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Pulmonary Aspergillosis

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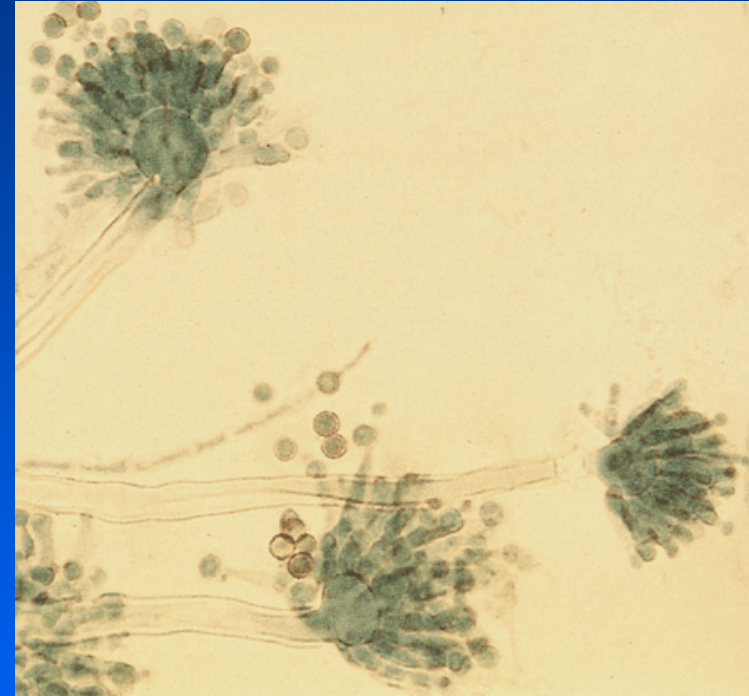
Overview

- Pulmonary aspergillosis background information
- Patient presentations
- Common radiographic findings for each type of pulmonary aspergillosis
- Summary



Aspergillus: the Facts

- *Aspergillus* - a fungus that is ubiquitous in the soil.
- It has low pathogenicity, therefore affected patients have either underlying chronic lung disease and/or impaired immunity.
- Manifestations of pulmonary aspergillosis depend on the virulence and number of spores inhaled, on the patient's immune status, and on the presence of any underlying chronic lung disease.



Franquet et al. *Radiographics* 2001



The 4 Types of Pulmonary Aspergillosis

1. Saprophytic aspergillosis
(aspergilloma/mycetoma)
2. Hypersensitivity reaction (allergic
bronchopulmonary aspergillosis)
3. Semi-invasive (chronic necrotizing)
aspergillosis
4. Angioinvasive aspergillosis



Patient 1 – Mr. H.

History:

- Mr. H. is a 46 y.o. man with h/o end-stage renal disease secondary to amyloidosis s/p living donor related renal transplant, sarcoidosis, and hepatitis B, C, and D who p/w non-productive cough and dyspnea x 2 weeks.
- He denies fevers, chills, sick contacts, or recent travel.
- He has been taking all of his immunosuppressive medications (CellCept, Prednisone, Prograf, Valcyte) regularly.
- He smokes 0.5 packs/day. Past IVDU. Denies EtOH use.

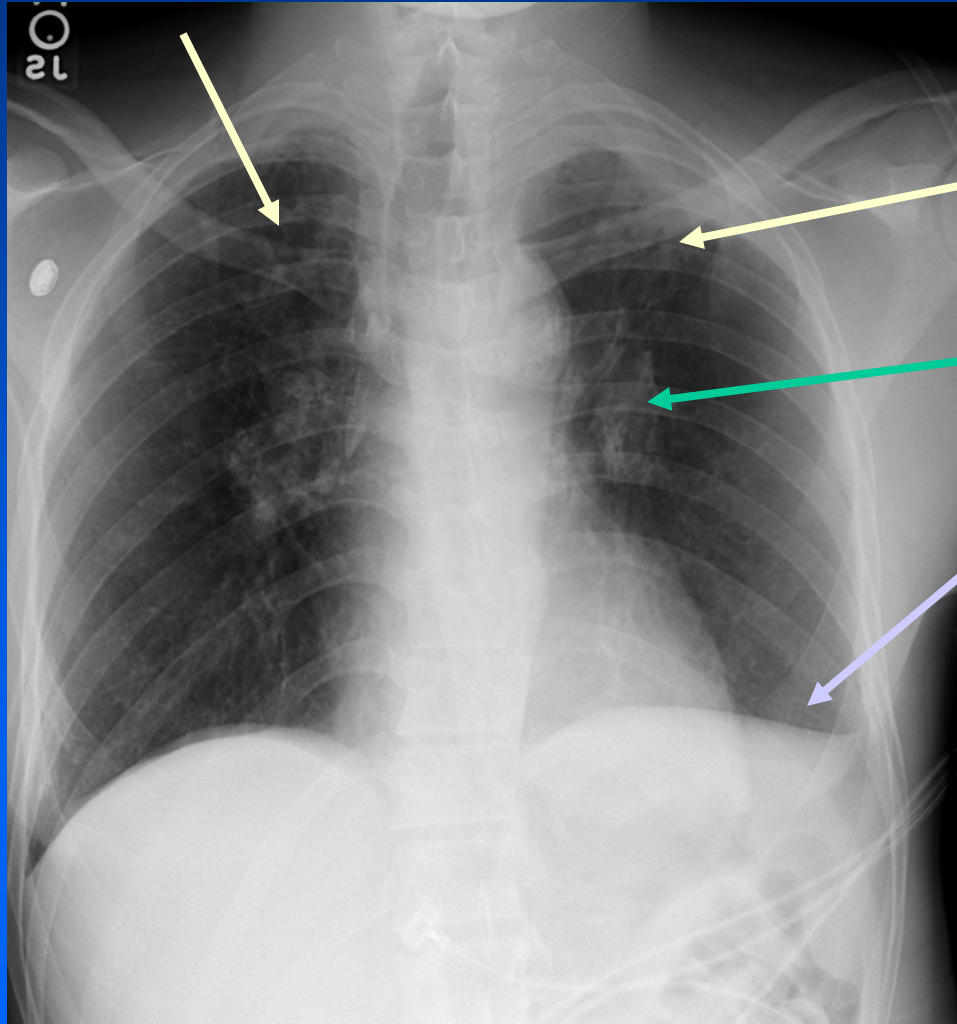
Physical Exam:

- Afebrile, RR 32, O2sat 95% on RA, sharp “barking” cough, bilateral posterior inspiratory crackles.

Labs: WBC 1.8, ANC 1160



Mr. H.'s Radiograph



Scarring and pleural thickening of the lung apices

Superior retraction and fullness of the hila bilaterally

Blunting of the left costophrenic angle

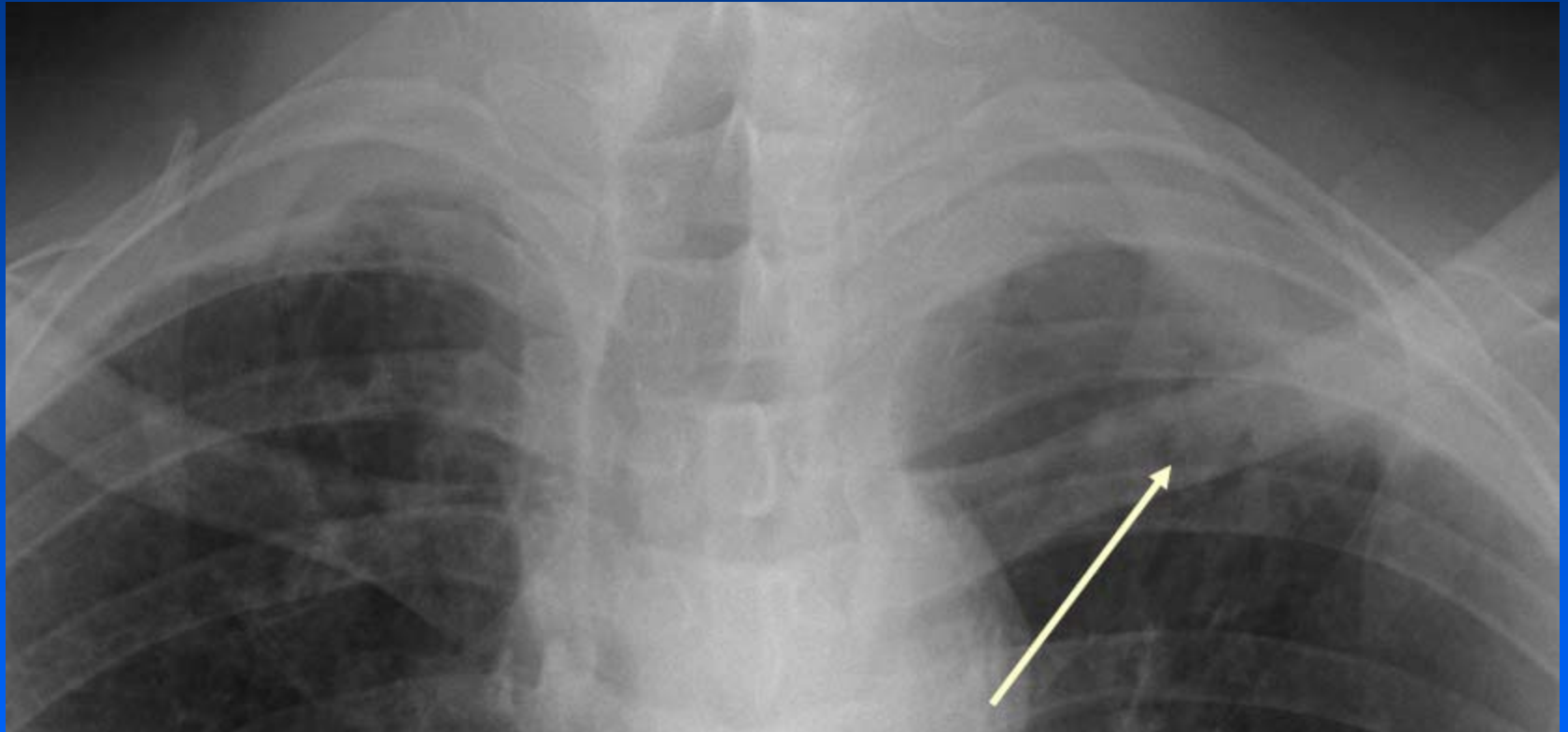
Patchy opacities scattered throughout both lungs.

All findings secondary to sarcoidosis and stable from CXR taken within the last 2 years.

PACS, BIDMC



A Closer Look at the Apices

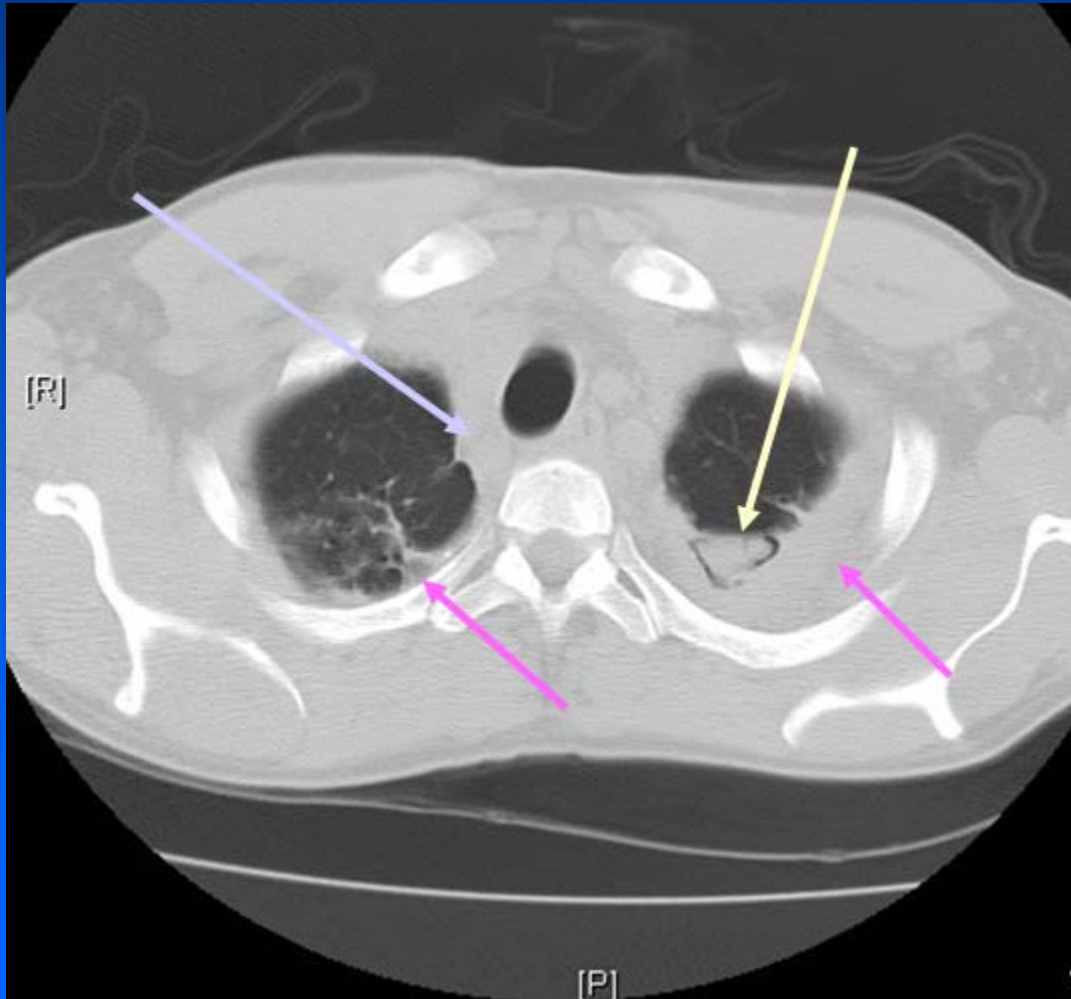


Nodular opacification
surrounded by air

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Mr. H.'s Chest CT



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Cyst in the left apex with rounded soft tissue opacity surrounded by a crescent of air.

Enlarged paratracheal/bronchial lymph nodes

L>R ground glass opacification at the apices with pleural thickening.

All findings are stable from previous chest CT except for the soft tissue opacity with “air crescent” sign in the L apex.



Differential Diagnosis

“Air-crescent” sign

- Aspergilloma/mycetoma
- Angioinvasive aspergillosis (during recovery)
- Tuberculosis
- Tuberculous cavity with a Rasmussen aneurysm
- Lung abscess
- *Pneumocystis carinii* pneumonia
- Cavitating bronchogenic carcinoma
- Hematoma



Narrowing the Ddx:

- Sputum culture was positive for *Aspergillus* species, all other cultures/stains (TB, PCP, RSV Ag) were negative.
- Diagnosis: Aspergilloma (a.k.a. mycetoma, fungus ball) or angioinvasive aspergillosis during the recovery phase.
- Given the patient's history of sarcoidosis and ANC of >1000 , it was felt that the radiographic finding is more likely aspergilloma.



Aspergilloma

- *Aspergillus* colonization of preexisting cavities to form a mycetoma (a fungal mass).
- The most common underlying causes are **tuberculosis, sarcoidosis and bronchiectasis**. The host is typically immunocompetent.
- Sometimes associated with bronchogenic cyst, pulmonary sequestration, pneumatoceles secondary to PCP in AIDS patients.
- Clinical manifestation – chronic cough, hemoptysis
- Treatment: 10% resolve spontaneously, anti-fungal medication (fluconazole, itraconazole, or IV amphotericin B)
- Surgical resection for patients with severe life-threatening hemoptysis or selective bronchial artery embolization



Patient 2 – Mr. R.

History:

- Mr. R. is a 73 y.o. man with history of transfusion dependent AML with chronic neutropenia x 2yrs, who presents with non-productive cough x 6 months, worse in the evenings.
- No improvement with short courses of Azithromycin or Levaquin.
- Denies fevers, chills, night sweats.
- Non-smoker, no EtOH use

Physical Exam:

- VS: T 98.8°F, BP 139/71, P 120, RR 20, O2 sat 96% RA
- Chest: clear to auscultation

Labs: WBC 2.3, 8% Neutrophils, ANC 184



Relation of Absolute Neutrophil Count to Risk of infection

Absolute neutrophil count/microL

Risk management

>1500

None

1000-1500

No significant risk of infection; fever can be managed on an outpatient basis

500-1000

Some risk of infection; fever can occasionally be managed on an outpatient basis

<500

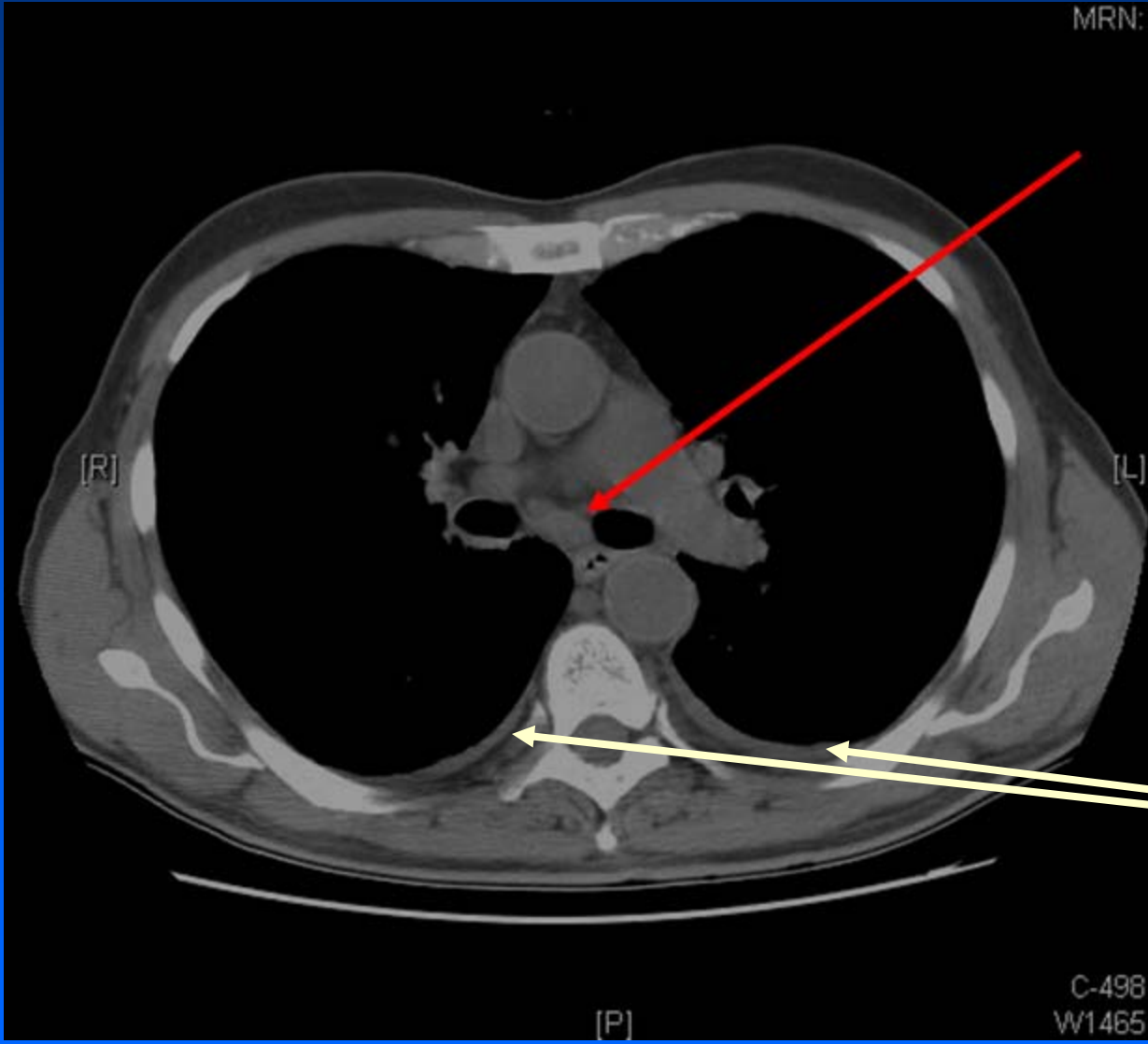
Significant risk of infection; fever should always be managed on an inpatient basis with parenteral antibiotics; few clinical signs of infection

<200

Very significant risk of infection; fever should always be managed on an inpatient basis with parenteral antibiotics; few or no clinical signs of infection



Mr. R.'s Chest CT



MRN:

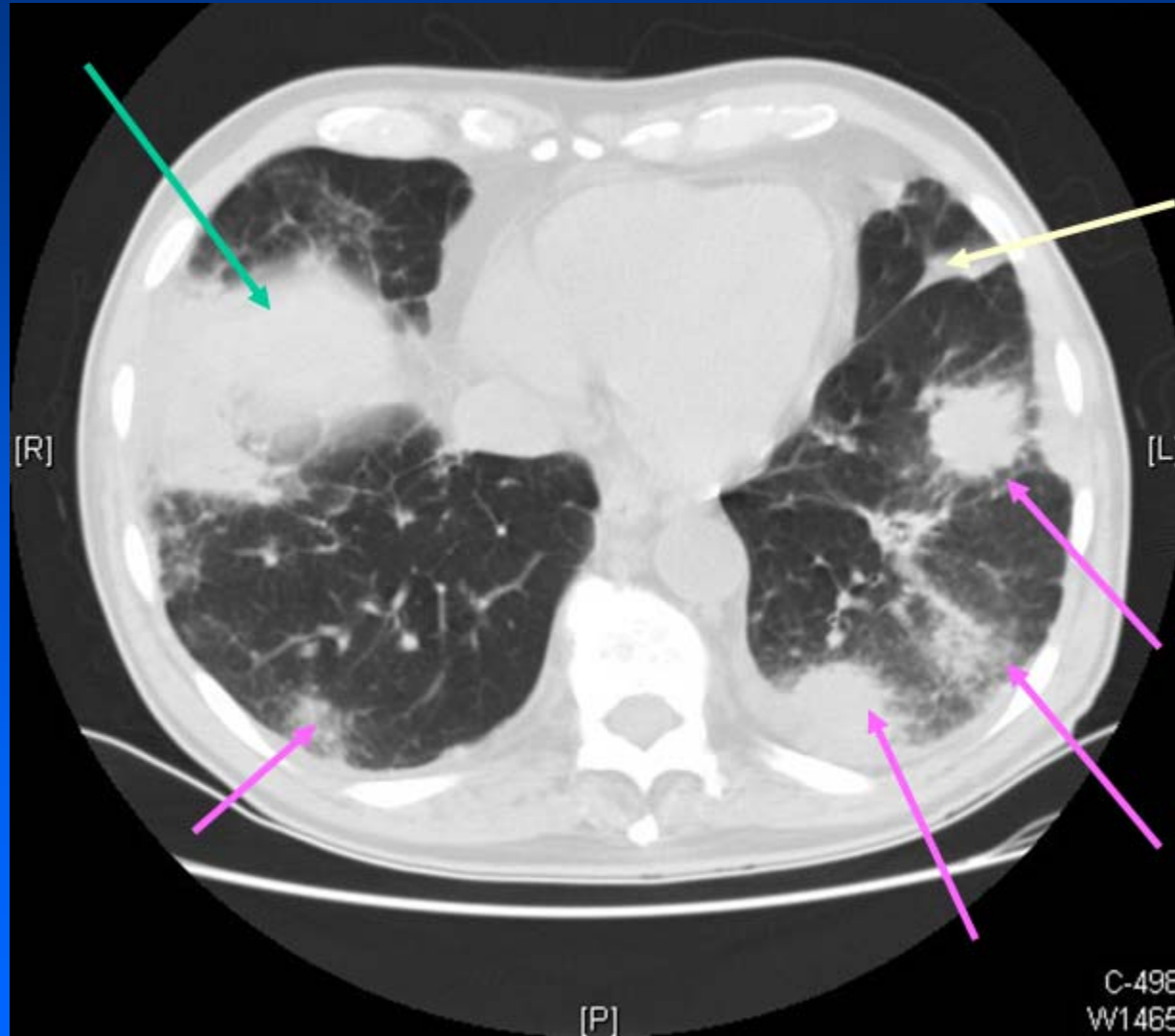
Enlarged
subcarinal lymph
nodes

Bilateral Pleural
Effusion

PACS, BIDMC



Mr. R.'s Chest CT



Left lung major fissure with pleural thickening/fluid

Multifocal rounded consolidations with irregular margins and surrounded by a “halo” of ground-glass opacification

Wedge shaped consolidation along the R major fissure surrounded by ground-glass opacification.



Differential Diagnosis

The differential for multiple nodules with ground-glass “halo” on CT should include any process that could cause hemorrhage around multiple nodules or infarcts.

- Angioinvasive aspergillosis
- Infection by TB, *Mucorales*, *Candida*, herpes simplex, and Cytomegalovirus
- Wegener’s granulomatosis
- Kaposi sarcoma
- Hemorrhagic metastases
- Bronchoalveolar carcinoma



Narrowing the DDx

- Pt was taken to bronchoscopy and for VATS.
- Pathology of a wedge resection of the right lower lobe showed necrotizing and organizing fungal pneumonitis, with fungal morphology consistent with *Aspergillus* species.
- Diagnosis: invasive pulmonary aspergillosis



Angioinvasive aspergillosis

- Occurs almost exclusively in **immunocompromised patients** with severe **neutropenia**.
- Pathology: invasion and occlusion of small to medium-sized pulmonary arteries by fungal hyphae leading to formation of necrotic hemorrhagic nodules or pleura-based, wedge-shaped hemorrhagic infarcts.
- Clinical manifestations: cough, pleuritic chest pain, hemoptysis
- Treatment: long-term antifungal medications, surgical resection



Angioinvasive Aspergillosis on HRCT

Findings

- Ill-defined nodules or focal consolidation with a halo sign (early)
- Cavitory nodules with air-crescent sign (late)
- HRCT is more sensitive in detecting nodules suggestive of fungal infection earlier in immunocompromised patients than radiograph and BAL culture.
- Bronchoscopy and VATS are often not an option in severely immunocompromised patients.
- Early detection and treatment with antifungal or surgical resection dramatically improve the prognosis of patients with angioinvasive aspergillosis.

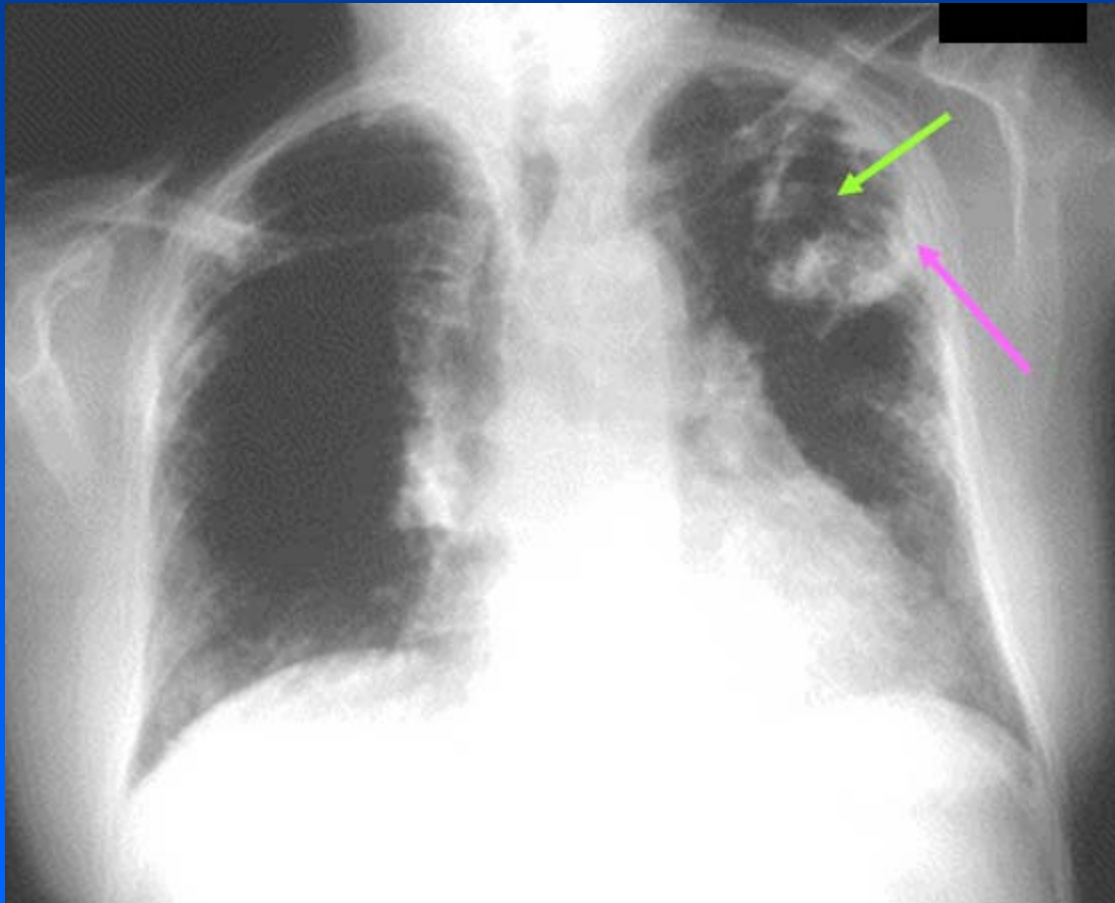


Chronic Necrotizing Aspergillosis

- Tissue necrosis and granulomatous inflammation (similar to that seen in reactivation TB), due to growth in the alveolar spaces with hemorrhage and bronchial wall invasion. No angioinvasion.
- Most commonly seen in patients with chronic debilitating illness (i.e. advanced age, diabetes, poor nutrition, alcoholism, steroid treatment).
- Clinical manifestations: insidious in nature. Chronic cough, sputum production, fever, weight loss, anorexia, hemoptysis.
- Diagnosis: abnormal findings on radiography and bronchoscopic biopsy consistent with tissue invasion
- Treatment: long-term antifungal medication



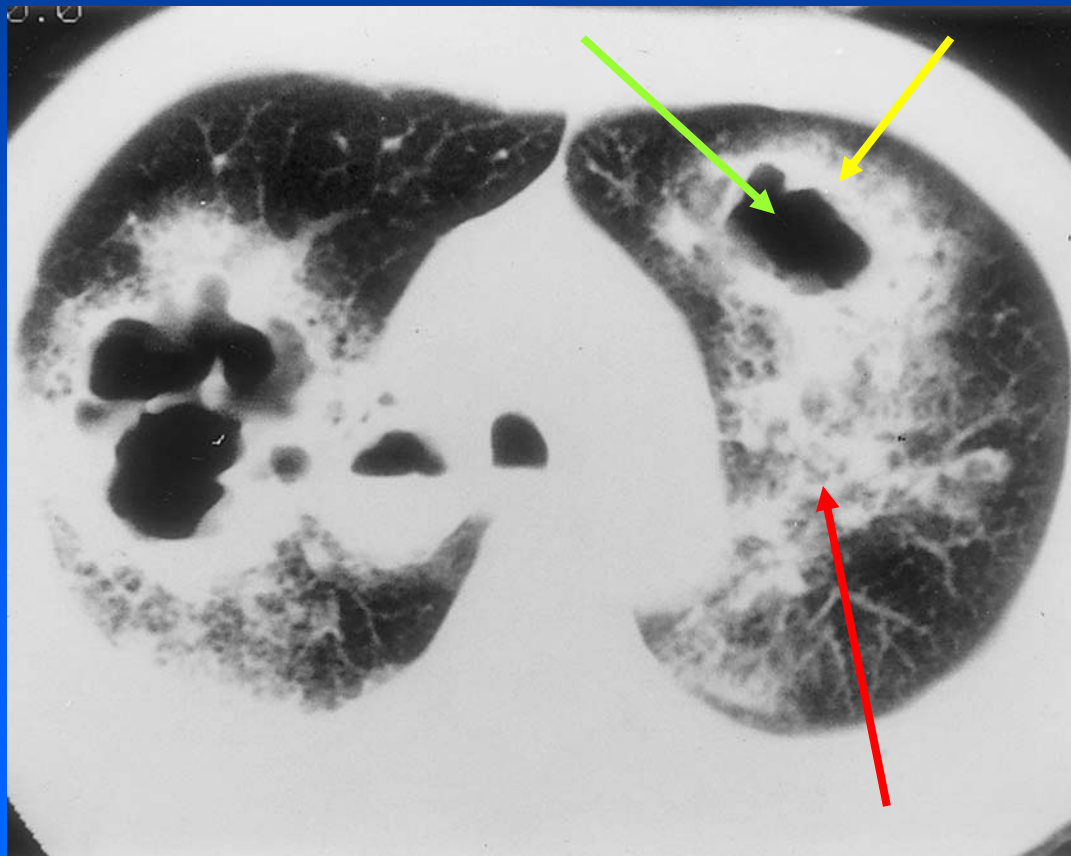
Radiographic findings of chronic necrotizing aspergillosis



CXR: Slowly progressive upper lobe consolidation predominantly with cavitation or pleural thickening, and multiple nodular areas of increased opacity.



Radiographic findings of chronic necrotizing aspergillosis



CT: cavitation with **bronchial wall thickening** and bronchial obstruction with **obstructive pneumonitis or collapse**.

DDx of thickening and narrowing of a central bronchus: mucormycosis, tuberculosis, amyloidosis, and sarcoidosis.

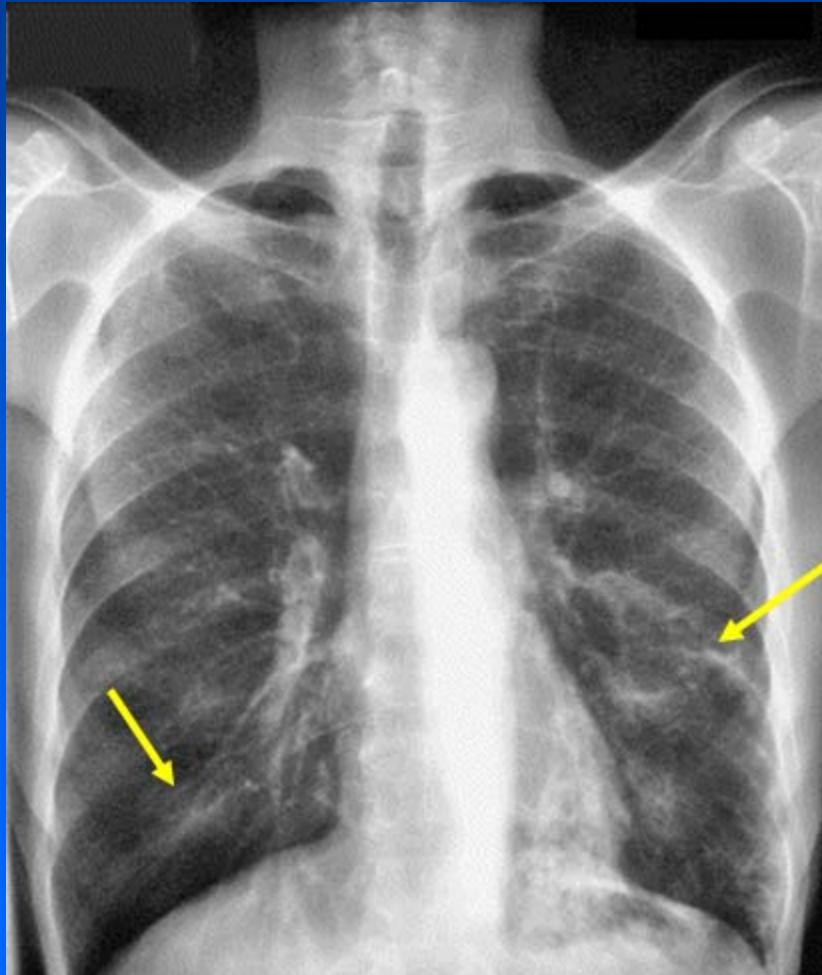


Allergic Bronchopulmonary Aspergillosis

- Most commonly seen in patient with long-standing asthma or cystic fibrosis.
- Complex hypersensitivity reaction to *Aspergillus* with immune complex deposition in the bronchial mucosa leading to necrosis and eosinophilic infiltrates with damage, resulting in bronchial dilation of the segmental and subsegmental bronchi
- Clinical manifestations: recurrent wheezing, low-grade fever, cough, sputum production. H/o recurrent pneumonia.
- Diagnosis: asthma, eosinophilia, elevated IgE, + skin test, pulmonary infiltrates and central bronchiectasis on CXR/CT.
- Treatment: corticosteroids



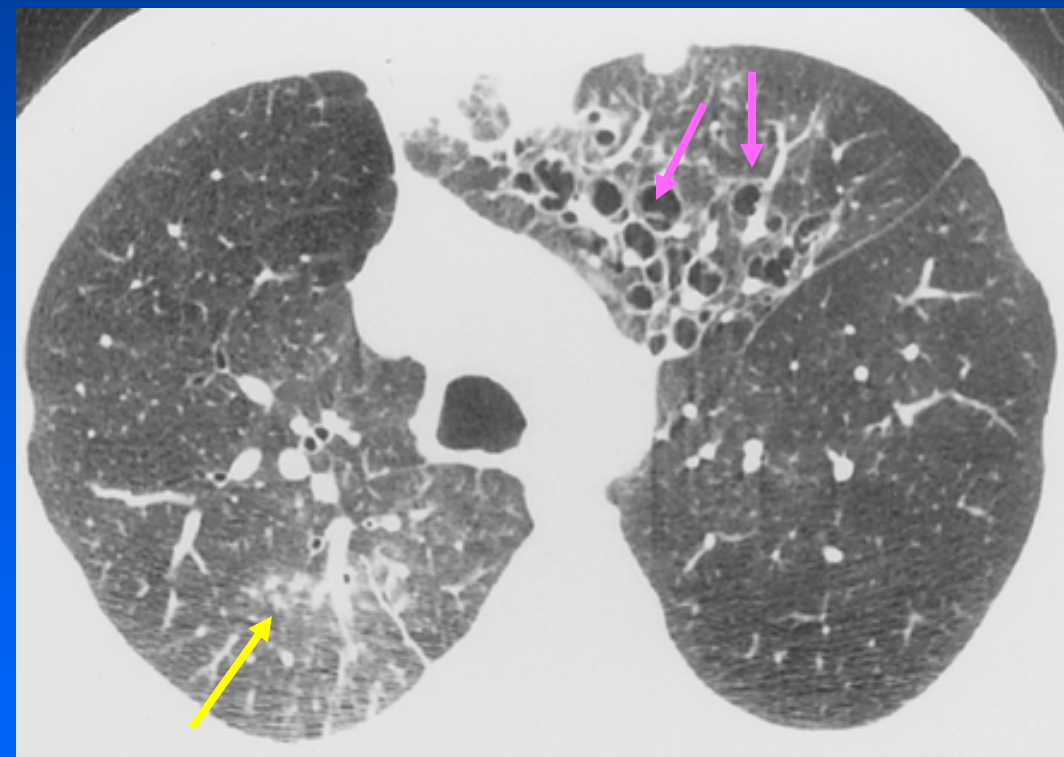
Radiographic findings in allergic bronchopulmonary aspergillosis



CXR - homogeneous, tubular, “finger-in-glove” areas of increased opacity in a bronchial distribution



Radiographic findings in allergic bronchopulmonary aspergillosis



On CT – **mucoïd impaction** and **bronchiectasis** involving the segmental and subsegmental bronchi of the **upper lobes**. 30% have high attenuation or calcification of the mucus plugs.

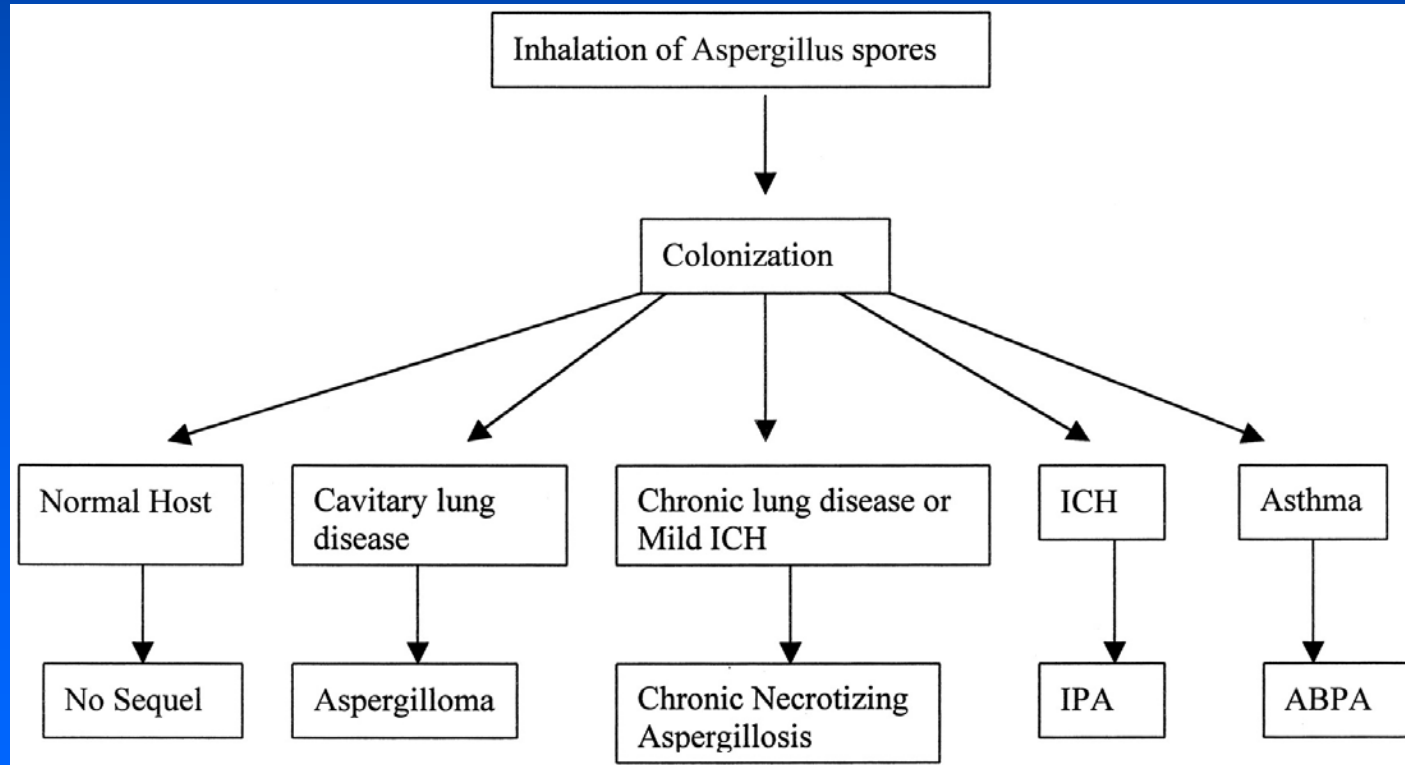
Ddx: other causes of mucoïd impaction (i.e. endobronchial lesions, bronchial atresia, bronchiectasis).

Franquet, T. *Radiographics* 2001



Summary

- There are 4 pulmonary manifestations of aspergillosis: saprophytic, allergic bronchopulmonary, chronic necrotizing, and angioinvasive.
- Aspergillosis typically affects patients with chronic lung disease and immunocompromised individuals. The different manifestations are dependent on the immune status of the patient.





Summary

- “Air-crescent” sign on CT or CXR is associated with aspergilloma in immunocompetent patients and with recovery from angioinvasive aspergillosis in immunosuppressed patients.
- CT “halo sign” indicates a rim of hemorrhage around a nodule/infarct and is highly associated with angioinvasive aspergillosis in immunosuppressed patients.
- Allergic bronchopulmonary aspergillosis is the result of a hypersensitivity reaction to *Aspergillus* in an immunocompetent patient, not an infection.



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