Lower Respiratory Infections and Tuberculosis

ACOI Board Review 2013
Mia Taormina, DO, FACOI
Overview

• Epidemiology
• Common clinical presentations
• Bacteriology – community pathogens and health care associated pathogens for pneumonia
• Antimicrobial therapy for various definitions of CAP and for HCAP/VAP
Community Acquired Pneumonia

- 5.6 million cases per year
- Number one cause of infectious disease related deaths in the US each year
- 10 billion dollars in healthcare costs
- Average rate of in-hospital mortality is 12%
### Expected Pathogens for CAP

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td>20-60%</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>3-10%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>3-5%</td>
</tr>
<tr>
<td>Gram negative bacilli</td>
<td>3-10%</td>
</tr>
<tr>
<td>Legionella species</td>
<td>2-8%</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>1-6%</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>4-6%</td>
</tr>
<tr>
<td>Viruses</td>
<td>2-15%</td>
</tr>
<tr>
<td>Aspiration</td>
<td>6-10%</td>
</tr>
<tr>
<td>Others</td>
<td>3-5%</td>
</tr>
</tbody>
</table>
Sample Case #1

- A 19 y.o. college freshman presents to the ER with fever, cough and a sore throat for 4 weeks
- She was prescribed erythromycin but low-grade fevers and nonproductive cough persisted
- One week after the onset of illness, persistent hoarseness developed
- No other constitutional symptoms, and her past medical history is negative
Diagnosis/Treatment

• This scenario should point you towards an “atypical” pneumonia given the patient’s age and protracted course
• Mycoplasma pneumoniae and chlamydia pneumonia should be at the top of your list
• Cold agglutinins positive?
• Treatment should be with a macrolide or doxycycline for outpatient treatment in a patient with no comorbidities and no recent antibiotic exposure
Sample Case #2

- A 56 y.o. man presents to the emergency department complaining of right-sided pleuritic chest pain, cough productive of thick greenish-yellow sputum, increasing dyspnea, fevers, and shaking chills—all of 2-day duration.
- He denies nausea, vomiting, and diarrhea.
- His past medical history is significant for CAD, DM, and COPD. No sick contacts. No recent travel.
Sputum Gram Stain
Community Acquired Pneumonia

- Presentations on CAP
  - Fevers/chills
  - Productive cough
  - Lobar consolidations

- Often case presentation is accompanied by CXR and/or sputum Gram stain

- Possibly a positive blood culture for Streptococcus species or a strep pneumo urine antigen test positive
Or…

• Take our same patient and add a few buzzwords:
  – Recent air conditioner maintenance
  – Vacation involving air conditioning
  – Vacation involving spa, hot tub, etc.

• Perhaps add nausea, vomiting, headache, mental status changes

• Hyponatremia, elevated LFTs, Legionella urine antigen positivity
Treatment…

- Depends on the severity of illness
- Oral outpatient antibiotics for those who are clinically stable with common medical comorbidities
- Inpatient treatment, non-ICU
- Inpatient treatment, ICU if the patient meets criteria for “Severe” CAP
Outpatient Treatment

- With common medical comorbidities such as DM, CAD, COPD, renal insufficiency, OR antibiotic use in the past 3 months
  - Respiratory fluoroquinolone
    - Levofloxacin, moxifloxacin
  - Beta-lactam plus a macrolide
    - Penicillin, cephalosporins + erythromycin, azithromycin
Inpatient Non-ICU

- Patients who are sick enough to be admitted to the hospital, do not meet criteria for ICU admission
  - Respiratory fluoroquinolone
    - Levofloxacin, moxifloxacin
  - Beta-lactam plus a macrolide
    - Usually ceftriaxone + azithromycin
  - Others?
    - Tygecycline, ceftaroline
Severe?

CRITERIA FOR SEVERE CAP:

• Minor criteria:
  – Respiratory rate >30 breaths/min
  – PaO2/FiO2 ratio >250
  – Multilobar infiltrates
  – Confusion/disorientation
  – Uremia (BUN level >20 mg/dL)
  – Leukopenia (WBC count, <4000 cells/mm3)
  – Thrombocytopenia (platelet count, <100,000 cells/mm3)
  – Hypothermia (core temperature, <36C)
  – Hypotension requiring aggressive fluid resuscitation

• Major criteria:
  – Invasive mechanical ventilation
  – Septic shock with the need for vasopressors
Inpatient ICU

• Beta-lactam plus a macrolide or a respiratory fluoroquinolone
  – Cefotaxime, ceftriaxone, ampicillin-sulbactam PLUS
  – Azitromycin OR
  – Levofloxacin

• Penicillin allergy?
  – Levofloxacin + aztreonam
  – Tygecycline
Sample Case #3

- A 72 y.o. man who presented with perforated diverticulitis requiring emergent exploratory laparotomy.
- Multiple medical co-morbidities.
- Remains intubated after surgery and fails to wean from the ventilator.
- POD #7 has a temperature of 102°F and bedside bronchoscopy reveals purulent secretions.
Radiograph
HCAP/VAP

• Initial antibiotic selection should include coverage for MRSA and pseudomonas
• For MRSA – vancomycin, linezolid, (tygecycline, ceftaroline)
  – Do not select daptomycin for pneumonia!
• When pseudomonas is a consideration:
  – Pipericillin-tazobactam, cefepime, imipenem/meropenem/doripenem PLUS
  – Ciprofloxacin or aztreonam or an aminoglycoside
Other bugs...

- **ESBL producing gram negatives**
  - Klebsiella, e. coli, enterobacter, others…
  - Consider ertapenem, quinolones if susceptible
- **Acinetobacter baumanii**
  - Frequent/overuse of aminoglycosides, quinolones, ureidopenicillins, and third/fourth generation cephalosporins
  - Many times sensitive to ampicillin-sulbactam
  - Often need to choose tigecycline or colistin
Sample Case #4

- A 16 y.o. boy with a history of asthma presents with a syndrome of high fevers, non-productive cough, shortness of breath, and nausea in November.
- Influenza swab is positive for Influenza A.
- Sent home on oseltamivir and improves initially.
- 1 week later presents with rapidly progressive shortness of breath, recurrent fevers, hypotension and requires emergent intubation and ICU admission.
Diagnosis?

• A scenario of post-influenza pneumonia or “necrotizing” pneumonia should make you think of Staph aureus/MRSA/CAMRSA as the causative organism.

• Add linezolid or vancomycin and treat for sepsis/septic shock.
HOT Topics

- Young patients with “atypical” pneumonia – give doxycycline
- Treatment for CAP in and out of the ICU
- Antibiotic choices for legionella pneumonia
- Community acquired pneumonia in a pregnant woman – look for a cephalosporin
- Which antibiotic should be stopped if a patient fails to wean from the ventilator – look for an aminoglycoside
- Pneumonia in an HIV+ patient with a HIGH CD4 count – think S. pneumoniae
- Post-influenza pneumonia – S. aureus/MRSA
- Drug of choice for influenza pneumonia – oseltamivir
- Histoplasmosis, blastomycosis, coccidiodomycosis
Questions?
Tuberculosis

• Epidemiology/pathogenesis
• Clinical presentation and classification of tuberculosis
• Diagnosis and treatment of LTBI and tuberculosis
• Definitions and treatment of MDR/XDR TB
• Infection Control
Epidemiology

Reported TB Cases
United States, 1982–2011*

*Updated as of June 25, 2012.
Epidemiology

TB Case Rates, United States, 2011

- ≤ 3.4 (2011 national average)
- >3.4

*Cases per 100,000.
Pathogenesis

- Inhalation of droplet nuclei
- Bacteria multiplies
- Macrophages consume the bacteria, then die
- Travel through the blood and lymphatic system
- Containment of infection
- Multiplication - DISEASE
TB Droplet Nuclei

• One cough produces 500 droplets
• The average TB patient generates 75,000 droplets per day before therapy is initiated
• This drops to 25 infectious droplets per day within two weeks of beginning effective multidrug therapy for TB
Sample Case

• A 46 y.o. Mexican woman presents to the ER with a c/o cough, fever, pleuritic chest pain and a 10 pound weight loss over the past month.

• Emigrated to the United States 15 years ago, no known TB contacts, received 3 doses of BCG vaccine.

• No hemoptysis, no night sweats.
Symptoms of Tuberculosis

( Established) pulmonary tuberculosis

Productive cough

Night sweats

Primary pulmonary tuberculosis

Structural abnormalities

Tuberculous pleuritis

Chest pain

Poor appetite

Miliary tuberculosis

Return of dormant tuberculosis

Cough with increasing mucus

Coughing up blood

Weight loss

Dry cough

Fever

Weakness

Extrapulmonary tuberculosis

Common sites:
- Meninges
- Lymph nodes
- Bone and joint sites
- Genitourinary tract

Gastrointestinal symptoms
Mantoux PPD

- **5mm** positive in HIV patients, transplant patients, those in contact with active TB cases, those with classic CXR findings
- **10mm** positive in healthcare workers, immigrants, those with DM, RI, chronic steroids use, IVDU
- **15mm** positive in the general population
- REGARDLESS OF BCG
Boosting?

- Happens with previous exposure to BCG or perhaps active TB
- First PPD “primes” the immune system and may not be positive
- Second PPD placed 1 week later could elicit a stronger “positive”
- Phenomenon makes it difficult to distinguish a “reactor” from a “converter”
Quantiferon TB-Gold, T-spot TB

- Serologic IFN-gamma based tests
- Eliminates operator error/bias
- Consideration of improved specificity, sensitivity when compared to Mantoux PPD
- Can possibly distinguish between false + PPD and BCG administration
Chest Radiograph
Chest Radiograph cont’d.

- Abnormalities often seen in the apical or posterior segments of upper lobe or superior segments of lower lobe
  - Cavitary lesions?
- Appearance can be variable in HIV patients
- Cannot alone confirm a diagnosis of TB, however a negative CXR in a possible case of TB usually indicates no infectious TB disease
Sputum Collection

- Sputum specimens are essential to confirm the diagnosis of TB.
- A poor specimen would contain too many epithelial cells indicative of saliva instead of sputum.
- 3 specimens, with cultures, ideally on 3 consecutive days with at least one specimen being spontaneous early morning sputum.
- NGT aspirate?
- Single bronchoscopy specimen?
AFB Smear Results

• Positive:
  – Need at least 10,000 AFB per mL
  – Positive in about half of those with active disease
  – Signal a highly infectious patient
  – Other mycobacterial infections?

• Negative:
  – Too few bacilli to be seen directly
  – CULTURES are still important if smear negative
  – Patient is likely less infectious to others

• Pleural effusion?
  – Look for AFB+ and greater than 50% lymphocytes!
## Classification System for TB

<table>
<thead>
<tr>
<th>CLASS</th>
<th>TYPE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No TB exposure</td>
<td>No history of exposure</td>
</tr>
<tr>
<td></td>
<td>Not infected</td>
<td>Negative PPD</td>
</tr>
<tr>
<td>1</td>
<td>TB exposure</td>
<td>History of exposure</td>
</tr>
<tr>
<td></td>
<td>No evidence of infection</td>
<td>Negative PPD</td>
</tr>
<tr>
<td>2</td>
<td>TB infection</td>
<td>Positive PPD</td>
</tr>
<tr>
<td></td>
<td>No disease</td>
<td>Negative bacteriologic studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No clinical or CXR evidence of TB</td>
</tr>
<tr>
<td>3</td>
<td>TB, Clinically active</td>
<td>M. Tuberculosis cultured</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical, bacteriologic, or radiographic evidence of disease</td>
</tr>
<tr>
<td>4</td>
<td>TB, Not clinically active</td>
<td>History of TB or Abnormal/stable CXR findings, Positive PPD, and no clinical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>evidence of active disease</td>
</tr>
<tr>
<td>5</td>
<td>TB Suspected</td>
<td>Diagnosis pending</td>
</tr>
</tbody>
</table>
Treatment of LTBI

• 9 months of daily INH therapy - standard
  – 4 months of daily rifampin therapy
• Substantially reduces the infected persons risk of developing TB
• Monitor patient for toxicity/adherence
Treating TB Disease

• Always treat with multiple drugs
• Never add a single drug to a failing regimen
• Treatment course depends on drugs selected – usually 6 months, sometimes 9 months
  – Four drugs (RIPE) – Rifampin, INH, Pyrazinamide, Ethambutol for 2 months
  – Two drugs for the remaining 4-7 months
    • INH and Rifampin (depending on drug sensitivities)
  – Substitute rifabutin for rifampin in HIV+ patients on certain HAART therapies
• DOT (Directly Observed Therapy) 3x/wk
Drug Resistance?

- Always send positive M. Tuberculosis cultures for sensitivity testing
- MDR TB – isolate that is resistant to both INH and rifampin
- XDR TB – MDR + resistance to FQ and at least 1 of the 3 injectible drugs (amikacin, kanamycin, capreomycin)
- Primary resistance – TB strain is already resistant to one or more drugs
- Secondary resistance – develops during treatment
Treatment options for MDR TB

• Depending on susceptibilities:
  – Use pyrazinamide and/or ethambutol if available PLUS
  – Use levofloxacin or moxiflocacin if available PLUS
  – Use amikacin or capreomycin or streptomycin or kanamycin if available

• Add 2\textsuperscript{nd} line drugs until you have 4-6 active agents
  – Cycloserine or ethionamide or PAS
  – Consider imipenem, linezolid, macrolides
  – New agent pending – bedaquiline (Sirturo)
Infection Control

• Alert staff, nurses, hospital infection control of possible cases of TB
• Negative pressure isolation room with filtration until 3 negative AFB smears
  – Consider in HIV/AIDS patients with undiagnosed pulmonary disease
• Use of N-95 respirator by staff
• Patient to wear surgical mask during transfers
HOT Topics

• Know the PPD cutoffs for LTBI and who to offer INH treatment – healthcare workers!
• Parapneumonic effusion with high lymphocytes (>50%) – think TB
• Know isolation requirements for patients with suspected TB
• Know treatment of TB in an immunocompetent patient – RIPE
• Substitute rifabutin for rifampin in treatment of TB in HIV patients on HAART
• Know the basics of MDR TB – resistant to both INH and rifampin and requires 4-6 active drugs
Questions?