstructive pneumonitis in the right lower lobe, and postobstructive pneumonia in the left lower lobe.
Lower Respiratory Culture	▪ Specimen: Sputum ▪ Culture: 2+ MOLD ▪ Gram Stain: 3+ WBC, Mixed Flora
Sputum Culture Speciation	▪ 1+ Aspergillus fumigatus ▪ 1+ Candida albicans ▪ 1+ Aspergillus species, not A. Fumigatus

Fig 2. Patient Chest X-Ray



Hospital Course

- Hospital Day 1– Patient started on albuterol, ipratropium, corticosteroids with shown improvement in peak flow. Patient alternated between venti mask and nasal cannula for supplemental oxygen.
- Hospital Day 2 – Patient continued to experience cough and chest tightness with frequent desaturations. Physical exam revealed poor air movement bilaterally in lower lobes and inspiratory wheezing in right upper lobe.
- Hospital Day 3 – Repeat CXR order (Table 2.) 7-day course of antibiotics for community acquired pneumonia was started. Sputum culture still NGTD.
- Hospital Day 4 – Duoneb reduced from TID to BID per patient request. Saturations persistently between 92-96% on 6L nasal cannula. CTA ordered to rule out PE (Table 2.)
- Hospital Day 5 – Patient experienced persistent hypoxia with non-productive cough and significantly worsened shortness of breath. Guaifenesin, Chest PT, Acepella, and Metanet were added to treatment regimen.
- Hospital Day 6 – Patient continued to improve decreasing supplemental oxygen requirement from 6L to 4L nasal cannula with o2 sat of 97%. Steroid tapered from BID to QD. Repeat COVID negative. Mucomyst added to treatment regimen
- Hospital Day 7 – Supplemental O2 weaned to 2L with 90% saturation on room air. Peak flow improved to 250 liters/min. Lower respiratory culture grew 2+ mold.
- Hospital Day 8 – Pt removed from supplemental oxygen with saturation of 95% on room air. Speciation revealed 2+ Aspergillus fumigatus
- Hospital Day 9 - Pt is discharged with pulmonary follow up outpatient.

Discussion

- The global burden of ABPA is approximately 4.5 million.
- Many patients go undiagnosed due to extreme variance in patient presentation.[8]
- To date there is no universally accepted diagnostic criteria for ABPA.[2,9]
- The main goals of treatment include:
  - Controlling asthma or cystic fibrosis symptoms,
  - Preventing and/or treating pulmonary exacerbation,
  - Remitting pulmonary inflammation, and
  - Reducing progression of pulmonary disease
- Corticosteroids remain the universally recommended initial treatment, but the course of treatment is individualized
- Itraconazole and voriconazole can be used to reduce fungal load, dampening the inflammatory reaction.[2-6,9]
- The use of monoclonal antibodies remains controversial but has been reported to show positive outcomes in patients with ABPA.[10]
- Treatment monitoring is recommended to be conducted bimonthly using serum IgE concentrations.[9]
- When left untreated, sequelae include:
  - Bronchiectasis
  - Severe persistent asthma
  - Pulmonary fibrosis
  - Eventual loss of pulmonary function[4,6,7]
- Research is currently being conducted on potential diagnostic biomarkers to hasten diagnosis and streamline treatment.[3]

Conclusion

- Due to scarcity in publication and notoriety, ABPA is rarely included among a clinician's differential when treating acute asthma or cystic fibrosis exacerbation.
- Delay in diagnosis has been linked to a number of lasting pulmonary sequelae in patients with ABPA.
- Corticosteroids remain the most widely used initial treatment for ABPA
- Itraconazole, Voriconazole, and off-label Omalizumab have also shown improved patient outcomes.
- There is currently no standardized diagnostic criteria or treatment protocol for ABPA

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