HIV related lung disease

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Learning objectives

At the end of the session you will

• Understand the impact of lung disease on HIV morbidity and mortality

• Be able to diagnose and treat the most common acute and chronic lung diseases associated with HIV/AIDS
HIV related lung disease

General Observations

• 60% of children have chronic changes on CXR by 2 years.

• HIV related lung diseases have increased the number of children admitted to hospital with acute lung disease by 20-40%.

• More likely to develop complications and require admission for longer periods of time.

• Chest diseases may require more sophisticated diagnostic techniques.
General Observations cont.

• Pulmonary manifestations are the most common initial manifestations

• Primary cause of death in 50% of HIV infected children

• Common pulmonary disorders are bacterial pneumonias, PCP, and LIP.
HIV related lung disease

- The spectrum of lung disease influenced by
  - Immunological status
  - Other co-morbid disease ie reflux
  - Use of anti-retroviral drugs
  - PCP prophylaxis
Acute Respiratory Disease in HIV infected children
Acute Respiratory Disease in HIV infected children

- Bacterial pneumonia
- *Pneumocystis jiroveci* pneumonia (PCP)
- Mycobacterium *Avium* Complex (MAC)
- Viral pneumonia
- CMV
- Fungal infections
Community Acquired Pneumonia

Background and Presentation:

• Most frequently identified pathogen:
  • *S. Pneumoniae*
    • 40 x ↑ risk of developing invasive pneumococcal disease

• May have ↑ risk of
  • gram negative infections
  • complicated viral pneumonias
Community Acquired Pneumonia

Clinical presentation:
- similar to uninfected children
- Fever
- Cough
- Tachypnoea
- Hypoxia
- Chest retraction

Investigations:
- CXR
- Acute phase reactants (CRP)
- White cell count
- Blood culture if hospitalized
- Sputum culture
Community Acquired Pneumonia

Out-Patient Treatment

- Manage according to IMCI guidelines
  - Amoxycillin (30-80 mg/kg/day tds)

- Standard dose Amoxycillin (30-40mg/kg/day) + Co-amoxiclav (30-40mg/kg/day) if suspects
  - penicillin resistant organisms
  - beta-lactamase-producing Haemophylus influenzae
  - Staphylococcus aureus

- Erythromycin if penicillin allergic
Community Acquired Pneumonia

In-Patient Treatment

- No CNS involvement
  - Penicillin + gentamicin ± cloxacilin
- CNS involvement
  - 3rd Generation Cephalosporin +/- Vancomycin (if suspecting resistant *S. pneumoniae*)
  - Discontinue vancomycin once penicillin resistant organism has been excluded
- Do NOT discontinue co-trimoxazole prophylaxis when treating intercurrent bacterial infections with other antibiotics
Pneumocystis jiroveci pneumonia (PCP)

- AIDS defining illness
- Occurs most commonly in children < 1 year
- High mortality
- Prevention (CTX prophylaxis) effective
- Early and appropriate treatment improves prognosis significantly
Pneumocystis Jiroveci cont.

- Signs and symptoms:
  - Onset- gradual: days-weeks
  - Febrile
  - Cough
  - HALLMARK: tachypnea with hypoxia
  - Lung auscultation may be normal

- Investigations:
  - Oxygen saturations- usually < 90% in room air
  - CXR- diffuse bilateral alveolar or interstitial infiltrate (patient may be hypoxic with normal CXR)
Management of PCP

- Begin treating for PCP immediately on suspicion (in addition to usual treatment of pneumonia), even if HIV status of child has not been established yet
- Treatment:
  - Oxygen
  - Co-trimoxazole (20 mg/kg/day of trimethoprim component) 6 hourly for 5 days, changing to oral for 3 weeks if adequate response
  - Consider adding Clindamycin 30-40mg/kg for severe disease
  - Prednisone 1-2 mg/kg daily for 2 weeks- r/o TB first
  - Morphine if severe distress and no ICU available

- Secondary PCP prophylaxis after discharge
Chronic Respiratory Disease in HIV infected children
Chronic Respiratory Disease in HIV infected children

- Lymphoid Interstitial Pneumonia
- Bronchiectasis
- Aspiration Associated Lung Disease
Etiology of HIV-associated Chronic Lung Disease

• Jeena P M et al. looked at causes of Persistent Lung Disease (PLD) and Chronic Lung Disease (CLD) in HIV infected and uninfected children in South Africa

• Chronic lung disease was defined as the presence of clinical and radiological features of lung disease for > 3 months
• 138/194 (71%) of the children with PLD/CLD had HIV
• Amongst HIV infected children with confirmed diagnosis
  • LIP 46%
  • TB 17%
  • Bronchiectasis 17%
  • Other interstitial pneumonitis 14%
Why is it so difficult to establish a cause of CLD?

- Imaging findings
  - often non-specific
  - have to be interpreted in association with clinical findings & CD4 count

- Isolation of the organism
  - sputum analysis, nasopharyngeal aspirate, BAL or lung biopsy

- Treatment
  - empirical basis before a definitive diagnosis is made
Added difficulty with establishing a cause of CLD in HIV-infected children

- High incidence of Tuberculosis
- Many children already have structural lung damage
- Late diagnosis of HIV
- No PCP prevention
- In the absence of HAART
  - Multiple organisms/ conditions
What are the consequences of chronic lung disease?

- Permanent destruction of lung
- Raised pulmonary pressures with secondary right heart failure
- Recurrent admissions
- Death from respiratory failure
LIP

- Lymphoid Interstitial Pneumonia
- Lymphocytic Interstitial Pneumonitis
Case definition

- ‘The presence of a diffuse, often symmetrical, reticulonodular or nodular pattern, occasionally with the presence of hilar or mediastinal adenopathy for at least 2 months without identifiable pathogen or antibiotic response, can be used as a clinical case definition.’

- The nodules are approximately 2-3 mm and are most easily recognized at the bases and the peripheral lung zones
Lymphoid Interstitial Pneumonia not exclusively in HIV seropositive patients

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<td>Complication of allogeneic bone marrow transplantation</td>
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<td>Pulmonary alveolar microlithiasis †</td>
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<td>Infections including Legionella pneumonia, tuberculosis, Mycoplasma, Chlamydia, Diphosphhydantoin use †</td>
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Lymphoid Interstitial Pneumonia

- LIP represents 25 - 40% of pulmonary disease in children (3% in adults)

- Three types:
  1. lymphocytic interstitial Pneumonia (LIP)
  2. pulmonary lymphoid hyperplasia (PLH)
  3. polyclonal polymorphic B-cell lymphoproliferative disorders.

- In African children BRONCHIECTASIS is a common consequence
Natural History

- Not fully understood

- Clinical course variable
  - remain stable or
  - progress slowly to respiratory failure
  - spontaneous remission has been known to occur
Spectrum of disease

- Depends on child’s immune status and viral load

- Is a CD8 response to the HIV virus.

- Radiographic findings continues to evolve as the lifespan of patients with HIV and LIP increase with HAART

- Improvement and or resolution with ART

- Conflict in the literature? poor or good prognostic sign
WHO Clinical Stage

- 2005 WHO stage 3
- No presumptive clinical diagnosis

- Definitive Diagnosis
  - CXR:
    - bilateral reticulonodular interstitial pulmonary infiltrates > 2 months
    - no response to antibiotic treatment
    - no other pathogen found.
  - Oxygen saturation persistently <90%
  - Characteristic histology

- May present with cor pulmonale with ↑ exercise induced fatigue
Clinical Presentation

- Onset insidious

On examination:
- Pulmonary findings
  - Cough and tachypnea
  - Chest deformities
  - Auscultatory findings rare
- Extra-pulmonary findings
  - Digital clubbing in advanced cases
  - Generalized lymphadenopathy
  - Hepatosplenomegaly
  - Parotid enlargement
- May present with symptoms or signs associated with intercurrent viral or bacterial respiratory illness
Extra-pulmonary findings

Parotid swelling

Finger clubbing
Features suggestive of chronic respiratory illness

- Pulmonary hypertension with right ventricular hypertrophy
- Increased anterio-posterior diameter of chest
- Intercostal recession
- Harrison’s sulci
- Subcostal retraction
- Hepatomegaly
Diagnosis

- Definitive diagnosis requires open lung biopsy

- However, in patients with HIV diagnosis may be made if
  - dyspnoea with hypoxia
  - classic radiographic findings of micronodular infiltrates
Chest X-ray

1. LIP CXR has reticular or finely reticulonodular interstitial opacities with nodules 3 mm

2. Coarse reticulonodular interstitial opacities with nodules between 3 mm and 5 mm

3. 1 or 2 plus at least one area of patchy alveolar opacity

4. Focal alveolar consolidation resembling pneumonia
Chest x-ray

- The radiographic findings of LIP includes a diffuse, symmetrical, reticulonodular, or nodular pattern with or without hilar or mediastinal adenopathy.
Other CXR findings

Lymph glands enlarge in LIP
Degree of enlargement: poorly described
May be difficult to distinguish from TB

Consolidation may be found
LIP with Cystic changes

LIP with RLL cyst
CT scan findings

- Subpleural micronodules
- Reticulonodular pattern
- Hilar lymphnodes
- Subcarinal lymphnodes
Complications of LIP

- Recurrent lower respiratory infections
- Bronchiectasis
- Cystic lung disease
- Cor pulmonale
Treatment

- **Supportive therapy**
  - ↓ exposure to cigarette smoke / inhaled irritants
  - nutritional support
  - oxygen for hypoxemia
  - bronchodilators for reversible airway obstruction
  - antibiotics for inter-current infection

- **HAART**
  - symptomatic HIV disease - stage 3.

- **Corticosteroid therapy**
  - only indicated if respiratory failure
  - exclude TB before starting
  - ensure CTX prophylaxis
Radiographic changes in response to HAART

12.06.2002

30.01.2003
TB LIP co-disease

- Diagnostic Dilemma as both are
  - common in sub-Saharan African children
  - presents with chronic symptoms,
  - hepato-splenomegaly
- CXR findings similar:
  - reticulo-nodular picture
  - enlarged glands
  - can cause cavities
LIP with Miliary TB

- Miliary TB more likely if
  - < 1 year of age
  - CNS involvement
  - CXR: widespread fine (< 2 mm) nodules (millet size)
LIP with TB
Long term outcome of LIP

• Largely unknown

• Conflicting evidence in literature

• Resolution of findings of LIP poor prognostic indicator if not on HAART
  • associated with reduction in CD4 count

• Resolution irrespective of patients clinical status
Summary

• LIP very common
• High morbidity
• Clinical Stage III disease
• WHO recommends HAART based on CD4 count
• BUT if severely symptomatic should get HAART irrespective of CD4 count
• All children with clinical features suggestive of LIP should have a CXR
• Diagnosis based on clinical features and CXR
Bronchiectasis

- Represents a common end stage of a number of nonspecific and unrelated antecedent events:
  - inflammatory destruction of bronchial and peri-bronchial tissue
  - irreversible dilatation of bronchial tree
  - permanent dilatation of sub-segmental airways
  - chronic daily cough
Bronchiectasis and HIV

- Both T and B cell dysfunction + impaired local defence mechanisms
  - impaired muco-cilliary clearance
  - recurrent pulmonary infections
- Incidence 16%
- Most common causes of bronchiectasis
  - LIP
  - unresolved or recurrent pneumonia
  - TB
WHO Clinical Stage

• 2005 WHO Clinical Stage 3 Condition

• Clinical Diagnosis
  • history of productive cough (copious amounts of purulent sputum)
  • with or without clubbing
  • halitosis
  • crepitations and/or wheezes on auscultation
  • anorexia and FTT non-specific

• Definitive Diagnosis
  • CT scanning the gold standard
  • CXR
CXR findings

- Honeycomb appearance (small cysts)
- and/or persistent areas of opacification
- and/or widespread lung destruction (fibrosis, volume loss)
CT-scan findings
Treatment

- Supportive
  - Hydration and mucous clearance
  - Postural drainage
- Systemic Antibiotic Therapy
  - During acute exacerbations
  - Treat for 2-3 weeks
Summary

• Suspect bronchiectasis in child with persistent night time coughing if other treatment modalities have failed

• Clubbing may not be present

• Indication for HAART

• Patients need:
  1. Chest physiotherapy and postural drainage
  2. Antibiotics for inter-current infections
Aspiration associated lung disease

- Common in HIV infected children
- GERD and naso-pharyngeal reflux may cause
  - Oesophagitis
  - FTT
  - Lung disease – Chronic with acute exacerbations
  - Strictures
Diagnosis

History
- regurgitation
- coughing spells
- milk via nose during feeds
- hoarse voice
- occasionally stridor

Clinical features
- oesophagitis
- Poor weight gain
- look for
  - lung disease
  - neurological disease
Investigations

• CXR
  • Recurrent, persistent or migrating lung infiltrates
• Barium swallow
  • Anatomical abnormalities
• Video Fluoroscopy
  • Suck and swallow in-coordination
• Endoscopy
  • Erosive esophagitis and complications
• Radionucleotide scintigraphy
  • GER, aspiration slow gastric emptying
• pH Studies
Treatment

Problematic

• Feeding adaptation

• Medical management – PPI

• Surgical – Nissan +/- PEG, Managing complications
Summary

• Careful history for reflux particularly important in infants

• If naso-pharyngeal in-coordination
  • look for CNS abnormality
  • consider HAART
South to South