Approach to Respiratory Infections in Immunocompromised Hosts

Lisa K Moores MD, FCCP, MACP
Associate Dean for Student Affairs
Professor of Medicine
F. Edward Hebert School of Medicine
The Uniformed Services University of the Health Sciences
Bethesda, MD
USA

Register now at congress.chestnet.org
Conflict of Interest Disclosure

I have no financial or intellectual disclosures related to this topic
Learning Objectives

• We have only 40 minutes together, so I am going to predominantly focus on the approach to these patients and pearls of wisdom to recall
• Cannot cover all the specific diseases.....but we will touch on a few....and others in the rest of the pulmonary infections presentations; will not touch on prophylaxis
• At the conclusion of this presentation, you will be able to:
  – Describe the approach to pulmonary infections in immunocompromised hosts
  – Recall that the type of immune deficiency and timeline are key in the differential diagnosis
  – List the common radiographic patterns that can be helpful in the approach to these patients
  – Recognize that non-infectious complications can occur as well
General Principles

• Type of immunodeficiency and timeline are the most important factors in narrowing the differential diagnosis

• Consider previous therapies, previous infections/cultures, travel, other exposures (cause of death and infections in organ donor)

• Early diagnosis and micro-organism specific therapy is the key

• BE AGGRESSIVE IN PURSUING A SPECIFIC MICROBIOLOGIC DIAGNOSIS*

• Multiple simultaneous pulmonary complications are common
General Principles

• Serological testing is generally not useful
• Microbiological testing should focus on antigen detection and nucleic acid detection (PCR)
• CT Chest is a key component of diagnostic work up
• Empiric anti-microbials should be started as soon as possible
Clinical Presentation

• Patients may not present with classic signs and symptoms of pneumonia due to their immunosuppressed state

• Signs and symptoms are non-specific and may include:
  • Fever, cough, and dyspnea
General Principles

• Certain subgroups are highly susceptible to infection
  – Aggressive tumors
  – Recent HSCT (esp. with GVHD)
  – Recent infections with CMV or known colonization with fungi or resistant bacteria
  – ANC below 500 (especially below 100)
  – High dose glucocorticoid therapy or recent intensification of immunosuppression
The type and degree of immunocompromise determine risk for infection.
Question 1

- A 23 year-old man with chronic granulomatous disease presents with fever and non-productive cough
- On physical examination, he is afebrile with normal oxygenation and faint crackles in the mid-right lung zone. The skin and cardiac exams are normal
- After a chest radiograph reveals a focal nodular opacity, a chest CT is obtained
Question 1

Which of the following is the most appropriate next step?

A. BAL galactomannan  
B. Serum galactomannan  
C. Sputum fungal culture  
D. Transbronchial biopsy  
E. No additional testing; begin empiric antifungal therapy  

Register now at congress.chestnet.org
Question 1

Which of the following is the most appropriate next step?

A. BAL galactomannan

B. Serum galactomannan

C. Sputum fungal culture

D. Transbronchial biopsy

E. No additional testing; begin empiric antifungal therapy
## Type of Immunosuppression and Infection Risk

<table>
<thead>
<tr>
<th>Immuno-deficiency</th>
<th>Example(s)</th>
<th>Clinical Pattern</th>
<th>Organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defects in immunoglobulins and/or complement proteins</td>
<td>Common variable immune deficiency</td>
<td>• Sinopulmonary infections</td>
<td>• Encapsulated bacteria (S. pneumo, H. flu, N. meningitidis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chronic GI infections</td>
<td>• Giardia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Meningitis</td>
<td>• Campylobacter</td>
</tr>
<tr>
<td>Granulocyte defects</td>
<td>• Neutropenia</td>
<td>• Recurrent skin and soft tissue infections</td>
<td>• S. aureus</td>
</tr>
<tr>
<td></td>
<td>• Chronic granulomatous disease</td>
<td>• Abscesses</td>
<td>• Gram negative bacilli</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Aspergillus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Nocardia</td>
</tr>
<tr>
<td>Defects in cell-mediated immunity</td>
<td>HIV Post transplant CTD</td>
<td>Progressive infections</td>
<td>Viruses</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mycobacteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fungi</td>
</tr>
</tbody>
</table>
Diagnostic Assessment

- Vital signs, exam
- Blood, urine, sputum, CSF cultures
- CBC, chemistries
- Urinary antigens
- Antigen and PCR assays of serum, BAL, CSF
- Skin examination
- Imaging
### Radiographic Patterns

<table>
<thead>
<tr>
<th>Signs</th>
<th>Diagnosis</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation &amp; air bronchogram</td>
<td>Pneumonia</td>
<td>Atelectasis, neoplasia, aspiration</td>
</tr>
<tr>
<td>Silhouette sign</td>
<td>Segmental or bronchopneumonia</td>
<td>Atelectasis, neoplasia</td>
</tr>
<tr>
<td>Bulging fissure sign</td>
<td>Lobar pneumonia, abscess</td>
<td>Neoplasia</td>
</tr>
<tr>
<td>Feeding vessel sign</td>
<td>Septic emboli</td>
<td>Metastasis</td>
</tr>
<tr>
<td>Air fluid level sign</td>
<td>Empyema, abscess</td>
<td>Neoplasia, Wegener's granulomatosis</td>
</tr>
<tr>
<td>Inhomogeneous enhancement</td>
<td>Abscess, empyema</td>
<td>Neoplasia, Wegener's granulomatosis</td>
</tr>
<tr>
<td>Split pleura sign</td>
<td>Empyema, bronchopulmonary fistula</td>
<td>Postoperative and pleurodesis associated changes</td>
</tr>
<tr>
<td>Ground glass opacities (GGO)</td>
<td>Atypical pneumonia</td>
<td>Neoplasia, drug toxicities, cardiac failure, vasculitis</td>
</tr>
<tr>
<td>Halo sign</td>
<td>Aspergillosis</td>
<td>Pseudomonas, HSV, CMV, Wegener granulomatosis,</td>
</tr>
<tr>
<td>Air crescent sign</td>
<td>Aspergillosis</td>
<td>Hydatid cyst of lung</td>
</tr>
<tr>
<td>Monad sign</td>
<td>Mycetoma</td>
<td>Wegener's granulomatosis, neoplasia</td>
</tr>
<tr>
<td>Reverse Halo</td>
<td>Aspergillosis, cryptogenic organizing</td>
<td>Tuberculosis, bacterial infections, Sarcoidosis, Wegener's</td>
</tr>
<tr>
<td>Crazy paving</td>
<td>PCP, viral like influenza</td>
<td>granulomatosis</td>
</tr>
<tr>
<td>Miliary pattern</td>
<td>Tuberculosis</td>
<td>Alveolar proteinosis, pulmonary edema and hemorrhages</td>
</tr>
</tbody>
</table>

S.K. Bajaj, B. Tombach / Radiology of Infectious Diseases 4 (2017) 29e37
<table>
<thead>
<tr>
<th>Imaging patterns</th>
<th>Associated infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground-glass opacity</td>
<td>• Pneumocystis</td>
</tr>
<tr>
<td></td>
<td>• Cytomegalovirus</td>
</tr>
<tr>
<td>Nodules &lt;1 cm diameter</td>
<td>• Viral pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Invasive aspergillosis</td>
</tr>
<tr>
<td></td>
<td>• Septic embolism</td>
</tr>
<tr>
<td>Nodules &gt;1 cm diameter</td>
<td>• Invasive aspergillosis</td>
</tr>
<tr>
<td>“Halo sign”</td>
<td>• Candidiasis</td>
</tr>
<tr>
<td></td>
<td>• Cytomegalovirus pneumonia</td>
</tr>
<tr>
<td>Cavitated nodules</td>
<td>• Septic embolism</td>
</tr>
<tr>
<td></td>
<td>• Invasive aspergillosis</td>
</tr>
<tr>
<td>Tree-in-bud pattern</td>
<td>• Infectious bronchiolitis</td>
</tr>
<tr>
<td>Consolidation Lobar</td>
<td>• Pneumococcus</td>
</tr>
<tr>
<td></td>
<td>• Klebsiella</td>
</tr>
<tr>
<td>Consolidation Rounded</td>
<td>• Pneumococcus</td>
</tr>
<tr>
<td></td>
<td>• Legionella</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>• Gram-negative bacteria</td>
</tr>
<tr>
<td></td>
<td>• Staphylococcus</td>
</tr>
</tbody>
</table>
Radiographic Patterns

<table>
<thead>
<tr>
<th>Radiographic Patterns</th>
<th>Common radiographic findings</th>
<th>Common CT findings</th>
</tr>
</thead>
</table>
| Pneumocystis pneumonia                        | Bilateral symmetric ground-glass opacities or fine reticulonodular pattern, mainly involving perihilar regions.  
|                                               | May be diffuse or involve mainly the lower or upper lung zones                              | Bilateral symmetric ground-glass opacities      |
| Pulmonary candidiasis                         | Unilateral or bilateral areas of consolidation                                             | May be patchy or diffuse                        |
|                                               | Poorly defined nodules                                                                      | May have “crazy paving” pattern                 |
| Angioinvasive pulmonary aspergillosis         | Bilateral poorly defined nodules                                                           | Multiple bilateral nodules                      |
|                                               | Single or multiple foci of consolidation                                                   | CT halo sign                                    |
| Pulmonary histoplasmosis                      | Single or multiple nodules                                                                 | Patchy or confluent consolidation              |
|                                               | Unilateral or bilateral areas of consolidation                                            | Multiple nodules, 1–3 cm diameter               |
|                                               | Cavitation is rare                                                                          | CT halo sign                                    |
| Viral pulmonary infections                    | Bilateral reticulonodular pattern                                                           | Wedge-shaped areas of consolidation             |
|                                               | Patchy bilateral areas of consolidation                                                    | Cavitation, with or without air-crescent sign   |
|                                               |                                                                                                | Diffuse nodular opacities 3 mm or less in diameter |
|                                               |                                                                                                | Nodules greater than 3 mm in diameter           |
|                                               |                                                                                                | Small linear opacities                          |
|                                               |                                                                                                | Focal or patchy areas of consolidation          |
|                                               |                                                                                                | Cavitation is rare                               |

X. Zheng, G. Zhang / Radiology of Infectious Diseases 1 (2014) 37e41

Register now at congress.chestnet.org
## CT changes in atypical Pneumonia.

<table>
<thead>
<tr>
<th>Pneumonia</th>
<th>GGO with lobular distribution</th>
<th>GGO diffuse pattern</th>
<th>Centrilobular nodules</th>
<th>Segmental consolidation</th>
<th>Interlobular septal thickening</th>
<th>Pleural effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>−</td>
</tr>
<tr>
<td>Legionella</td>
<td>+++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Mycoplasma</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>++</td>
<td>+</td>
<td>++ (+/- halo)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Sign indicate the relative frequency of the findings from lowest to highest.*
Halo Sign

Ground glass opacity surrounding a nodule or mass

Histopathology: focus of infarction surrounded by alveolar hemorrhage
<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fungi</td>
<td>Aspergillosis, Mucormycosis, Cryptococciosis</td>
</tr>
<tr>
<td>Viruses</td>
<td>HSV, VZV, RSV, CMV, influenza A</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Actinomyces, bacterial pneumonia, septic emboli</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>Mycobacterium tuberculosis, MAC</td>
</tr>
<tr>
<td>Parasites</td>
<td>Paragonimus westermani, Toxocara canis</td>
</tr>
<tr>
<td>Systemic diseases</td>
<td>Granulomatosis with angiitis, sarcoidosis, amyloidosis</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>Lung cancer, lymphoma, metastases</td>
</tr>
</tbody>
</table>

The incidence of HS on:

- Day 0 was 96%
- Day 3 was 68%
- Day 7 was 22%
- Day 14 was 19%

Diagnostic Criteria for Invasive Fungal Disease

Host Factors
- Neutropenia
- Allogeneic stem cell transplant
- Corticosteroids

Clinical Criteria
- CT findings
- Tracheobronchitis
- Sinonasal infection
- CNS infection

Mycologic Criteria
- Direct test (cytology, direct microscopy, culture)
- Indirect test (antigen detection)

Galactomannan (GM) Antigen Detection

- Polysaccharide in the cell wall of *Aspergillus*
  - Thought to be released during angioinvasion

- False positives
  - Other fungi (e.g., *Penicillium*, *Fusarium*, *Histoplasma*)
  - Use of tazobactam
  - Plasmalyte

- BAL GM
  - Higher sensitivity
  - Higher PPV
  - Higher diagnostic odds ratio than serum GM

Question 1

A. BAL galactomannan
B. Serum galactomannan (less sensitive than BAL GM)
C. Sputum fungal culture (very low sensitivity)
D. Transbronchial biopsy (more invasive option)
E. No additional testing; begin empiric antifungal therapy (OK to begin therapy, but additional testing necessary)
A 52 year old man who underwent cadaveric kidney transplant four months ago presents with 6 days of fever, dyspnea, chest pain, and headache. Medications include cyclosporine, mycophenolate mofetil, and prednisone 15 mg/day.

On physical examination, temperature is 38.5°C and oxygen saturation is 92% on ambient air. He appears lethargic. The cardiopulmonary and skin exams are normal. The neurologic exam is non-focal and there is no nuchal rigidity.

Chest radiograph reveals several nodular opacities in both lungs abutting the pleura. Lumbar puncture demonstrates a lymphocytic pleiocytosis with increased CSF protein. A CT-guided biopsy of the largest pulmonary nodule is obtained.
Question 2

Which of the following is the most appropriate therapy?

A. Acyclovir
B. Ampicillin
C. Fluconazole
D. Liposomal amphotericin B and flucytosine
E. Trimethoprim/sulfamethoxazole
Question 2

Which of the following is the most appropriate therapy?

A. Acyclovir
B. Ampicillin
C. Fluconazole
D. Liposomal amphotericin B and flucytosine
E. Trimethoprim/sulfamethoxazole
For transplant patients, infections occur in a predictable pattern based on time from transplant.
Timeline of Infections after Solid Organ Transplantation

- **Nosocomial, technical**
  - < 1 month
    - Drug resistant species (MRSA)
    - Aspiration
    - CLABSI
    - CAUTI
    - Wound infection
  - 1-6 months
    - BK virus
    - Cryptococcus
    - M. tuberculosis
    - Pneumocystis
    - Nocardia
    - Herpes viruses
  - > 6 months
    - CAP
    - UTI
    - Aspergillus
    - Nocardia
    - Late-viral infections

Infections in SOT

- Treatments result in dysfunctional neutrophils
- Lung is the primary site of infection in heart and lung transplant
- In liver, kidney, small bowel recipients, abdominal infections, followed by lung
- IMI more common in lung and small bowel transplants
  - Use of prophylaxis has led to increase in non-aspergillus infections
  - Liver transplant patients particularly susceptible to *mucorales* spp
- In lung transplant patients, must also consider airway anastomotic infections
Timeline of Infections after Hematopoietic Stem Cell Transplantation

Pre-engraftment 0-30 days
- Gram negatives
- Gram positives
  - Candida
  - Aspergillus
- HSV

Post-engraftment 30-100 days
- Encapsulated bacteria
  - Nocardia
  - Aspergillus
- Pneumocystis
- CMV
- VZV

Late > 100 days

Chi AK. *Chest*. 2013;144(6):1913-22

Register now at congress.chestnet.org

Connecting a Global Community in Clinical Chest Medicine
Cryptococcosis

Forms of Disease

- Meningoencephalitis
- Pulmonary
- Cutaneous
- Disseminated disease

Third most common invasive fungal infection in SOT recipients after candidiasis and aspergillosis

Cryptococcosis: Clinical Features

Meningoencephalitis

- Fever, headache, lethargy, personality changes
- CSF: Lymphocytic pleiocytosis, low glucose, elevated protein, elevated opening pressure

Pulmonary disease

- Fever, chest pain, dyspnea, cough, hemoptysis
- Imaging: Solitary-few nodules ± cavitation, hilar/mediastinal adenopathy, pleural effusions

Cutaneous Cryptococcosis

Most common: papulonodular lesions with umbilicated center resembling molluscum contagiosum

Cryptococcosis: Treatment

**Induction**
Liposomal amphotericin B + flucytosine
2 weeks

**Consolidation**
Fluconazole 400-800 mg/d
8 weeks

**Maintenance**
Fluconazole 200-400 mg/d
6 months-1 yr

Question 2

Which of the following is the most appropriate therapy?

A. Acyclovir (drug of choice for HSV encephalitis)
B. Ampicillin (drug of choice for *Listeria* meningitis)
C. Fluconazole (used for consolidation/maintenance, but inadequate for induction)
D. Liposomal amphotericin B and flucytosine
E. Trimethoprim/sulfamethoxazole (drug of choice for PJP and *Nocardia*)
Question 3

- A 46 year old non-smoking woman with HIV presents with two weeks of dyspnea on exertion and non-productive cough. She was diagnosed with HIV five years ago and has intermittently received care. When last seen six weeks ago, she had a CD4 count of 185 cells/μL and a HIV RNA of 53,000 copies/mL. She has not been taking any medications and has not had recent travel.

- On exam, temperature is 38.0°C and oxygen saturation is 82% breathing ambient air. She has bilateral crackles and egophany. There are no rashes. A representative image from chest CT is shown.
In addition to community-acquired pneumonia coverage, which of the following should be started?

A. Acyclovir
B. Amphotericin B
C. Ganciclovir
D. Trimethoprim/sulfamethoxazole
E. Voriconazole
In addition to community-acquired pneumonia coverage, which of the following should be started?

A. Acyclovir  
B. Amphotericin B  
C. Ganciclovir  
D. Trimethoprim/sulfamethoxazole  
E. Voriconazole
In patients with HIV, the CD4 count correlates with infection risk
Risk of Pulmonary Infection by CD4 Cell Count

CD4 cell count
500  →  200  →  100  →  50  →  0

- Bacterial Pneumonia
- Bacteremia/sepsis
- Increased GNR & S. aureus risk
- Reactivation TB
- Primary TB
- Atypical TB
- Pneumocystis jirovecii pneumonia
- Cryptococcus neoformans
- Nocardia spp
- Aspergillus spp, Toxoplasma
- CMV, other viruses
- NTM
- Disseminated endemic fungi

Bacterial Pneumonia

- Most frequent infection in HIV infected patients
- IVDU, smoking, older age, viral load, and previous recurrent pneumonia
- Can occur at any CD4 count, but incidence and severity increase as the CD4 count decreases
- Clinical presentation similar to non HIV infected patients
- CDC added recurrent pneumonia as an AIDS defining illness in 1992
Bacterial Pneumonia

- *Streptococcus pneumoniae* most common cause
  - Effectiveness of vaccination controversial
- *Haemophilus influenzae* second most common
- *Pseudomonas aeruginosa* and *Staphylococcus aureus* can be seen as community acquired pathogen in these patients
- *Legionella* infection uncommon, but still more prevalent than in non HIV infected individuals and may portend a worse prognosis
- Other uncommon include *Rhodococcus equi* and *Nocardia* spp
Decline in HIV/AIDS Mortality Rates

Trends in Annual Age-Adjusted* Rates† of Death among Persons Living with Diagnosed HIV Infection Ever Classified as Stage 3 (AIDS)

1987–2016 — United States

ART available

*Standard: age distribution of 2000 US population
† Per 1,000 persons ever classified as having stage 3 infection (AIDS).

Register now at congress.chestnet.org
Effect of ART on Incidence of Infections

http://www.cdc.gov/ncidod/EID
HIV Chest Radiographic Patterns

**Focal**
- bacteria, TB, PCP
- lymphoma

**Mediastinal LN**
- TB, MAC, KS, fungi,

**Diffuse**
- PCP, TB, bacteria, fungi, CMV, KS

**Pleural Effusion**
- bacteria, TB, KS, ↓albumin
- CHF, fungi, lymphoma (PEL)

**Diffuse Nodules**
- TB - miliary
- KS - large
- Fungi - small

**Cavities**
- TB (high CD4+),
- PCP, *R. equi*, Nocardia
Pneumocystis Pneumonia

- PCP caused by *Pneumocystis jirovecii*, a ubiquitous fungus that shares some biological features with protozoa
- Use of routine prophylaxis and HAART have led to sharp decline in incidence, but still the most common AIDs defining illness
- HIV patients typically have a more subacute course and longer duration of symptoms
## PCP/PJP Presents Differently in HIV-Negative Patients

<table>
<thead>
<tr>
<th></th>
<th>HIV-Positive</th>
<th>HIV-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td>Subacute (weeks)</td>
<td>Acute (&lt;1 week)</td>
</tr>
<tr>
<td></td>
<td>Survival &gt;80%</td>
<td>Survival 50-90%</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td>Diffuse bilateral opacities</td>
<td>Diffuse bilateral opacities</td>
</tr>
<tr>
<td><strong>β-D-Glucan</strong></td>
<td>Sensitivity: 90-95%</td>
<td>Sensitivity: 90-95%</td>
</tr>
<tr>
<td></td>
<td>Specificity: 65-90%</td>
<td><strong>Specificity: 85-90%</strong></td>
</tr>
<tr>
<td><strong>LDH</strong></td>
<td>Sensitivity: 92-100%</td>
<td><strong>Sensitivity: 64-100%</strong></td>
</tr>
<tr>
<td></td>
<td>Specificity: 25-85%</td>
<td>Specificity: 25-85%</td>
</tr>
<tr>
<td><strong>BAL microscopy</strong></td>
<td>&gt;90% sensitive (high organism burden)</td>
<td>62-85% sensitive (low organism burden)</td>
</tr>
</tbody>
</table>

---

- CXR is initially normal in many patients; eventually develop bilateral interstitial infiltrates emanating from the hila
- HRCT extremely sensitive for detecting PCP
- FOB with BAL preferred diagnostic procedure
- TMP-SMX remains DOC; adjunctive corticosteroids can be used in severe disease
*Pneumocystis* cannot be cultured; gold standard is staining

Serum biomarkers are suggestive but non-specific

TB in HIV Infected Patients

- HIV is currently the largest risk factor for developing TB disease
- Second most common opportunistic infection (may be most common in some geographic regions)
- May be new infection or reactivation, depending on geography
- Rates are lower when ART is initiated sooner
  - Ongoing viral replication a risk factor
- Presentation dependent on CD4 count; higher levels present with postprimary infection; lower counts will present with military/disseminated disease
TB in HIV infected Patients

- Treatment principles similar to those in HIV- patients
- Can be complicated by drug interactions and overlapping toxicities, which can lead to subtherapeutic levels
- ART should be initiated as soon as TB therapy tolerated
  - This may lead to increased incidence of IRIS
  - One month of concomitant prednisone can reduce incidence
In addition to community-acquired pneumonia coverage, which of the following should be started?

A. Acyclovir (CD4 not low enough for viruses, HSV pneumonia rare)
B. Amphotericin B (radiographic pattern less consistent with fungal disease)
C. Ganciclovir (CD4 not low enough for viruses, drug of choice for CMV)
D. Trimethoprim/sulfamethoxazole
E. Voriconazole (radiographic pattern less consistent with fungal disease)
Consider non-infectious complications of immunosuppressive medications
Non-Infectious Complications

- Drug reactions
  - Consider and exclude infective and other potential causes
  - Establish a temporal relationship
  - Radiological findings are wide and include ARDS, NSIP, HP, and OP patterns
- Lymphoproliferative disorder
  - Often related to EBV
  - Multiple bilateral nodules/masses, lymphadenopathy and patchy air space opacification are common
Non-Infectious Complications

• Rejection
  – Acute rejection: Volume loss and septal thickening fl/pleural effusion
  – Chronic rejection: BOS mosaic attenuation, air-trapping, and bronchial dilatation

• Alveolar hemorrhage
  – High mortality. Bilateral infiltrates on radiographs,
  – bilateral ground-glass opacification and consolidation on HRCT
  – Hemoptysis is not always a feature.

• Pulmonary edema/emboli
  – Remember PE and pulmonary edema as a cause for respiratory symptoms
HIV Noninfectious

• **Neoplastic**
  – Kaposi’s sarcoma (almost exclusively in MSM)
  – Lymphoma, usually B-cell
  – Primary effusion lymphoma: “liquid lymphoma”, associated with HHV-8, poor prognosis
  – Lung cancer (adenocarcinoma)
PAH in HIV

• WHO Group 1
• 1/200 cases of HIV infection
• Not related to HIV infection of pulmonary vascular endothelium
• NOT associated with HHV8
• Unrelated to CD4+ count
• Treat as other Group 1 PAH
Immune Restoration Inflammatory Syndrome (IRIS)

- “Unmask” current or latent infection
  - CMV: retinitis, uveitis, vitritis, colitis, pancreatitis
  - MAC: lymphadenitis, adrenals, skin
  - Hepatitis C: acute hepatitis
- “Paradoxical worsening” TB, PCP, cryptococcal meningitis, Kaposi sarcoma
- Sarcoidosis
Summary

• Type of immune deficiency is paramount
• Timing of symptoms post-transplant (SOT or HSCT) helps narrow the DDX
• Radiographic patterns are helpful
• Consider non-infectious etiologies as well
Join colleagues from around the region to gain access to the CHEST learning and training experience at our regional congress. This unique program will go beyond the classroom-style setting to connect you to leading experts who will teach and develop you and your team.

Learn More: athens.chestnet.org