Non-CF Bronchiectasis

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Objectives

• Better understand the pathogenesis of bronchiectasis
• Know how to determine the etiology of bronchiectasis
• Be able to better manage patients with bronchiectasis
• Recognize and manage exacerbations of bronchiectasis
Epidemiology

- Prevalence increasing by about 9% per year from 2000-2007.
- Higher in women and older patients.
- Highest in Asians.
- Is increased prevalence due to greater use of HRCT?
Burden on Patients

• More frequent and long hospitalizations.
• More frequent office visits.
• More extensive/expensive medical treatments.
• Mortality from 10-16% over 4 years.
  – Higher mortality with lower FEV1, higher dyspnea scores, P.A. + cultures, low BMI, male sex, advanced age, COPD, number of affected lobes.
  – Lower mortality in idiopathic cases and with regular vaccines, scheduled visits.
Pathogenesis

Neutrophil Inflammation (Proteases) → Airway Destruction and Distortion (Bronchiectasis)

Bacterial Colonization → Abnormal Mucus Clearance
When to Consider the Diagnosis

- Chronic cough/sputum or recurrent respiratory infections.
- P.A., staph, other GNRs, MAC in sputum.
- Recurrent pneumonia.
- Recurrent hemoptysis.
- Difficult to treat asthma.
- COPD with frequent exacerbations.
- Diagnosis of COPD in nonsmoker.
- Diagnosis made by HRCT of the chest.
Radiographic signs of bronchiectasis. A = Bronchus terminating in a cyst; B = lack of bronchial tapering; C = signet ring sign; D = mucus plug.

Am J Respir Crit Care Med 2013;188, 647-656.
Etiology Based on Distribution of Bronchiectasis on CT

• Both upper lobes with hilar retraction:
  – Post-primary tuberculosis, sarcoidosis, radiation fibrosis.
• Diffuse bronchiectasis:
  – CF, ciliary dysfunction syndrome, childhood pneumonias, CVID.
• Central bronchiectasis with mucus plugs:
  – ABPA.
• Bronchiectasis in dependent lung, with air-fluid levels:
  – Chronic aspiration.
• RML/lingular bronchiectasis with tree-in-bud opacities:
  – Atypical mycobacterial infection.
• Bronchiectasis and fibrosis not conforming to a lobar distribution:
  – Radiation fibrosis.
• Lobar distribution of bronchiectasis:
  – Post-infectious, including bacterial, tuberculous, and fungal.
Diagnosis - Etiology

• Additional history helpful
  – History of recurrent infections, especially sinusitis
  – Infertility
  – History of difficult to control asthma
  – Family history of bronchiectasis, COPD, emphysema, CF
  – Inflammatory arthritis, dry eyes, dry mouth
  – Inflammatory bowel disease – UC or Crohn’s
  – MGUS, multiple myeloma, CLL, stem cell transplant
  – HIV infection
  – Inhalation injury, radiation
  – Childhood infections - pertussis
  – GERD
Etiology

• Cystic fibrosis
• Autoimmune diseases
  – Rheumatoid arthritis
  – Sjögren’s syndrome
• Cilia abnormalities
  – Primary ciliary dyskinesia (PCD)
• Connective tissue diseases
  – Tracheobronchomegaly (Mounier-Kuhn syndrome)
  – Marfan’s disease
  – Cartilage deficiency (Williams-Campbell syndrome)
• Hypersensitivity
  – Allergic bronchopulmonary aspergillosis (ABPA)
Etiology

• Immune deficiency
  – Immunoglobulin deficiency
  – HIV infection
  – Job’s syndrome (hyperimmunoglobulin E syndrome)

• Inflammatory bowel disease
  – Ulcerative colitis
  – Crohn’s disease

• Injury
  – Pneumonia/TB/Atypical Mycobacteria/childhood infections
  – GERD/Aspiration
  – COPD
  – Smoke inhalation
  – Radiation
Etiology

• Malignancy
  – Chronic lymphocytic lymphoma
  – Stem cell transplantation; graft-versus-host disease

• Obstruction
  – Tumor
  – Foreign body
  – Lymphadenopathy

• Other
  – $\alpha_1$-Antitrypsin deficiency
  – Sarcoidosis
  – Yellow nail syndrome
  – Young’s syndrome
Etiology - Testing

- Bacterial, fungal, and mycobacterial sputum culture
- Immunoglobulins A, E, G (subclasses), and M
- Before and after titers to pneumococcal vaccine
- ANA, RF, anti-CCP, SSA, SSB antibodies
- $\alpha_1$-Antitrypsin level and phenotype
- In some cases:
  - Bronchoscopy
  - Gastrointestinal evaluation
Etiology – Cystic Fibrosis

• When and how should CF testing be done in adults with bronchiectasis?
  – Clinical suspicion
    • Diffuse bronchiectasis
    • Chronic sinusitis
    • Bilateral absence of the vas deferens/infertility
    • Pancreatitis/exocrine pancreatic insufficiency
    • Absence of other etiology on initial testing
  – CF testing
    • Adults who escaped diagnosis in childhood may have atypical CF and the sweat chloride test can be non-diagnostic.
    • Sweat chloride - $100-$200. CFTR sequencing - $2000-$3000 for CFTR sequencing).
Etiology – PCD

• When and how should PCD testing be done in adults with bronchiectasis?
  – Clinical suspicion
    • Diffuse bronchiectasis
    • Chronic sinusitis
    • Infertility
    • Situs inversus (~50% of cases – Kartagener’s syndrome)
    • Absence of other etiology on initial testing
Algorithm for the diagnosis of PCD

Clinical history

(Children >6 yrs and post 1994 only) → Nasal nitric oxide

Nasal nitric oxide <250 ppb

Inability to perform screening tests or high index of clinical suspicion with normal screening test results

↔ Adults

Saccharine test

Nasal mucociliary clearance time >60 min

Light microscopy

Abnormal ciliary beat frequency or beat pattern

Electron microscopy

Known ultrastructural defect

PCD diagnosis confirmed

J Clin Pathol 2012;65:267-271
Etiology

Annals ATS 2015 12, 1764-1770.
Management of Non CF Bronchiectasis

Am J Respir Crit Care Med 2013 188, 647-656.
Airway Clearance

- Mobilize secretions and interrupt the cycle of inflammation and infection
- Choices
  - Traditional CPT/postural drainage
  - Oscillatory positive expiratory pressure (PEP)
  - High frequency chest wall oscillation (The VEST)
  - Autogenic drainage
  - Active cycle breathing with huff coughs
  - Nebulized isotonic or hypertonic saline
  - NOT inhaled dornase alfa (Pulmozyme)
Airway Clearance – Inhaled Therapy

• Nebulized hypertonic saline
  – Recommended for CF
  – Cochrane review conclusion
    • It is not possible to draw firm conclusions regarding the effect of nebulized hypertonic saline for non-CF bronchiectasis.
    • The data suggest that it is unlikely to have benefit over isotonic saline in patients with milder disease.
Exercise

- Eight weeks of exercise improves exercise capacity, dyspnea, fatigue.
- Increased time to first exacerbation and reduces number of exacerbations at 12 months.
Bronchodilators

• In the patients with asthma/ABPA and COPD, bronchodilators should be used per the usual guidelines.
• In patients with other types of bronchiectasis, the use of bronchodilators should be tailored to the individual patient as there is little evidence for effectiveness.
Anti-inflammatory Therapy - Steroids

• Oral steroids – useful for ABPA, otherwise risks outweigh benefits
• ICS – Reduces sputum volume.
• ICS/LABA reduces cough, improves QOL.
• Possible increased risk of hemoptysis.
Anti-inflammatory Therapy - Macrolides

• Exert immunomodulatory effects on host inflammatory responses without immunosuppression.
• Modify mucus production, inhibit biofilm production, suppress immune mediators, moderate leukocyte recruitment and function.
• Three large RCTs have shown effectiveness.
• NTM infection must be excluded.
• Concerns for potential development of macrolide resistant bacterial strains.
• No increased CV events found in the three trials.
Complications

- Hemoptysis
- Pneumonia
- Metastatic infection
- Cor pulmonale
- Hypoxemia
- Atypical mycobacterial infection
- Exacerbations
Definition of Exacerbation

• Sometimes difficult to separate from baseline symptoms.
  – Increased sputum volume, purulence, viscosity.
  – Increase in cough, wheezing, dyspnea, hemoptysis
  – Decline in lung function
  – Systemic symptoms – fever, malaise, sweats, anorexia
Treatment of Exacerbations

• Obtain sputum for routine C&S and AFB.
• Chest radiograph as indicated.
• Intensify secretion clearance techniques.
• Use bronchodilators similar to COPD exacerbation treatment.
• Start antibiotics based on the patient’s prior cultures and sensitivities.
• Adjust antibiotics when results of sputum culture and sensitivity analysis available.
# Microbiology

<table>
<thead>
<tr>
<th>Microbiology</th>
<th>n=189 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. influenza</em> type B</td>
<td>63 (33)</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>25 (13)</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>39 (21)</td>
</tr>
<tr>
<td><em>M. catarrhalis</em></td>
<td>41 (22)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>25 (13)</td>
</tr>
<tr>
<td><em>Coliform</em> spp.</td>
<td>19 (10)</td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td>5 (3)</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>4 (2)</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Others</td>
<td>13 (7)</td>
</tr>
</tbody>
</table>

Treatment of Exacerbations: Antibiotics

• If no prior cultures available, start fluoroquinolone with activity against P.A. Higher doses may be needed.
• Addition of nebulized tobramycin may assist in eradication of P.A.
• For resistant P.A. infection, parenteral therapy with ceftazidime equal to extended spectrum penicillin plus aminoglycoside. Combination treatment recommended in BTS guidelines for non-CF patients.
• Two weeks of antibiotics recommended. May require PICC line for home management.
Surgery

Surgery

• With localized disease and failure of treatment or recurrent hemoptysis, lobectomy or segmentectomy can be considered.
• Should be done in specialized centers.
• Thoracoscopic surgery challenging due to vascular pleural adhesions and bronchial artery hypertrophy.
• Recent series from U. of Colorado included 171 patients who had 212 surgical procedures with 0% mortality and overall complication rate of 8.9% — Persistent air leak in 5.6% was most common

Lung Transplantation

• Non-CF bronchiectasis indication in 4.3% of bilateral lung transplants
• Patients have generally good outcomes
• Indications for referral:
  – FEV₁ below 30% predicted or a rapid decline in FEV₁.
  – Exacerbation of pulmonary disease requiring an intensive care unit stay.
  – Increasing frequency of exacerbations requiring antibiotic therapy.
  – Refractory and/or recurrent pneumothorax.
  – Recurrent hemoptysis not controlled by embolization.
Conclusions

• Determination of the etiology possible and important.
• HRCT CT is diagnostic and can suggest etiology.
• Airway clearance techniques are the initial and very important treatment.
• Macrolide therapy is a new and effective tool in preventing exacerbations.
• Antibiotics should be used judiciously and based on sputum culture data.
• Surgery for localized disease and lung transplant are important tools.