For Those Who Lover Sputum: Bronchiectasis

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Objectives

• Increase understanding of the general characteristics of non-CF Bronchiectasis
• Develop an approach to work-up & management
• Categorize & review heterogeneous causes

Disclosure: No Conflicts of Interest
Key References


• Pasteur MC et al, BTS Guidelines for Non-CF Bronchiectasis *Thorax* 2010;65:i1-i58

• *Clinics in Chest Med*, May 2013

• Barker AF: *NEJM* 2003; 346:1383-1393

• Ten Hacken NHT, et al: *BMJ* 2007;335:1089-93
Bronchiectasis

• Irreversible abnormal dilation of bronchial tree
• Inflamed, collapsible airways
• Bacterial Colonization (\textit{S. aureus}, \textit{H. influenzae}, \textit{P. aeruginosa})
• Chronic productive cough (wet vs. dry)
  – Collected sputum→3 layers (foam, clear, purulent)
  – cough 90%, sputum 76%, dyspnea 72%, hemoptysis 56%
• Exam: rales 70%, rhonchi 44%, wheeze 34%.
• Obstructive physiology
  – Low FEV1, FVC preserved
  – Decreased DLCO
Parts of some airways become widened.

Extra mucus collects in the widened airway. This is prone to infection.
Bronchiectasis

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Total Prevalence: ~52/100,000

Prevalence may be increasing
SI F>M predominance

Useless Morphology Classification

• Bronchiectasis can be:
  – Focal (lobe/segment)
  – Diffuse

• Cylindrical: creates tram track lines

• Varicose: beaded bronchi.

• Cystic: occ large cysts imitate cavity or give grape cluster pattern
Vicious Cycle Hypothesis

• Microbial colonization initiates & perpetuates airway inflammation
• PMNs infiltrate lungs & cause structural airway damage
• Impaired mucociliary clearance.
• Optimal for bacterial growth & certain spp. Selection (eg, *S. aureus*, *H. flu*, *P. aeruginosa*)
Lung inflammation triggered

Inflammatory response activated
- Mucus production
- Cellular defenses
- Chemical defenses

Pulmonary defenses ineffective: lung infection

Increased:
- Mucus production
- Inflammation

Lung damage

Mucus plugging/airway obstruction

Mucus retained
Bronchiectasis Differential Diagnosis

- **Idiopathic (50→10%...)**
- Airway obstruction
- Primary Ciliary Dyskinesia Syndrome (PCD)
- **Immunodeficiency (Ig Def, CLL/Rx, GVHD, HIV)**
- **Post-infectious**
- Diffuse Panbronchiolitis
- Inflammatory Disease
- Alpha-1-Antitrypsin Syndrome
- **Cystic Fibrosis**
Airway Obstruction

• Foreign Body Aspiration
  – Lower lobes, posterior segment upper lobe
• Obstruction broncholith, slow growing/B9 tumor
• Lymph nodes enlargement
  – Middle Lobe Syndrome
Differential Diagnosis

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Primary Ciliary Dyskinesia (PCD)

- Incidence ~ 1/15000 – 1/60000
- Autosomal recessive (some DNAH11)
- Classic triad
  - Bronchiectasis
  - Sinusitis
  - Variable male sterility
- Situs inversus (50%) = Kartagener’s
- Classic ultrastructure defect…
Nasal NO for PCD Diagnosis

- Proper SOP, nNO <77: Sensitivity 98%, Spec 99%
- 6 other centers: Identified correctly 70 out of 71 PCD
- Technology more user friendly
- nNO for screening then confirm by EM, \textit{in vitro/vivo} assess

Leigh et al. \textit{Ann ATS} 2013;10:574-81
Differential Diagnosis

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• Airway obstruction
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• Post-infectious
• Diffuse Panbronchiolitis
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• Cystic Fibrosis
Immunodeficiency

- Hypogammaglobulinemia presents in children
  - Recurrent sinopulmonary infections (middle ear)
  - Can be acquired in elderly
  - Measure IgA, IgG, and IgG subclasses
  - Measure response to protein, polysaccharide vaccine
  - NB: D/t dysregulated T-cell function lung/LN bx may show granuloma → misDx sarcoid/TB/NTM
  - Treatment: IVIG infusion q mo.

- Heme-Malig: CLL, post rituximab, GVHD
- AIDS associated bronchiectasis (recurrent infection)
- Jobs Syndrome
Differential Diagnosis

• Idiopathic (50→10%...)
• Airway obstruction
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• Post-infectious
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Post-Infectious

- Viral, Mycoplasma
- TB
- Pertussis
- Nontuberculous mycobacteria & Nodular Bronchiectasis
- Aspergillus
- Severe/recurrent bacterial pneumonia
  - Post-op. nosocomial pneumonia
  - Associated with kyphoscoliosis
What do you know about Nodular/Bronchiectasis Form of MAC Lung Infection? What about Rapid Growers? NTM Lung Infection a/w Pre-existing Bronchiectasis or CF?

Fascinating Stuff???
Post-Infectious

- Viral, Mycoplasma
- TB
- Pertussis
- NTM and nodular bronchiectasis
- Aspergillus
- Severe/recurrent bacterial pneumonia
  - Post-op. nosocomial pneumonia
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**Allergic Bronchopulmonary Aspergillosis (ABPA)**

1. Asthma
2. Skin test reactivity to *Aspergillus fumigatus*
3. Serum precipitins to *Aspergillus fumigatus*
4. IgE elevation (>1000 ng/ml or >500 IU/ml)
5. Specific IgE (IgG) antibodies to *Aspergillus fumigatus*
6. Proximal Bronchiectasis
7. Pulmonary Infiltrates (eg. fleeting, upper lobes, mucoid impaction)
8. Eosinophilia with pulmonary infiltrates

Note: Positive sputum culture not essential for diagnosis

Allergic Bronchopulmonary Mycosis (other Aspergillus spp, Candida, other fungi)

Adapted from Patterson & Greenberger
Post-Infectious

- Viral, Mycoplasma
- TB
- Pertussis
- NTM and nodular bronchiectasis
- Aspergillus
- Severe/recurrent bacterial pneumonia
  - Post-op. nosocomial pneumonia
  - Associated with kyphoscoliosis
Differential Diagnosis

• Idiopathic
• Airway obstruction
• Dyskinetic Cilia Syndrome
• Immunodeficiency (Agammaglobulinemia)
• Post-infectious
  • Diffuse Panbronchiolitis
  • Inflammatory Disease
  • α-1 Antitrypsin Syndrome
  • Cystic Fibrosis
Diffuse Panbronchiolitis (DPB)

- Japanese, Korean, M:F 2:1, onset 20-80 y.o
- Clinical characteristics
  - Chronic sinusitis 75%, precedes lung disease (yrs or decades)
  - Productive cough, dyspnea, wheezing, weight loss, clubbing uncommon
  - Sputum: *H. influenzae*, *S. aureus*, *P. aeruginosa*
  - Acquisition of Psa→poor survival (8%@ 5 yr)
  - PFTs: obstructive, mixed obstructive/restrictive
  - Histopath: localized to resp bronch. transmural inflammation (lymphocytes, foamy macrophages)
  - **No:** exocrine dysfunction, ↑ sweat Cl, CFTR abnormality
Survival Curves According to Year of Diagnosis

Group A = 1970 - 1979, n= 190
B = 1980 - 1984, n= 221
C = 1985 - 1990, n= 87

WHY?
DPB and Macrolide Rx

- Serendipitous discovery 1982
- Standard: E-mycin 400-600 mg/day continuous
- No significant change in bacterial flora & serum levels (1 \( \mu \text{g/ml} \)) don’t exceed MICs
- Clinical factors improved
  - Randomized blinded trial (Yamamoto et al, 1991)
    - 3 mos E-mycin vs. placebo
    - Improved DOE, sputum volume, CRP, PFTs, CXR)
  - PFTs
  - *P. aeruginosa* infected group improves also
  - Mortality rates decreased
- Other macrolides tested (clari-, roxi-, azithromycin)

*In vitro* data: Macrolides modulate inflammatory response & Inhibit *P. aeruginosa* virulence factors (eg, biofilm)
Differential Diagnosis

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Young’s Syndrome

- Similar to CF
- Sinusitis, bronchiectasis, azoospermia
- Normal Sweat Cl, NPD
- Normal pancreas function
- No genetic link yet found
- Infertile middle age males
- Decreasingly found (toxic exposure births/prior era?)
Inflammatory Diseases & Bronchiectasis

- Sjogren’s Syndrome
- Rheumatoid Arthritis
- Ulcerative Colitis >> Crohn’s disease
Alpha-1-Antitrypsin Deficiency

- Radiographic:
  - Cystic bronchiectasis 10-20%
  - Emphysema co-exists or overshadowed
  - No other predisposing illness

- Uncertain clinical correlation (sputum production)

- No pathophysiologic association
  - All causes bronchiectasis: no increase in AAT alleles
    (Cuvilier et al: Chest 2000)
Differential Diagnosis

- Idiopathic (50→10%...)
- Airway obstruction
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- Post-infectious
- Diffuse Panbronchiolitis
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- Cystic Fibrosis
Differential Dx
(Mnemonic: IA_SPICE)

- **I**diopathic
- **A**irway Obstruction
- **S**jogren’s & other Inflammatory (RA, IBD)
- **P**ost-Infectious (TB, non-tuberculosous mycobacteria, Aspergillus, Pertussis, NP, virus)
- **I**mmunodeficiency (Ig, AIDS)
- **C**F & other genetic/congenital (Primary Ciliary Dyskinesia, Sequestration, $\alpha$-1 Anti-trypsin)
- **E**soteric (Diffuse Panbronchiolitis, Yellow Nail Syn., Tracheobronchomegaly [Mounier-Kuhn], Cartilage deficiency [Williams-Campbell], Swyer James)
How do you evaluate a patient for bronchiectasis?
Evaluation for Bronchiectasis

• History
  – Poorly resolving/recurrent pneumonia
  – Purulent sputum (quantify)
  – H/O of difficult asthma management
  – Family history/GI problems/infertility

• Exam
  – nasal polyps
  – localized rales, wheezes, or rhonchi
  – clubbing
Evaluation for Bronchiectasis
Lab Data

• Spirometry

• Sputum Gram Stain & Culture (quantitative)
  – S. aureus, H. influenzae
  – P. aeruginosa (mucoid?)
  – AFB smear/culture (AM x3 Mail Back)

• Consider:
  – Immunoglobulin electrophoresis & quantification of IgG subclasses; pre/post PVX/DT titers
  – Sweat Chloride, CF genetics (Ambry lab), NPD
  – RF, CCP, ANA, SSA, SSB antibodies
  – Exhaled nasal Nitric Oxide screen, then EM, genetics,
  – Asthma?, Eos?, Aspergillus skin test, IgE (ARUP ABPA panel)
  – Bronchoscopy for cultures (eg, elderly: NTM, other bacteria)

• Radiology Evaluation
  – Chest x-ray & High Resolution Chest CT
  – Sinus CT
What are the radiographic features of bronchiectasis?
Radiography

- Bonchograms (history of medicine)
- CXR and High Resolution CT
  - Signet Ring
  - Tram Tracks
  - Engagement Ring
  - Railroad tracks
Swollen airway wall

Air in dilated airway

Normal Airway

Swollen airway wall
CT Characteristics:

- High resolution = Thin sections (1.5-3 mm)
- Normal:
  - Bronchus
  - Vessel
- Engagement (Signet) ring:
  - Bronchus
  - Vessel
- Railroad tracks
HRCT: Other Characteristics

• Lack of tapering bronchi

• Clusters = Grape-like appearance

• Enlarged bronchi can appear cystic vs. Blebs of emphysema (thinner walls)
Lack of Tapering Bronchi
Grape-like Clusters
Cystic Bronchi
HRCT bronchiectasis Dx

- Central $\rightarrow$ ABPA
- Upper lobe $\rightarrow$ CF
- Lobar $\rightarrow$ Post-infectious; obstructive (eg, LN, FB)
- Correlation: # abnormal airways and severity
Traction Bronchiectasis

- Radiographic finding w/o clinical features of bronchiectasis
- Pulmonary Fibrosis
- Radiation injury
How do you identify acute exacerbation of bronchiectasis?
Symptoms of Acute Exacerbation of Bronchiectasis

- Change in sputum production
- Increased dyspnea
- Increased cough
- Increased wheezing
- Malaise, fatigue, lethargy, decreased exercise tolerance
- ± Fever (T>38)
- Changes in chest exam
- Reduced pulmonary function
- Radiographic changes (subtle vs. new infiltrate)

Adapted from Odonnell et al: Chest 1998
How do you treat bronchiectasis?
Rx Extrapolated from CF…

- Antibiotics generally effective for chronic Rx
  - Suppress bacteria burden: ↓ bacteria = ↓ evil cytokines
    - Nebulized tob, gent, colistin effective, small trials
    - Nebulized aztreonam (Cayston) not effective
  - Eradication Rx for *P. aeruginosa* likely effective
  - Cycling antibiotics: no supportive data, but often done

- Exacerbation: IV antibiotics aimed at predom spp
  …little supportive data

- Pulmozyme trial…not good, maybe harmful

- Anti-inflammatory Rx
  - Avoid long term steroids except ABPA
  - ICS weak data; ICS/LABA no supportive data (ex. Asthma too)
  - Macrolide randomized control trial data supportive
    Azithro MWF (EMBRACE, BAT trials) & E-mycin 250 bid (BLISS)

Bronchiectasis Treatment Overview

- Manage/alter underlying cause
- Antibiotics
  - Acute exacerbation, parenteral abx based on culture & susceptibilities
  - Preventive strategies-uncertain benefit
    - Cycling Abx (no real data to support)
    - Inhaled Abx (tobramycin [gent], colistin, not aztreonam)
- 7% saline neb bid
- Bronchodilators (widely used…no good data)
- Chest physiotherapy (various modalities) & Aerobic exercise
- Pulmozyme…No
- ICS (minimal if any benefit)
- Macrolides (must r/o NTM)
- Nutrition
- Surgery
Comprehensive Overview

Bronchiectasis Confirmed by HRCT

Clinical History and Laboratory Evaluation to Identify Etiology

Treat Underlying Cause (eg, AAT Replacement, IgG Replacement)

Initiate Airway Clearance
1. Nebulized Agent
2. Chest Physiotherapy
3. Postural Positioning

Sputum Culture

Exercise Program or Pulmonary Rehabilitation

Consider Macrolide Therapy if Patient Experiences Frequent Exacerbations

Normal Flora
- Observe

Non-Pseudomonas
- Antibiotic targeted toward specific bacteria and local sensitivity patterns*

Pseudomonas
- Attempt eradication
- Suppressive antibiotics (nebulized)

NTM
- Monitor future cultures for NTM
- If > 2 positive cultures consider treatment according to ATS/IDSA guidelines
- Avoid macrolide monotherapy