Manifestations of Pulmonary Aspergillosis

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Case Presentation: Patient P.R.

- **CC:** P.R. is a 69-year-old Caucasian female with a hx of COPD and heavy smoking who presents with hemoptysis.

- **HPI:** The pt. was sitting at the hairdresser’s one day when she suddenly began to cough up several tablespoons of blood. She denies fevers/chills/sweats or syncope. She has lost 18 lbs. in the past 18 months. She denies recent foreign travel.

- **PMH:** COPD (oxygen-dependent)
  Interstitial Lung Disease
  Anemia

- **Social Hx:** 25 pack-year smoking history
Case Presentation, continued: P.R.

Physical Exam:

Gen:  Cachectic, bedridden, on oxygen
CV:   RRR
Lung: Bibasilar crackles, R>L
Abdomen: non-tender, non-distended
Neuro: non-focal

Labs:  WBC 22    HCT 37

What is this patient’s baseline?
Radiographic features: Lungs are hyperinflated with diaphragmatic flattening. Increased interstitial markings throughout. Volume loss in the right lung, with shift of hilum. Pleural thickening bilaterally (R>L).
P.R.: CXR on presentation

Radiographic features: CXR initially read as “no significant change from baseline.” But CT performed later that day revealed a right apical mass. Can you see it on CXR?
Differential Diagnosis:
Solitary Nodule (<4 cm)

Common:

• Bronchial adenoma
• Bronchogenic carcinoma
• Granuloma (TB, histo, coccidiomycosis)
• Hamartoma
• Metastasis
Differential Diagnosis with Clinical Hx

Clinical history includes weight loss, hemoptysis…

- **Bronchogenic carcinoma** (smoking-linked: squamous, small cell ca.)

- **Tuberculosis** (reactivation in apices?)
P.R.: CT on presentation

Radiographic features:

- R. apical cavity filled with dependent, **sponge-like debris**.
- Volume loss in the right lung.

Note: Irregularly shaped, sponge-like mass in a cavity is highly suspicious for...

**mycetoma**, or “fungus ball.”
Differential Diagnosis:
Mass Within a Cavity

Most common cause: **Fungus Ball**
(most common species is *Aspergillus fumigatus* or *Aspergillus flavus*, so it is also termed “aspergilloma”)

Other causes:  
Blood clot in tuberculous cavity  
Abscess with inspissated pus  
Cavitated tumor with debris
Aspergillus is a ubiquitous dimorphic fungus found especially on decaying vegetation. It can cause pulmonary disease under unique circumstances: (1) pre-existing cavitary lung disease and (2) immunocompromised states. Histologically, it consists of branching, septate hyphae. Its most common portal of entry is the respiratory tract.
The Varied Forms of *Aspergillus* Infection

- **Mycetoma** – a fungal mass growing inside a pre-existing lung cavity.

- **Semi Invasive and Invasive Pulmonary Aspergillosis** – organism erodes through tissue and into blood vessels.

- **Allergic Aspergillosis** – fungus acts as an antigen and initiates hypersensitivity reaction in the respiratory tree (usually in asthmatics).
What Is a Mycetoma?

• **Definition**: A fungal mass growing inside a pre-existing lung cavity that can be associated with significant morbidity and mortality in certain patient populations.

• **Risk fx**: Chronic lung disease
  
  Hx of cavitary lung disease
  - TB, sarcoid, histoplasmosis, PCP (in HIV+)
  - Lung abscess
  - Cancer
  - Bronchiectasis, emphysematous bullae
  - Pulmonary infarcts

• **Epidemiology**: approximately one in a million

• **Uncommon for mycetoma to progress to invasive form.**
Mycetoma: Clinical Considerations

- **Clinical features**
  - Patients often asymptomatic
  - If symptomatic, **hemoptysis** is the most common CC. Over 70% will experience hemoptysis during their course. > 25% will have severe hemoptysis (> 150 ml/d).
  - In HIV+ patients: **fever** may be present.

- **Diagnosis**
  - Radiologically: CXR, CT
  - Bronchoscopy (obtain specimen for culture)
  - Sputum culture

- **Menu of tests**: Follow with CXR, CT if symptoms worsen or do not improve. Try lateral decubitus on CXR. Note: CT is the more sensitive test.
**Mycetoma: Radiologic Features on CXR**

**Classic features:**

- **rounded mass** in pre-existing cavity
- **“air-crescent”** sign
- **pleural thickening**
- **upper lobe propensity**

Note: Mycetoma has worsened over 2 weeks.

Patient P.R.: AP View
(2 weeks after presentation)
Mycetoma: “Air-Crescent” Sign on CXR

The “air-crescent” or “meniscus” sign indicates the presence of a mass within a pre-existing cavity. This is a patient with a fungus ball in the right apical cavity.
Mycetoma: Mass Within Old Cavities

Figure A.
Fig. A. shows a **fungus ball** growing within an old tuberculous cavity (CXR). Note the very thin **air crescent**.

Figure B.
Fig. B. shows cavitary pulmonary sarcoidosis with an **aspergilloma**, gross cut surface of the lung.
Mycetoma: Radiologic Features on CT

P.R.: Axial CT, 2 weeks after presentation.
P.R.: Axial CT, on presentation.

Classic features: (1) Irregular, sponge-like mass in an apical cavity. (2) Pleural thickening. (3) Air-crescent consolidation sign. Note further consolidation adjacent to mass. Also note presence of bullae, which are risk factors for mycetoma.
Mycetoma: Additional CT Images

Fig. A. is an axial CT of an HIV+ positive patient with a left lung aspergilloma. Note mass and walled cavity. This patient went on to develop invasive aspergillosis.

Fig. B. is an axial CT of a fungus ball in the right lung. Note attachment to chest wall.
Mycetoma: Treatment and Prognosis

• **Treatment:**
  - Asymptomatic: nothing
  - Symptomatic: 1. Surgical excision of affected lung
  2. Arterial embolization of bleeding vessel
  3. Intracavitary placement of antibiotics
  4. IV amphotericin B x 2 weeks and lifelong oral itraconazole (as in P.R.’s case)

• **Prognosis:**
  – Non-AIDS → 8% mortality (massive hemoptysis)
  – AIDS (CD4 < 100) → 50% disease progression

Immune status largely determines prognosis.
What is Invasive Pulmonary Aspergillosis? (IPA)

• **Definition**: A fungal infection of the lung in which the organism erodes through lung tissue and invades blood vessels, resulting in hemorrhagic infarction of lung tissue. Broadly disseminated infection may also occur. This infection is associated with a high mortality rate.

• **Risk factors**: Immunosuppression (neutropenia)
  - BMT
  - Hematologic malignancy
  - Solid organ transplant recipients
  - AIDS (CD4 < 50) (esp. hx of pulmonary CMV, PCP)
  - High-dose steroid use + Diabetes may result in semi-invasive Aspergillosis
IPA: Clinical Considerations

- **Clinical Features**: fever, cough, dyspnea, pleuritic chest pain, new pulmonary infiltrate unresponsive to antibiotics.

- **Diagnosis**:
  1. **Tissue biopsy** with isolation of fungus on culture or histopathology. (open lung or bronchoscopy with transtracheal biopsy)
  2. **Brochoalveolar lavage (BAL)** positive for *Aspergillus*, in the appropriate clinical context.
  3. **CT**: nodule with “halo sign,” plus BAL positive for *Aspergillus*

Note: Sputum, blood cultures rarely positive.
IPA: Menu of Tests

- **Radiologic tests**: CXR, CT.

- According to one study…
  - **CXR**: > 70% of pts. with IPA had abnormalities suggestive of IPA. 10% were normal. But is it specific?
  - **CT**: > 85% of pts. with IPA had abnormalities suggestive of IPA.

- Follow patients clinically. If suspect that infection is worsening: CXR, CT again. **CT more sensitive.**
IPA: Radiologic Features on CXR

Diverse features:
- Patchy or diffuse infiltrates (> 70%)
- Multiple nodules (often abutting pleural surface) (14%)
- Cavitary disease (central cavitation within pulmonary opacities) (> 30%)
- “Air-crescent” sign – this time referring to lung infarction and retraction, leaving a rim of air around the opacity. A good prognostic sign: 67% survival with sign.

CXR: AP View, lateral decubitus. This is a 4-year-old immunocompromised child with IPA.
Fig. A. illustrates patchy infiltrates in a diabetic patient with IPA. This infection can mimic other bilateral pneumonias on CXR. Fig. B. illustrates multiple bilateral nodular densities as well as two large, irregular, thick-walled cavities in the right lung.
IPA: Radiologic Features on HRCT

Axial HRCT of a 50-year-old patient with leukemia who developed IPA.

Classic feature: Pulmonary mass(es) or nodules surrounded by a zone of lower attenuation: the “halo sign.” This represents an inner mass of coagulative necrosis with a rim of hemorrhagic infarction. This patient has a soft-tissue nodule in the RUL.
Axial HRCT of a 29-year-old patient with leukemia who developed IPA.

Extensive destruction: This picture shows bilateral, mostly peripheral (abutting pleural surface), areas of consolidation representing hemorrhagic infarction of lung tissue.
IPA: Treatment and Prognosis

• **Treatment:**
  IV amphotericin B x 2 weeks plus lifelong oral itraconazole. Surgical intervention may be necessary. Therapy often ineffective.

• **Prognosis:**
  Depends on severity of immunosuppression.
  Overall: 26-65% mortality
  AIDS patients: > 80% mortality
In Summary…

- **Aspergillus** is a ubiquitous fungus that occasionally takes up residence in the human respiratory tract under the following conditions: (1) pre-existing cavitary lung disease or (2) states of severe immunosuppression.
- **Worrisome manifestations** of this infection include (1) minimally-invasive mycetomas and (2) invasive pulmonary aspergillosis.
- **Radiology** – CXR, CT – contributes a great deal to detection and diagnosis.
- **Mycetomas** are virtually pathognomonic on CT but are sometimes obscured on CXR. They are a common cause of the “air-crescent sign.” **IPA** often mimics other pneumonias on CXR, but it is often associated with a “halo sign” on CT, representing angioinvasion.
- **Immunosuppression** is crucial to the development of IPA, but not to the development of mycetomas. In both circumstances, however, **immune status largely determines outcome.**
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