Patient 1: Mr. G

Mr. G is a 38yo man, previously healthy, presenting with
- 6 weeks of anorexia
- 30lb weight loss
- Increasing shortness of breath over one week
- Dyspnea on exertion
- Nonproductive cough over one week
Patient 1’s Chest Radiograph

“Multifocal Ill-defined Opacities”
DDx for Multifocal Ill-defined Opacities

ARDS, aspiration pneumonia, bronchopneumonia, eosinophilic pneumonia, fungus disease, metastatic disease, pneumoconiosis, PCP, pulmonary edema, PE with infarction, sarcoid, TB, viral/mycoplasma pneumonia....

Diffuse opacity is a very common and nonspecific finding, and must be correlated with clinical data.
Patient 1 was tested on admission, and found to be HIV positive, with a CD4 count of 26 cells/mm$^3$. 
Correlation of CD4 Counts with Opportunistic Organisms and Radiographic Findings

<table>
<thead>
<tr>
<th>CD4 count</th>
<th>Radiographic findings, infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200 cells/mm³</td>
<td>Bacterial pneumonia, TB (cavitary or non-cavitary consolidation)</td>
</tr>
<tr>
<td>&lt;200 cells/mm³</td>
<td><em>Pneumocystis carinii</em> pneumonia (reticular interstitial pattern) MOST common pulmonary infection below 200 cells/mm³</td>
</tr>
<tr>
<td></td>
<td><strong>Additional infections to keep in mind below 200 cells/mm³</strong></td>
</tr>
<tr>
<td></td>
<td>50-200 cells/mm³</td>
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<tr>
<td></td>
<td>Disseminated fungal infections and Kaposi’s sarcoma</td>
</tr>
<tr>
<td></td>
<td>&lt;50 cells/mm³ AIDS-related lymphoma, MAI, CMV (nodular or reticular patterns)</td>
</tr>
</tbody>
</table>
Patient 1’s FIRST Chest CT

Diffuse “Ground Glass Opacity”
Ground glass opacity is a CT finding consisting of an area of increased attenuation with preservation of the bronchial and vascular lung markings.

It is a common, but nonspecific, finding, occurring most commonly in acute pneumonia, pulmonary hemorrhage, pulmonary edema, interstitial diseases.

- AIDS $\rightarrow$ PCP
- Lung transplant $\rightarrow$ CMV
- Recent BMT $\rightarrow$ Infection and diffuse alveolar hemorrhage
Our Patient Has…

*Pneumocystis carinii* Pneumonia

Classic symptoms are:
- low-grade fever
- non-productive cough
- progressive dyspnea

The causative organism is unicellular, originally classified as a protozoan, but recently recategorized as a fungus. The strain that infects human lung tissue is now known as *P. jirovecii*.
Pneumocystis Pneumonia

- This is an AIDS-defining illness. The first five documented cases of AIDS in 1981 were cases of PCP in Los Angeles.

- Nearly 70% of all AIDS patients are infected with this organism at least once. It almost always strikes at CD4 levels below 200 cells/mm³. PCP also infects patients with cancer, organ transplant or those receiving immunosuppressive drugs.
Lab Diagnosis and Treatment

- PCP is diagnosed by microscopic examination of bronchoalveolar fluid or induced sputum, as it does not grown in culture.

- Treatment most commonly consists of Trimethoprim-sulfamethoxazole, despite an emerging resistance.

- HIV+ patients with CD4 counts below 200, as well as other immunocompromised patients should receive prophylaxis.

- Other drugs used to treat PCP include Dapsone, Atovaquone and Pentamidine.
Findings in PCP

- Chest Radiograph: Up to 39% are normal. Bilateral perihilar or diffuse infiltrates are classically seen.

- CT: Most commonly, patchy or diffuse ground glass opacities are seen, along with occasional septal thickening in more chronic cases.

- In PCP, the ground glass opacity is thought to represent fine alveolar exudate.

- HRCT is believed to be >90% accurate in diagnosis.
Rare Findings

- Rare presentations: focal lobar consolidation, lung nodules, bronchiectasis, mediastinal adenopathy, pleural effusion.
- Adenopathy and effusions are almost never seen, and should trigger further investigation for a different organism.
- A cystic form of PCP is becoming increasingly common over the last decade.
Cystic Changes in PCP

- In its cystic form, PCP manifests as *thinn-walled, irregularly-shaped air cysts* in the peripheral lung.

- The cysts prefer the upper lung lobes – some believe this to be due to aerosolized pentamidine therapy in the 1990’s.

- After infection resolves, cysts may persist or shrink in size. Permanent interstitial fibrosis is often seen as a long-term change.
Patient 1’s Worsening Chest Radiograph

Large cyst in Right middle lobe
PCP changes are seen earlier (and better) on CT, than CXR!

Cystic changes ALREADY visible in the anterior right middle lobe
Risk of Spontaneous Pneumothorax

- 35% of patients with these subpleural air cysts will manifest a spontaneous pneumothorax.
- A patient with cystic changes on radiograph or CT may thus present with acute onset dyspnea and pleuritic chest pain.
- Refractory air leaks in these patients may require surgical intervention. This form of PCP has a poor prognosis.
Later CXR and CT of Patient 1, with a Pneumothorax from PCP-related Cystic Changes
Lessons from Patient 1...

- Radiologic findings are too nonspecific, unless correlated with clinical information, such as a CD4 count.
- CT is vastly more sensitive than plain film in detecting PCP.
- The most common patterns seen in PCP are:
  - Diffuse, bilateral infiltrates on plain film
  - Ground glass opacity on CT
  - Peripheral thin-walled cysts on CT and plain film → watch out for pneumothorax!
Patient 2: Mr. D

62 year old man diagnosed with CLL four years previously, treated with various chemotherapy regimens, including steroid therapy.

Now presenting with:
- increasing dyspnea on exertion
- nonproductive cough
- decreasing oral intake
- increasing fatigue
Patient 2’s Chest X-Ray

Paratracheal prominence, possibly due to adenopathy
Patient 2’s Chest CT

Irregular opacity surrounded by “halo” of ground glass opacity
The CT “Halo Sign”

- The CT “Halo Sign” occurs when a dense nodule or focal area of consolidation is surrounded by a “halo” of ground glass opacity.
- This can be caused by hemorrhagic pulmonary nodules in diseases such as Wegener's Granulomatosis, metastatic angiosarcoma, Kaposi’s sarcoma.
- This sign may indicate **angioinvasive pulmonary aspergillosis**, especially in patients with acute leukemia. The necrotic nodule is surrounded by a hemorrhagic halo. Later, these may become cavitating lesions.

(Collins 2001)
Our Patient Has…

**Aspergillosis**

This is the most common fungal pneumonia in neutropenic cancer patients. Nearly 20% of Bone Marrow Transplant patients are also affected. Although it can occur in AIDS patients, it is less common. Mortality is known to be 60-90%. Unfortunately, our patient succumbed to his disease.

Therapy consists of a prolonged course of Amphotericin B.

Types of Aspergillosis

The clinical and radiologic manifestations are dependent on the category of pulmonary manifestation:

- Local/Noninvasive
- Semi-invasive
- Angioinvasive
- Airway-invasive
Findings in Local/Noninvasive Aspergillosis

- A mycetoma or “fungus ball” is formed within a pre-existing cavity in the lung tissue.
- It may cause hemoptysis.
- Characteristically, an “air crescent sign” is seen, corresponding to the sliver of air between the mycetoma and the lung tissue.

Aspergilloma

The Air Crescent Sign

This sign is seen when a mass grows within a cavity in the lung, or when an infected area of the lung necrotizes and cavitates.

In Angioinvasive Aspergillosis, the air crescent sign indicates immune response to the infection. Other rare causes: hydatid disease, hematoma, lung abscess, necrotic neoplasm.
Findings in Semi-Invasive Aspergillosis

- Also known as chronic necrotizing aspergillosis
- Associated with diabetes, alcoholism, malnutrition, steroid therapy and advanced age
- CT shows segmental consolidation in one or both lungs. Multiple nodular opacities may also be seen.
- Findings often mimic reactivation tuberculosis
Findings in Angioinvasive Aspergillosis

Fungal Hyphae Invade and Occlude Pulmonary Arteries

Findings in Angioinvasive Aspergillosis

- More common in severely neutropenic patients, like our patient, Mr. D.
- Hemorrhagic nodules lead to the CT “Halo Sign”. Wedge-shaped areas of necrosis may be seen.
- “The Air Crescent Sign” is often seen, as necrotic pulmonary tissue separates from the surrounding tissues leaving partially air-filled cavity. This usually indicates the return of immune function.
Findings in Airway-Invasive Aspergillosis

- Also known as aspergillus bronchopneumonia
- Most common in neutropenic cancer and AIDS patients
- CT findings are consistent with peribronchial disease. On HRCT, branching, nodular opacities create the “Tree in Bud Sign” due to the filling of airways with purulent material, thus making them higher attenuation.
The Tree-In-Bud Sign


A spring tree in bloom  Centrilobular opacities connected to branching lines

(Do you see the similarity?)
Lessons from Patient 2...

- The most common fungal infection in neutropenic cancer patients is Aspergillosis.
- There are four manifestations of pulmonary aspergillosis: local, semi-invasive, angioinvasive, and airway invasive.
- The CT “Halo” sign is most indicative of angioinvasive aspergillosis.
- The “Air Crescent” sign may indicate either local aspergilloma or resolving angioinvasive infection.
- The “Tree in Bud” sign is seen in airway invasive aspergillosis.
References

- Aronchick JM. Pulmonary Infections in Cancer and Bone Marrow Transplant Patient. *Semin Roentgenol* 2000; 35: 140-151
- Maki D. Pulmonary Infections in HIV/AIDS. *Semin Roentgenol* 2000; 35: 124-139
References

Acknowledgments

- Dr. Karen Lee, Dr. Eamon Kato and Dr. Nishino, for their invaluable help.
- Dr. Gillian Lieberman, our course director
- Pamela Lepkowski, our course administrator
- Larry Barbaras, our webmaster