Pulmonary Aspergillus

Key Points:
- Aspergillus pulmonary disease takes three main forms: invasive aspergillosis, aspergilloma, and ABPA (allergic bronchopulmonary aspergillosis). The first two are much more severe and present very differently from ABPA.
- Invasive aspergillosis usually occurs in patients who are already immunocompromised; it is diagnosed by biopsy stains plus biopsy culture, but persistently positive sputum cultures in the appropriate patient population have a high PPV.
- Aspergillomas are fungus balls in cavities that are usually pre-existing; treatment is surgical resection.
- ABPA most commonly presents like treatment-resistant asthma with brown sputum and fleeting pulmonary infiltrates as well as eosinophilia.

From most to least severe…
1. Invasive aspergillosis: Usually occurs in patients who are somehow immunocompromised. Aspergillus is angioinvasive, so it may result in pleuropulmonary hemorrhage or more commonly infarction.
   - Usually presents with persistent fevers; may have chest pain, cough and hemoptysis
   - CXR may be normal in up to 10% of cases, or may show wedge-shaped pleural-based densities late in the disease; chest CT will pick up more subtle infarctions early on and is rarely normal
   - Diagnosis is made by evidence of the fungus on special stains of biopsied lung PLUS positive cultures for Aspergillus from the biopsy specimen. Positive sputum cultures, while not diagnostic, should be taken seriously in immunocompromised patients, as they have a positive predictive value of 80-90% in that population. BAL washings are similarly useful but not diagnostic.
   - Treatment usually begins with IV amphoterocin and then a transition to po itraconazole later in the course. Two studies have been performed with po itraconazole alone that showed efficacy comparable to IV ampho, but standard practice still seems to be to begin with IV ampho.
   - Fungus ball (a.k.a. “mycetoma”) develops in parenchymal cavity; classic “crescent” sign around fungus ball within cavity
   - Cavitary lung lesions may be created by the aspergillus itself (less common) or may be pre-existing from TB, sarcoid, malignancy, other fungal disease (histo, cocci), Wegener’s, RA, or cystic fibrosis
   - Most common presentation is hemoptysis (75%), which may be massive
   - Diagnosed by typical CXR findings plus positive serologic tests for aspergillus OR multiple positive sputum cultures
   - May progress to invasive aspergillosis
   - Treatment is surgical resection; however, the procedure carries a high morbidity and mortality. Others have tried oral itraconazole or intra-cavitary amphotericin, but these are less successful than surgery. Alternatively, bronchial artery embolization has been performed in some patients, but this is mostly useful as a temporizing measure in cases of life-threatening hemoptysis.
3. ABPA: Allergic Bronchopulmonary Aspergillosis; think of this as more of a hypersensitivity reaction than an infection
   - Presents as asthma not responsive to conventional treatment; classically with eosinophilia of blood and sputum, and brownish phlegm production. In some cases, wheezing may be absent.
   - Commonly occurs in patients with CF
   - Seven diagnostic criteria proposed: (presence of 6 = probable ABPA; 7 = diagnostic)
     i. Episodic asthma
     ii. Peripheral blood eosinophilia
     iii. Scratch test reactivity to Aspergillus
     iv. Serum precipitins to Aspergillus
     v. Elevated serum IgE levels
     vi. History or presence of fleeting pulmonary infiltrates
     vii. Central bronchiecstasis
   - No good RCT’s on treatment, but standard care is corticosteroids (prednisone 0.5 mg/kg/d) +/- itraconazole
References
-- Fishman’s *Pulmonary Diseases and Disorders*, 3rd ed. 1998.