Pneumocystis Carinii Pneumonia (PCP) in the HAART Era

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Outline

• OIs in the HAART Era: Late Presentation

• Clinical Aspects of PCP

• PCP and the IRIS
Historical Context and Background

- PCP caused by Pneumocystis jiroveci, a ubiquitous organism classified as a fungus but shares biologic characteristics with protozoa.
Late Presentation in the HAART Era

Patients Starting ART at Higher CD4+ Cell Counts Overall, but Disparities Remain

- CD4+ cell count at start of ART (cells/mm³), 2009[1]

- In San Francisco study, overall trends of starting ART at higher CD4+ counts, but pts initiating ART at CD4+ counts > 350 cells/mm³ significantly more likely to be white, older, MSM, nonpoor, and diagnosed by private provider[2]

PCP Basics

• Remains a significant cause of death, which is associated with not receiving or failing to comply with HAART or PCP prophylaxis

• 95% of patients who developed PCP have a CD4 count below 200 cells/mm3
Clinical manifestations:

- Generally gradual in onset
- fever (79 to 100 %)
- cough (95 %), and
- progressive dyspnea on exertion (95 %)
- Oxygenation desaturation at rest or with exercise
Radiologic findings

Commonly diffuse, bilateral interstitial or alveolar infiltrates (CXR or CT)

Normal CXR in 25% at initial presentation

Presence of pleural effusion makes PCP unlikely diagnosis
Diagnostic Procedures

Demonstration of organisms in respiratory specimens collected by:

- Sputum induction - most rapid & least invasive. Depends on skill of lab

- Broncho-alveolar lavage - more sensitive

- Endoscopic aspirates - in intubated patients.

- Transthoracic needle biopsies.
PCP Differential Diagnosis

• Pulmonary TB

• Pulmonary KS

• Atypical bacterial Pneumonias
# HIV-Related PCP: Treatments

<table>
<thead>
<tr>
<th></th>
<th><strong>TMP/SMX</strong></th>
<th><strong>Pentamidine</strong></th>
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<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>folate antagonist DHFR inhibitor?</td>
<td></td>
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<tr>
<td><strong>Usual dose</strong></td>
<td>TMP 15-20 mg/kg/d SMX 75-100mg/kg</td>
<td>4 mg/kg/d</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>po, iv</td>
<td>iv, im</td>
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<tr>
<td><strong>Clearance</strong></td>
<td>renal</td>
<td>renal</td>
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<tr>
<td><strong>Toxicities</strong></td>
<td>fever, rash, hepatitis, renal failure, hypoglycemia, serum sickness, marrow hepatitis, fever, leukopenia, suppression rash, hypotension, pancreatitis</td>
<td>fever, rash, hepatitis, renal failure, hypoglycemia, serum sickness, marrow hepatitis, fever, leukopenia, suppression rash, hypotension, pancreatitis</td>
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<tr>
<td><strong>Cure (initial Rx)</strong></td>
<td>58-86%</td>
<td>44-99%</td>
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Alternative Antimicrobial Therapy

• Clindamycin 600-900mg iv 6-8hr + Primaquine 15-30 mg/kg base oral x 21/7

• Atovaquone 750 mg suspension bid with a meal x 21/7

• Trimetrexate + Leucovorin

• Dapsone + Trimethoprim
**Adjunctive Corticosteroid Therapy for AIDS Associated Pneumocystis Pneumonia**

- **Indications:**
  - Presumed or confirmed PJP
  - Moderate-severe hypoxemia
  - $PO_2 < 70$ mm Hg (room air)
  - Anti PJP therapy < 72 hours

- **Regimen:**
  * Prednisone 1mg/kg (PO) x 21 days

*Steroids preferably started *BEFORE* antimicrobials !!!!!!!

Use of corticosteroids

- Patients with PCP typically worsen after two to three days of therapy, presumably due to increased inflammation in response to dying organisms.

- Corticosteroids given in conjunction with anti-Pneumocystis therapy decrease the incidence of mortality and respiratory failure associated with severe PCP.


- Regimen:
  - Dose: 1mg/kg body weight per day
  - 21 days
Typical Radiological Findings
Radiological Improvement can be drastic!
Prophylaxis

- Risk of PCP recurrence without prophylaxis is 60%-70% per year
- Risk is 40%-50% per year for those with CD4 < 100
- PCP prophylaxis reduces the risk of PCP by 9-fold
- Patients who get PCP despite prophylaxis have a lower mortality rate
PCP and IRIS

- ACTG 5164 showed that HIV-infected patients recently diagnosed with an OI benefit from early ART (2wks compared to 8 wks).

- Pulmonary IRIS in PCP Case One case report of patient with high CD4 count\(^1\)

- 3 cases of life-threatening PCP in a setting of early ART (Day 13, Day 23 and Day 4)\(^2\)
  - IRIS episode occurred after completion of PCP therapy and following clinical improvement.
  - There is a need for further studies to identify risk factors of those patients who are likely to develop life-threatening IRIS

- One case of life-threatening IRIS in a PCP patient 3 days after initiation ART, plus review of case series and case reports (n=32)\(^3\)
  - Time to PCP IRIS varied widely (3-301 days. All cases associated with brisk viral load reduction

Acknowledgements

• IDI Clinic Archive

• Clinical Care Options HIV