

Bronchiolitis: A Clinical Approach

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Disclosures

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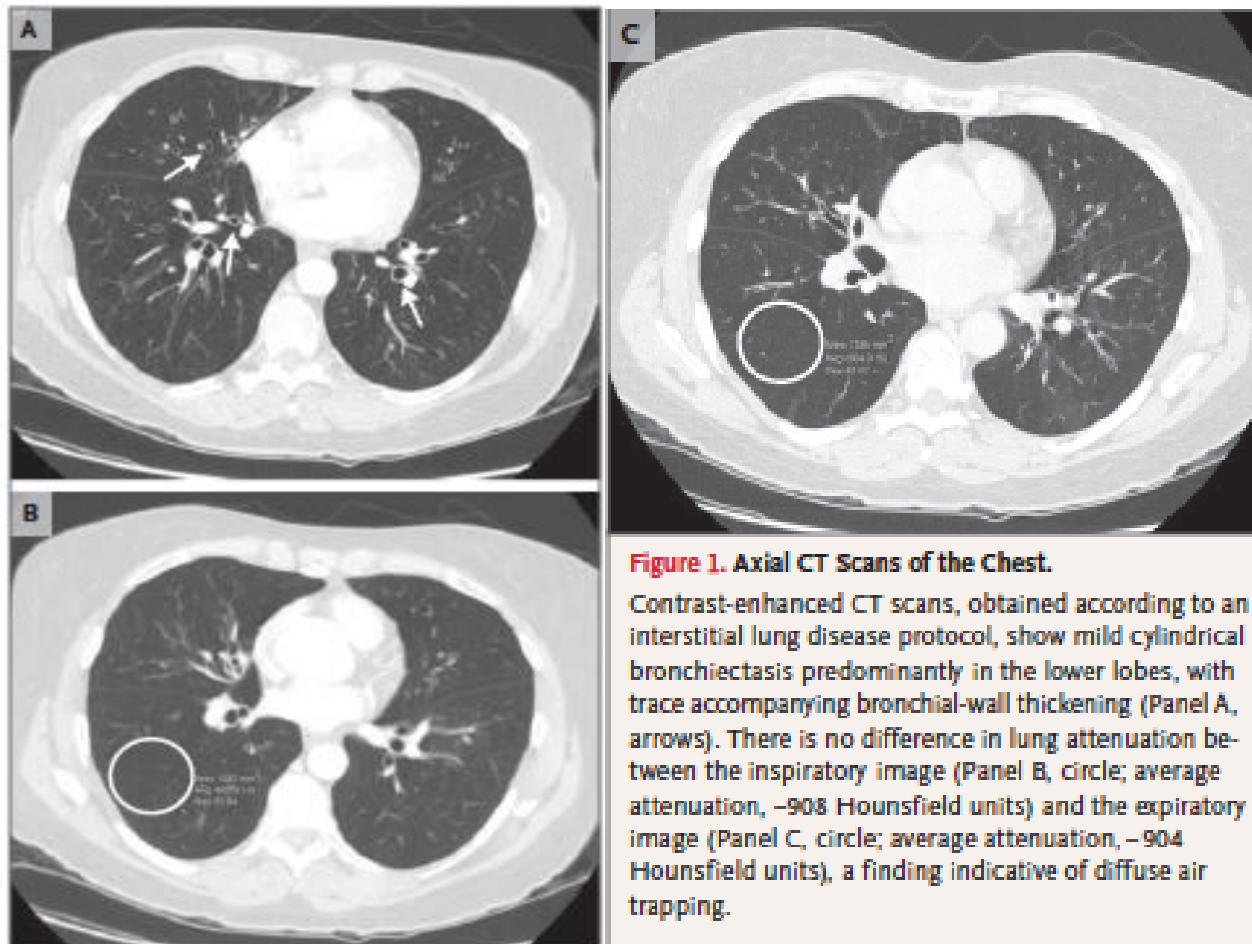
Clinical Summary

- 60 F with a non-productive cough followed by progressive dyspnea
- No improvement with ICS/LABA
- Ambient air saturation of 94%
- PE-CT with mild bronchial wall thickening and mild LLL bronchiectasis

Table 1. Results of Pulmonary-Function Testing.*

Variable	7 Mo before This Evaluation	4.5 Mo before This Evaluation	13 Days before This Evaluation	On This Evaluation
FEV ₁ before bronchodilator (liters)	1.06	1.32	0.88	0.90
FEV ₁ before bronchodilator (% of predicted value)	45	56	35	38
FEV ₁ after bronchodilator (liters)	1.25	1.32	0.96	0.91
Change in FEV ₁ from before bronchodilator to after (%)	18	0	9	1
FVC before bronchodilator (liters)	2.61	3.16	1.89	2.04
FVC before bronchodilator (% of predicted value)	90	109	59	69
FVC after bronchodilator (liters)	3.02	3.28	2.50	2.01
Change in FVC from before bronchodilator to after (%)	15	4	32	-1
Ratio of FEV ₁ to FVC	0.41	0.42	0.47	0.44
Total lung capacity (liters)	4.69	5.48	5.37	5.56
Total lung capacity (% of predicted value)	100	117	109	113
Residual volume (liters)	1.76	1.76	2.72	3.24
Ratio of residual volume to total lung capacity	0.44	0.41	0.51	0.58
Ratio of residual volume to total lung capacity (% of predicted value)	116	109	126	149
Diffusion capacity of the lung to transfer carbon monoxide (ml/min/mm Hg)	12.80	14.30	10.67	10.32 (corrected for hemoglobin)
Diffusion capacity of the lung to transfer carbon monoxide (% of predicted value)	62	69	44	49
6-minute walk test (ft)			1212 (with lowest measured arterial oxygen saturation of 93%)	

* FEV₁ denotes forced expiratory volume in 1 second, and FVC forced vital capacity.



Clinical Summary

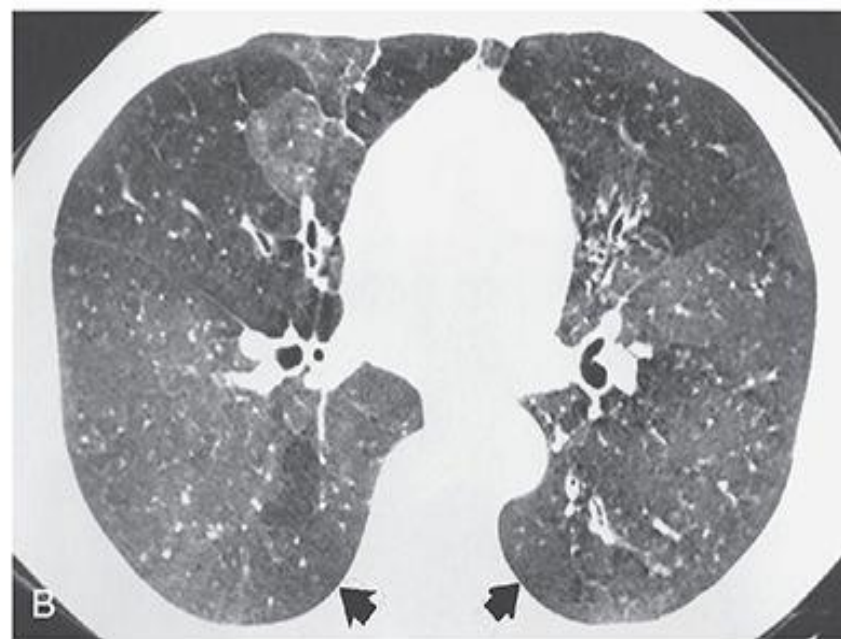
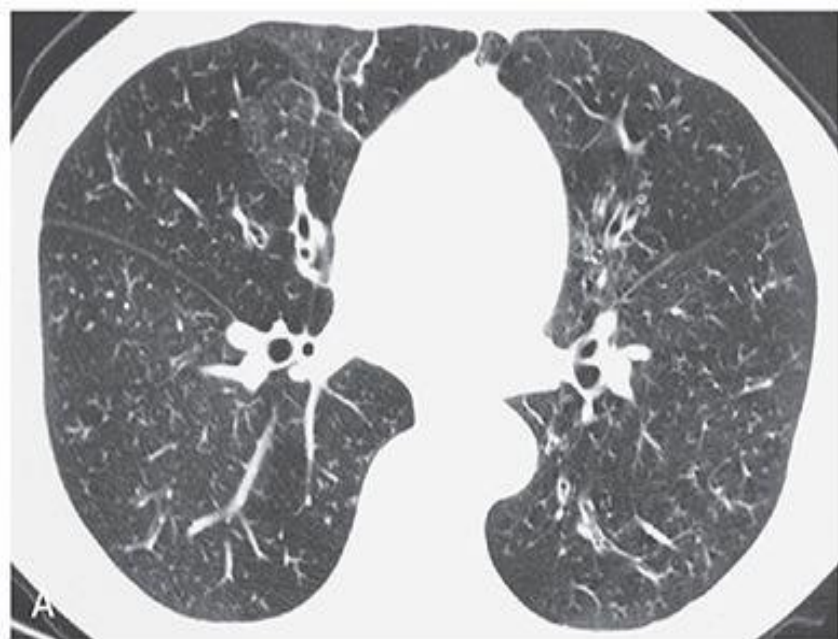
- Severe obstructive ventilatory deficit
 - Progressive over 7 months
 - Loss of bronchodilator response
 - Preserved lung volumes
 - Increasing hyperinflation
 - Worsening diffusion impairment
- BAL without infectious organism(s) and negative for pepsin

Bronchiolitis

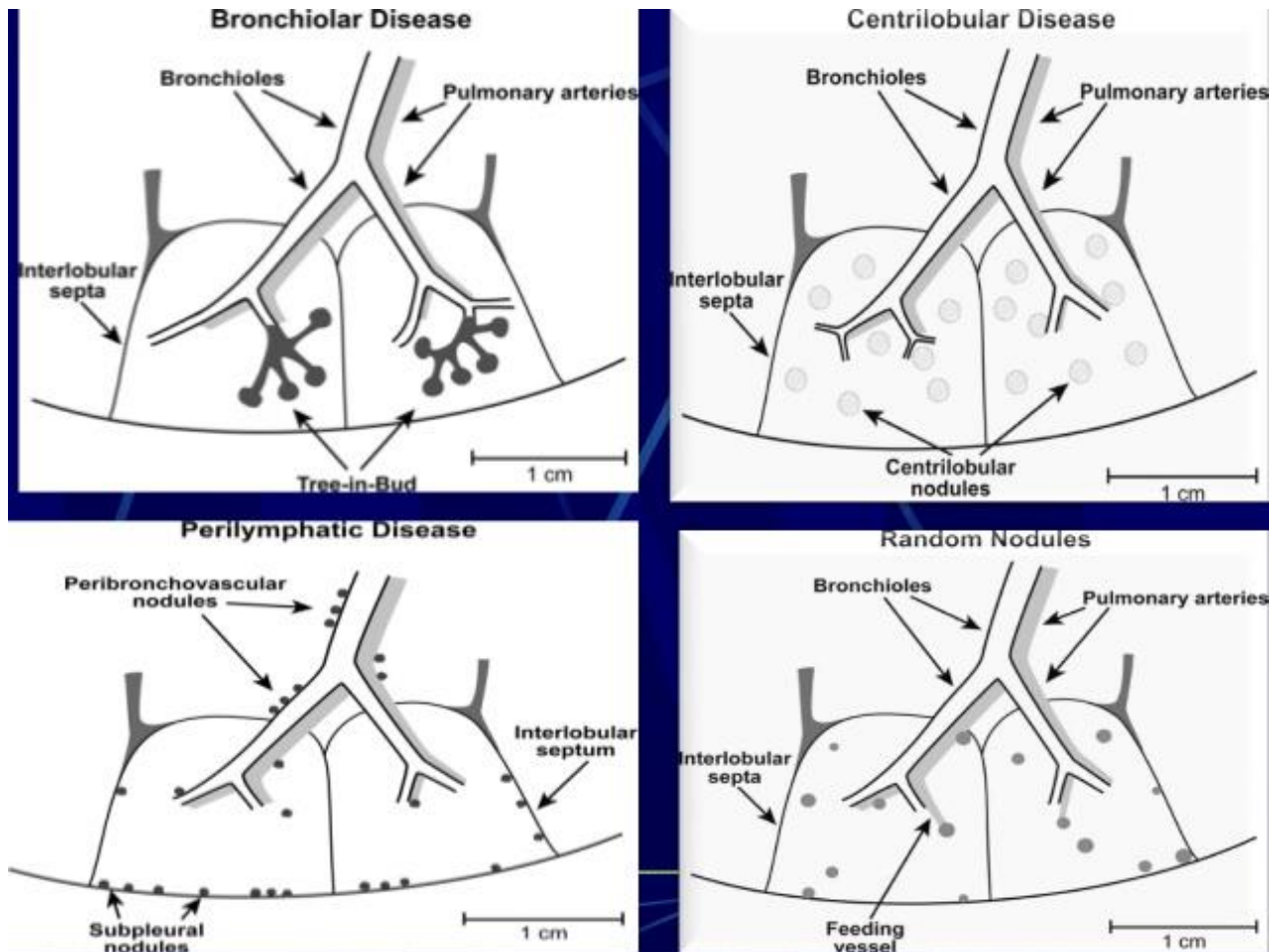
- Disease of the small airways (<2mm)
- Dyspnea and cough
- Airway obstruction +/- reduced DLCO
- Chest radiograph often clear
- HRCT with centrilobular nodules and / or mosaic attenuation or “gas trapping”

Mosaic Attenuation

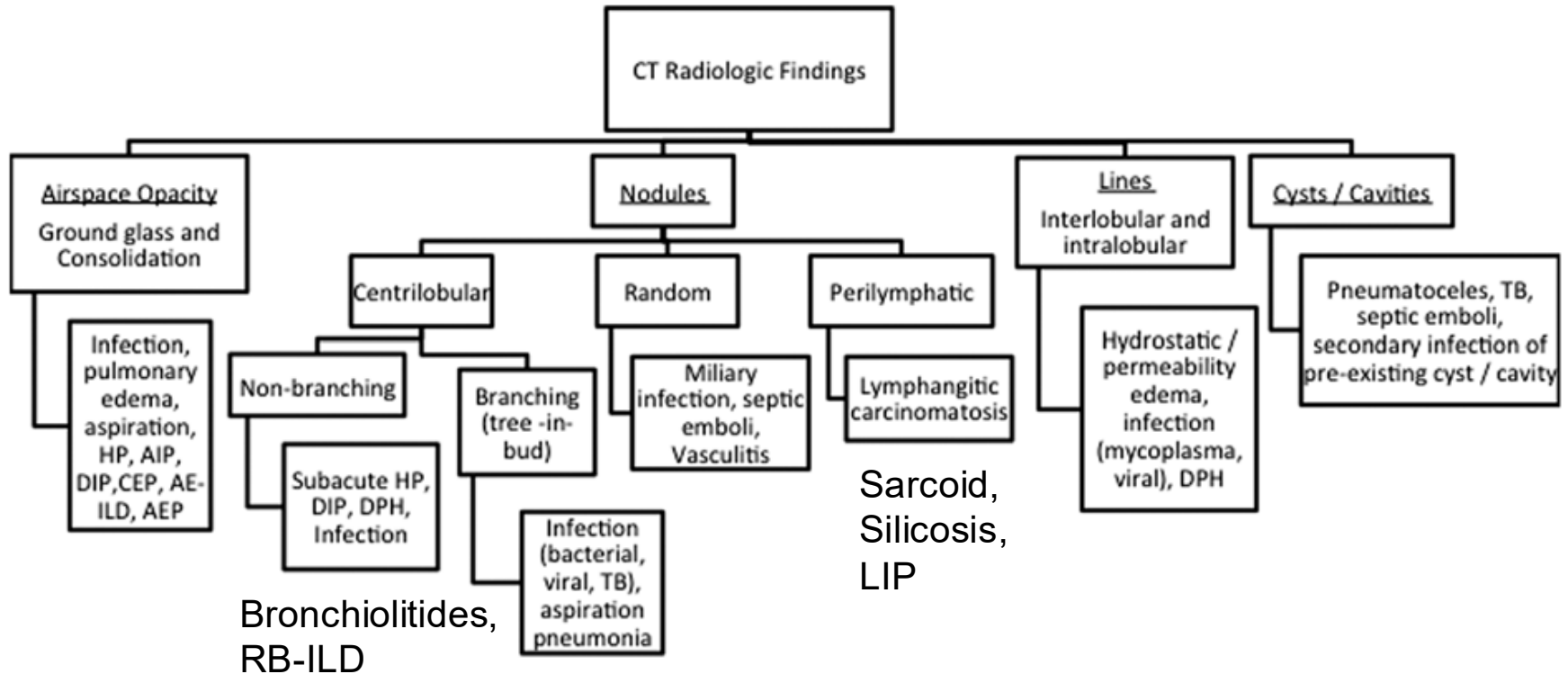
- Mosaic Attenuation – “Patch work” appearance on CT
 - Small airways disease (areas of low attenuation d/t decreased ventilation) – asthma, bronchiolitis, HP
 - Chronic thromboembolic disease (areas of low perfusion)
 - (Parenchymal disease (increased attenuation d/t ground glass))
- Gas Trapping – aka air trapping
 - D/t small airways disease
 - Areas of the lung that do not have normal (increased) attenuation w/ expiration (HRCT)



Nodule Distribution



DDX by Nodule Type



Types of Bronchiolitis

- Acute bronchiolitis
- Panbronchiolitis
- Respiratory bronchiolitis
- Follicular bronchiolitis
- Granulomatous bronchiolitis
- Obliterative (constrictive) bronchiolitis

ILD and Bronchiolitis

- Respiratory Bronchiolitis (RB-ILD)
- Hypersensitivity Pneumonitis
- Sarcoidosis
- Granulomatous-lymphocytic ILD
- Cryptogenic Organizing Pneumonia
- Airway Centered Interstitial Fibrosis

Idiopathic Bronchiolocentric Interstitial Pneumonia

Standardized Clinical Terms and Definitions for Interstitial Lung Disease A Consensus Statement from the Fleischner Society

Idiopathic bronchiolocentric interstitial pneumonia

- Cryptogenic HP
- Antigen-indeterminate HP
- Airway-centric/centered disease
- Airway-centric/centered fibrosis
- Airway-centered interstitial pneumonia
- Airway-centered interstitial fibrosis
- Bronchiolocentric pattern of interstitial pneumonia
- Acknowledges the multiple possible causes of this imaging and biopsy pattern
- Calls attention to the need for careful consideration of all potential causes of airway-centered interstitial pneumonia
- Harmonizes the classification and terminology across major interstitial pneumonia patterns and multidisciplinary diagnoses
- Facilitates future research to identify and better define potentially unique disease subtypes

Ryerson et al, AJRCCM, 2025

Acute Bronchiolitis

- Most commonly seen in children
- Viruses - RSV, influenza, parainfluenza, adenovirus
- Bacteria - Mycoplasma
- Usually self-limited
- Rarely, progresses to constrictive bronchiolitis

Panbronchiolitis

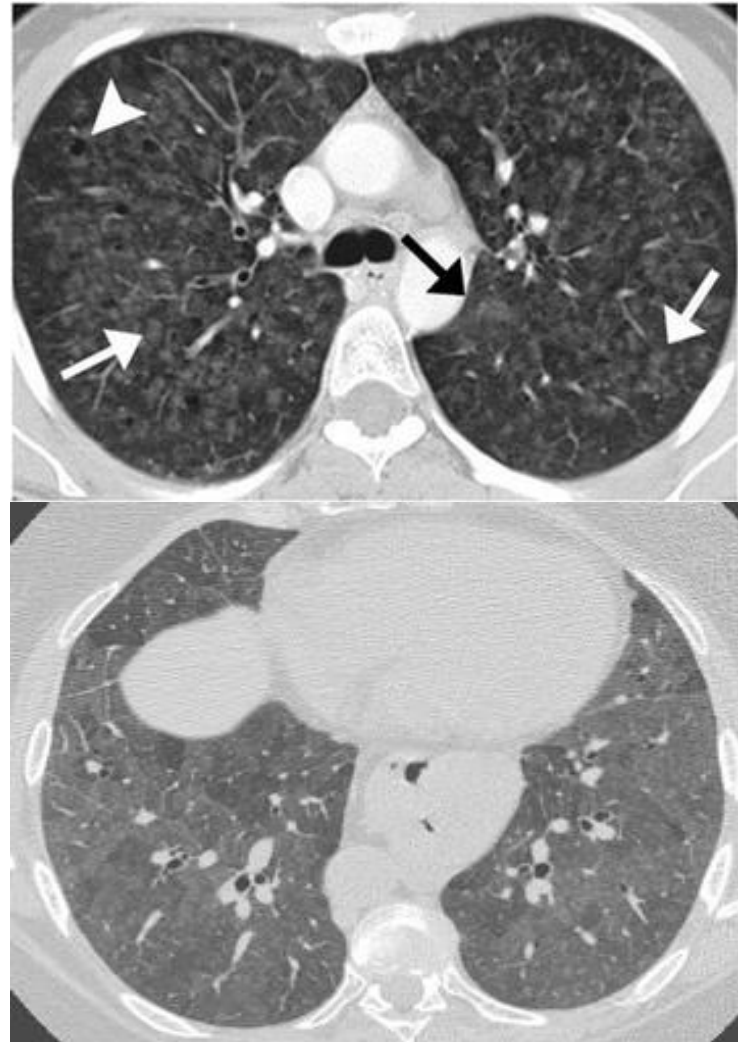
- Diffuse – distribution
- Pan – all levels of bronchioles affected
- Usually affects Japanese males
- Onset 4th – 5th decade of life
- Associated with chronic sinusitis and recurrent infections (H. influenza and Pseudomonas)



- DDX
 - Chronic bronchitis / bronchiectasis
 - PCD / CK
 - Immunodeficiencies
 - RA / IBD – related bronchiolitis
- Treatment
 - Suppressive macrolide therapy

Respiratory Bronchiolitis

- Seen in smokers
- May be incidental finding on pathology
- Dyspnea + radiographic abnormalities = RB-ILD
- CT Chest with centrilobular nodules (poorly defined) and ground glass opacities (often upper lobes)
- Smoking cessation +/- immunosuppression



Follicular Bronchiolitis

- Centrilobular nodules
+ ground glass
- Connective tissue diseases
 - Rheumatoid Arthritis
 - Sjogren's syndrome
- Immunodeficiencies
 - HIV
 - CVID
- Treatment based on
underlying condition



Granulomatous Bronchiolitis

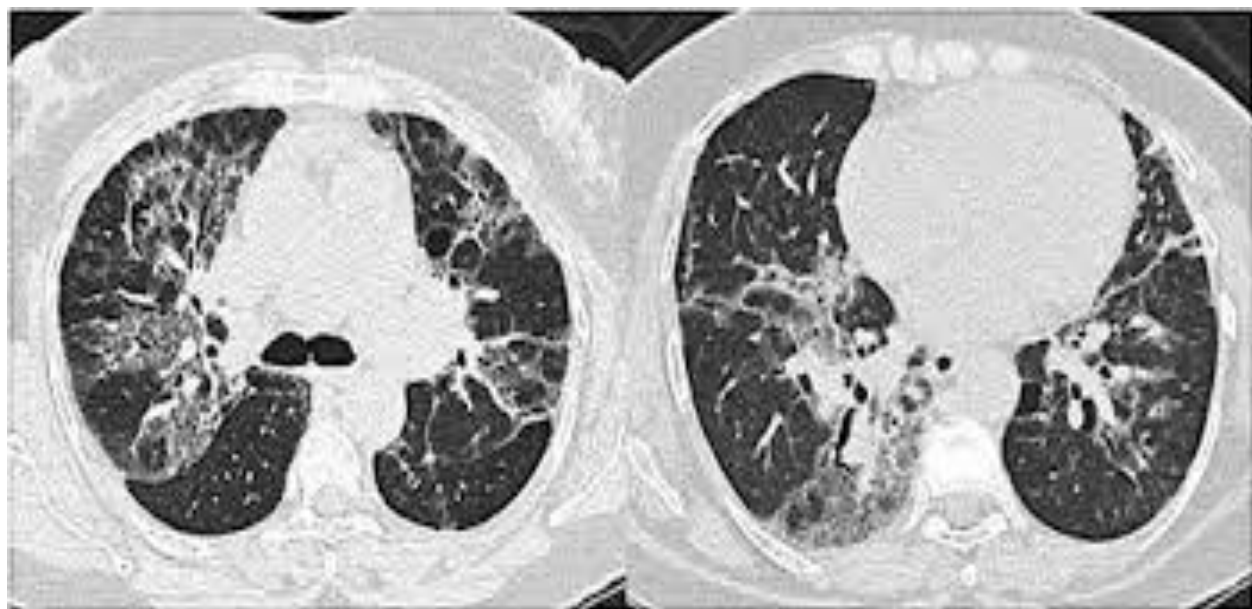
- Pathologic diagnosis
- Inflammatory bowel diseases
- Interstitial lung diseases
 - Hypersensitivity pneumonitis
 - Sarcoidosis
 - GL-ILD
- Infectious causes
 - TB and NTM

Cryptogenic Organizing PNA

- Previously called bronchiolitis obliterans organizing pneumonia (BOOP)
- Injury to alveolar epithelium
- Idiopathic interstitial pneumonia
- HRCT with patchy areas of consolidation / nodules and ground glass

Airway Centered Interstitial Fibrosis

- Female predominant
- Onset 40-60's
- Progressive
- CT Chest with bronchial wall thickening, traction bronchiectasis, and ground glass (peribronchovascular)



Obliterative Bronchiolitis

- Also called constrictive bronchiolitis
- Symptoms of dyspnea + cough
- Non-reversible airflow obstruction
- Diffusion impairment
- Mosaic attenuation / gas trapping on HRCT

Causes

- Post-infectious
- Medications – penicillamine, gold
- Toxins
 - Sulfur dioxide and hydrogen sulfide
 - Nitrogen oxides (fertilizers)
 - Food flavoring (diacetyl)
 - *Sauropus androgynus* (katuk)

Constrictive Bronchiolitis in Soldiers Returning from Iraq and Afghanistan

RESULTS

Among the soldiers who were referred for evaluation, a history of inhalational exposure to a 2003 sulfur-mine fire in Iraq was common but not universal. Of the 49 soldiers who underwent lung biopsy, all biopsy samples were abnormal, with 38 soldiers having changes that were diagnostic of constrictive bronchiolitis. In the remaining 11 soldiers, diagnoses other than constrictive bronchiolitis that could explain the presenting dyspnea were established. All soldiers with constrictive bronchiolitis had normal results on chest radiography, but about one quarter were found to have mosaic air trapping or centrilobular nodules on chest CT. The results of pulmonary-function and cardiopulmonary-exercise testing were generally within normal population limits but were inferior to those of the military control subjects.

CONCLUSIONS

In 49 previously healthy soldiers with unexplained exertional dyspnea and diminished exercise tolerance after deployment, an analysis of biopsy samples showed diffuse constrictive bronchiolitis, which was possibly associated with inhalational exposure, in 38 soldiers.

Causes

- Post-transplant
 - Allogeneic HSCT
 - Lung (Bronchiolitis Obliterans Syndrome)
- Systemic Diseases
 - Ulcerative colitis, Crohn's disease
 - RA, scleroderma
- Idiopathic

Clinical Course and Diagnosis

- Progressive
- Can lead to respiratory failure
- Bronchiolectasis and bronchiectasis – late in disease
- Diagnosis made via VATS (except for BOS)
- Narrowing to obliteration of airway lumen c/w constrictive bronchiolitis

Treatment - BOS

ORIGINAL ARTICLE

A randomised controlled trial of azithromycin therapy in bronchiolitis obliterans syndrome (BOS) post lung transplantation

Paul A Corris,^{1,2} Victoria A Ryan,³ Therese Small,¹ James Lordan,¹ Andrew J Fisher,^{1,2} Gerard Meachery,¹ Gail Johnson,¹ Chris Ward²

Table 2 Mean difference in FEV₁ between treatment groups for the intention-to-treat (ITT, n=46), 'as treated' (n=46) and Completer (n=33) populations

Outcome FEV ₁ (L)	Mean difference in FEV ₁ (azithromycin minus placebo)	95% CI for population mean difference	p Value
	ITT analysis 46 patients, 177 measurements		
Mean difference in FEV ₁ between treatment arms, adjusted for baseline FEV ₁ , randomisation stratification variables (disease and transplant) and time since randomisation	0.035	−0.112 to 0.182	0.6
	'As treated' analysis 46 patients, 177 measurements		
Mean difference in FEV ₁ between treatment arms, adjusted for baseline FEV ₁ , randomisation stratification variables (disease and transplant) and time since randomisation	0.306	0.181 to 0.431	<0.001
	Completers analysis 33 patients, 124 measurements		
Mean difference in FEV ₁ between treatment arms, adjusted for baseline FEV ₁ , randomisation stratification variables (disease and transplant) and time since randomisation	0.278	0.170 to 0.386	<0.001

Treatment - BOS

Clinical Research: Supportive Care

Fluticasone, Azithromycin, and Montelukast Treatment
for New-Onset Bronchiolitis Obliterans Syndrome after
Hematopoietic Cell Transplantation



Kirsten M. Williams^{1,2,*}, Guang-Shing Cheng³, Iskra Pusic⁴, Madan Jagasia⁵, Linda Burns⁶,
Vincent T. Ho⁷, Joseph Pidala⁸, Jeanne Palmer⁹, Laura Johnston¹⁰, Sebastian Mayer¹¹,
Jason W. Chien¹², David A. Jacobsohn¹, Steven Z. Pavletic², Paul J. Martin³, Barry E. Storer³,
Yoshihiro Inamoto¹³, Xiaoyu Chai³, Mary E.D. Flowers³, Stephanie J. Lee³

- Phase II, open-label, multicenter study
- 6% with treatment failure (decline in FEV1 > 10%) at 3 months in FAM group compared to historical controls (40%)

Returning to the Patient..

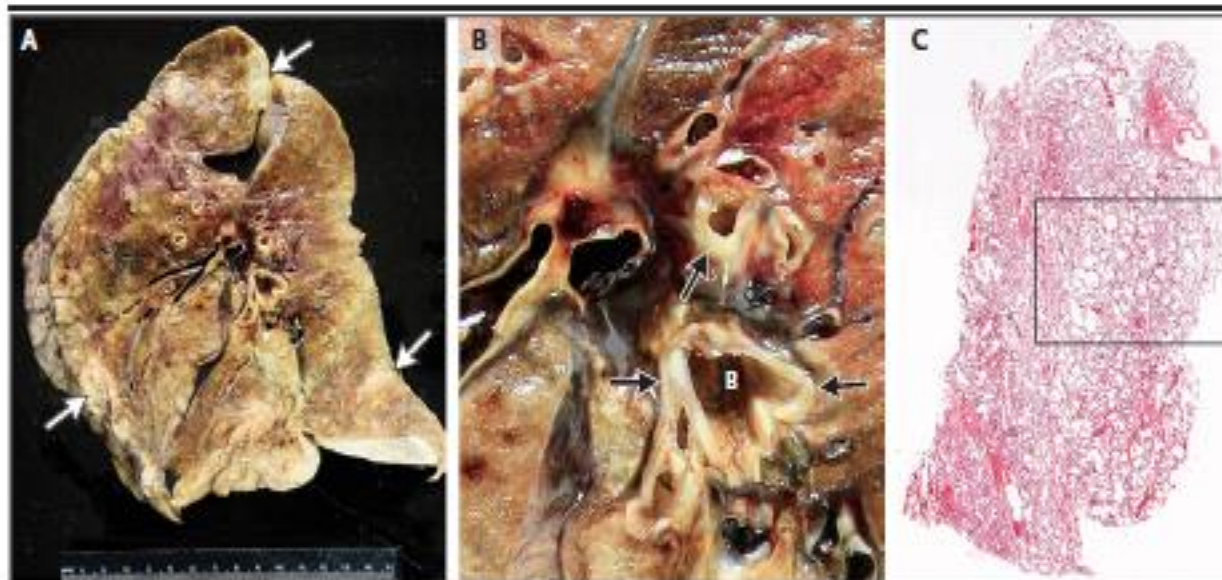


Figure 3. Lung-Explantation Specimen.

A photograph of the explanted right lung (Panel A) shows central bronchiectasis and peripheral organizing pneumonia beneath the pleura (arrows). A photograph of the explanted lung at higher magnification (Panel B) shows the ectatic bronchi (B) and thickened walls (arrows). Scanning magnification of a histologic section of the explanted lung (Panel C) shows extensive dilatation of peripheral air spaces and a virtual absence of recognizable bronchioles (particularly in the rectangle).

Questions ?