

Update in Internal Medicine 2026

Saturday, May 2 • 8 a.m. – 4 p.m.

UT Southwestern Medical Center, T. Boone Pickens Medical Education & Conference Center



Clinical Approach to Interstitial Lung Disease

Megan Kypreos, MD

Assistant Professor

UT Southwestern Medical Center

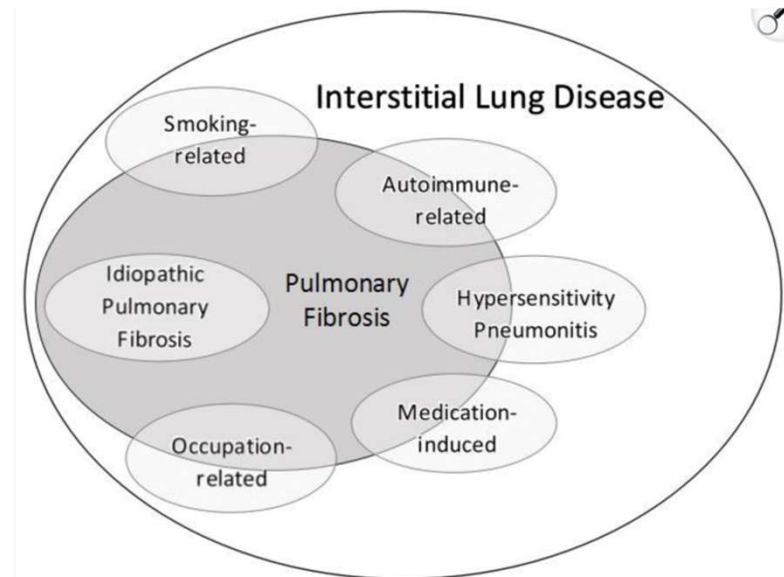
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Medical Center

Objectives

- Define interstitial lung disease and understand the importance for internists
- Distinguish the various etiologies of interstitial lung disease using an algorithm
- Develop an approach to the diagnostic evaluation of interstitial lung disease using an algorithm
- Apply the diagnostic algorithm to a case
- Understand the benefits and side effect profiles of the three antifibrotic medications

Definition of Interstitial Lung Disease

- Group of lung diseases comprised of a combination of inflammation and fibrosis of the lung parenchyma
- Encompasses more than 100 conditions



Kalchiem-Dekel, O. et al. Interstitial Lung Disease and Pulmonary Fibrosis: A Practical Approach for General Medicine Physicians with Focus on the Medical History. *J. Clin Med.* 2018, 7(12):476. doi: 10.3390.

Importance for the Internist

- Interstitial lung disease is increasingly recognized on CT chest imaging
- Early interstitial lung disease can be present in 2-7% of non smokers and in 4-9% of smokers over the age of 60
- Course can be progressive with a high mortality
- Therapies decrease the rate of progression but do not reverse or halt fibrosis

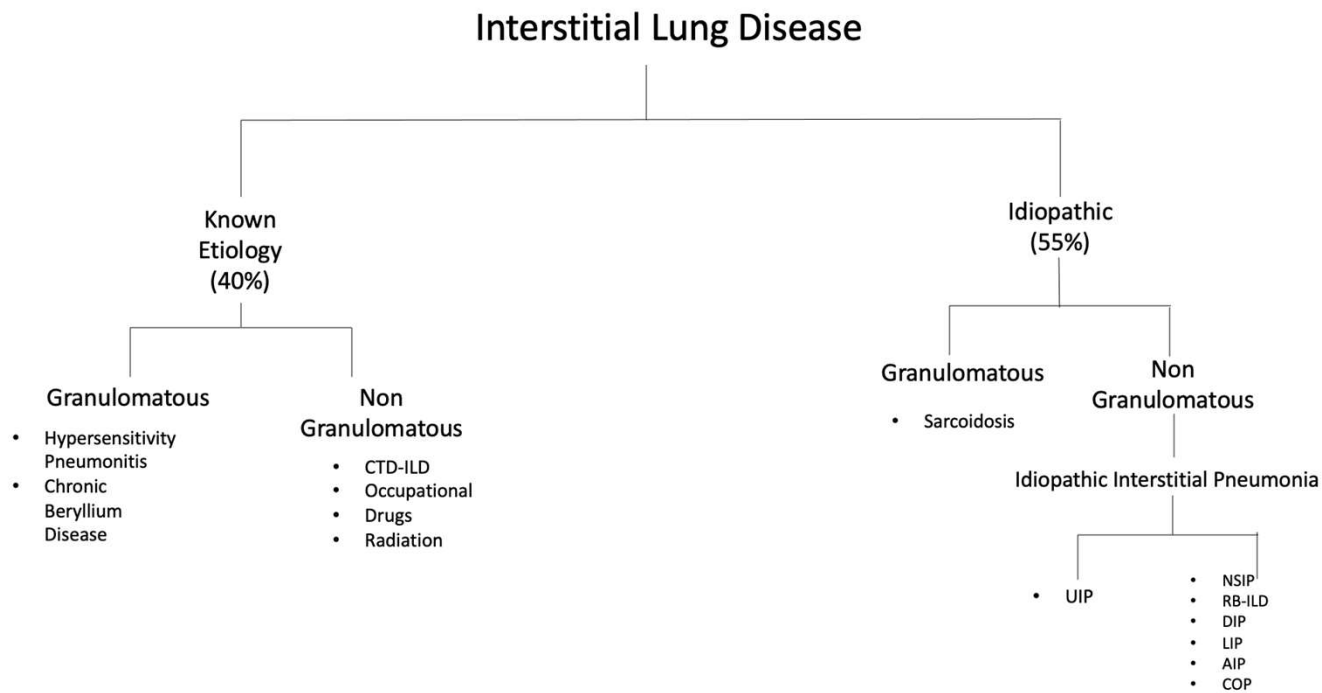
Hatabu, H., et al. Interstitial lung abnormalities detected incidentally on CT: a Position Paper from the Fleischner Society. *Lancet*, 2020, 8(7):726-737.

Clinical Presentation

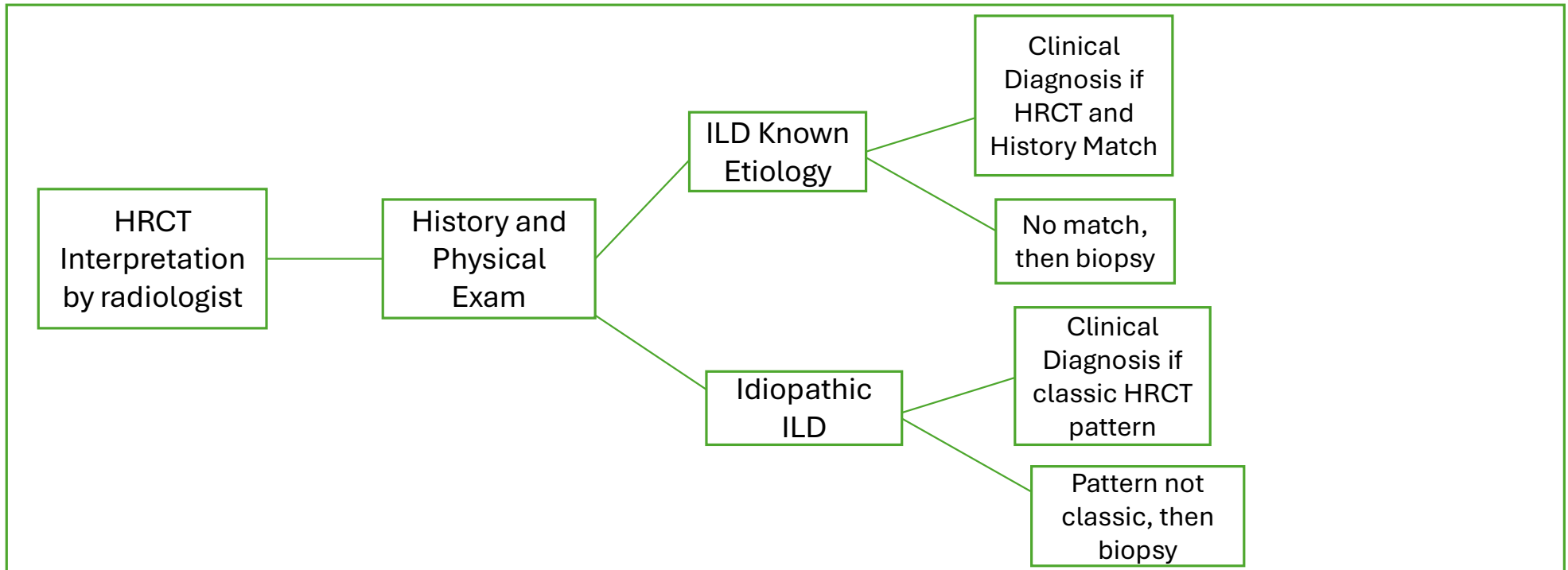
- Primary symptoms are dry cough and dyspnea on exertion
- Duration of symptoms is subacute to chronic (months to years)
- May have evidence of a systemic disease
 - Autoimmune, granulomatous, drug induced
- Imaging:
 - Chest x ray will show alveolar and/or interstitial involvement
- Pulmonary Function Testing:
 - Restricted and diffusion capacity will be reduced
- Physical Exam:
 - Crackles on lung auscultation



Etiologies of Interstitial Lung Disease



Evaluation of Interstitial Lung Disease



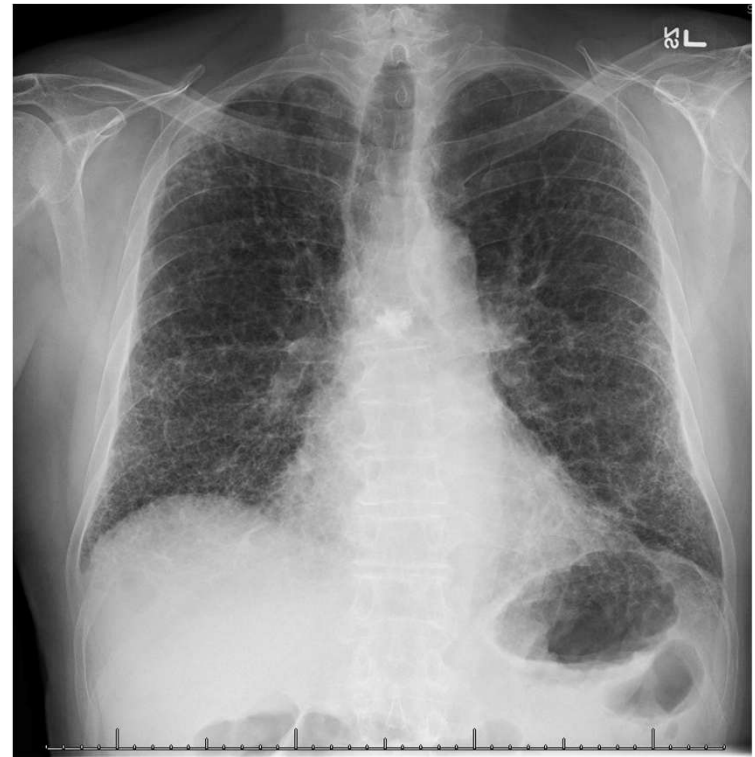
Case

A 65 year old male presents to his primary care physician with a dry cough that has been present for the past year and a half. He has also noticed dyspnea on exertion for the last nine months that has been progressive.

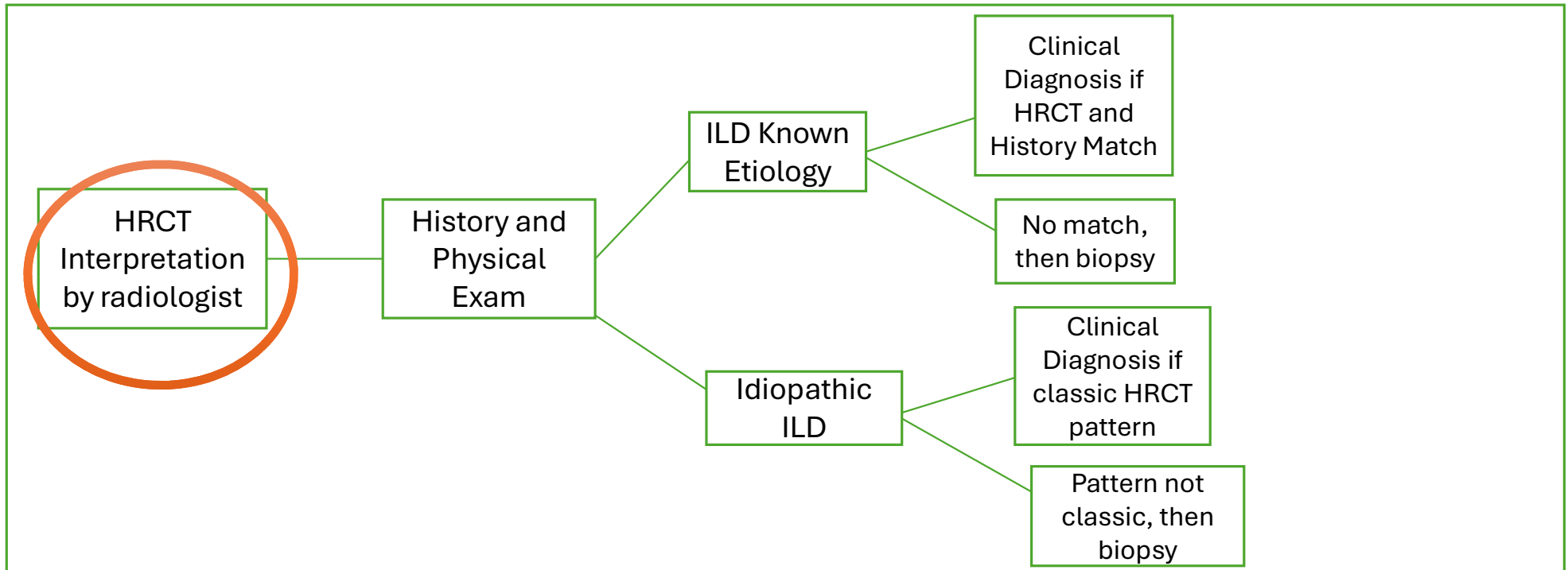
Case

Chest x ray is obtained and radiology interpretation states that reticulations are present predominately in the bilateral lower lobes

What is the next step?



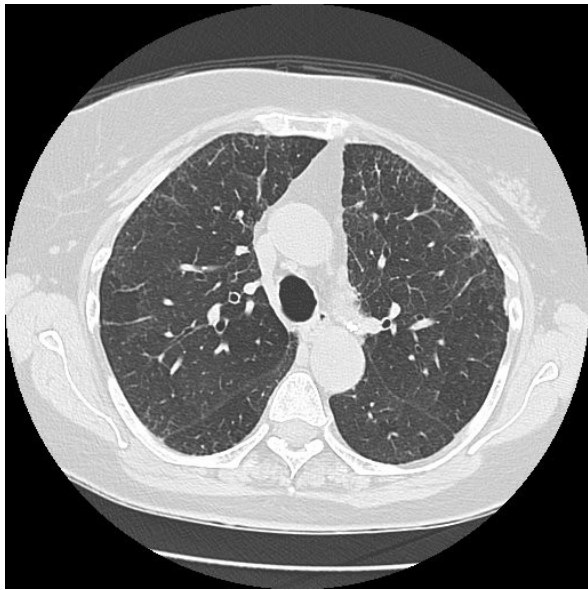
Evaluation of Interstitial Lung Disease



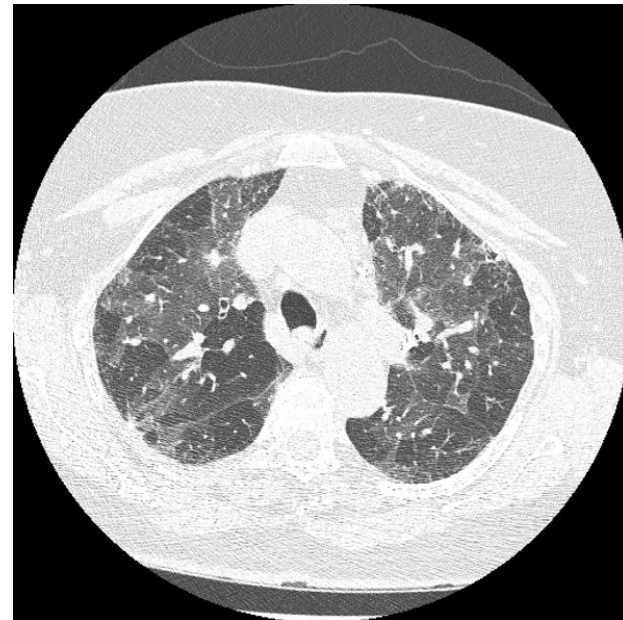
High Resolution CT Chest

- Takes very thin slices and uses a high resolution algorithm
- HRCT findings have been shown to correlate with pathologic findings
 - Pattern and histology findings alone do not make a diagnosis

High Resolution CT Chest

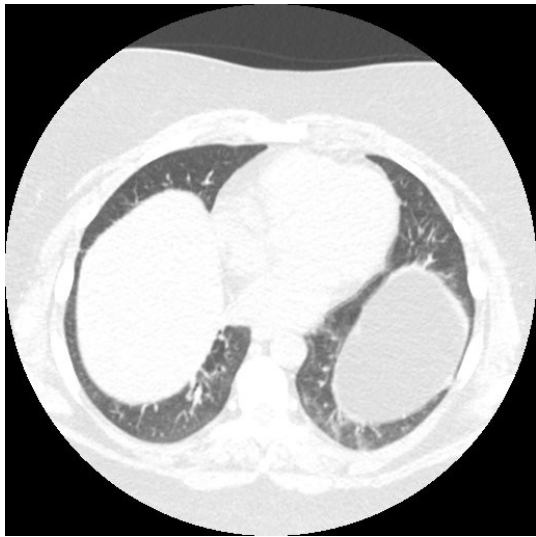


Inspiratory

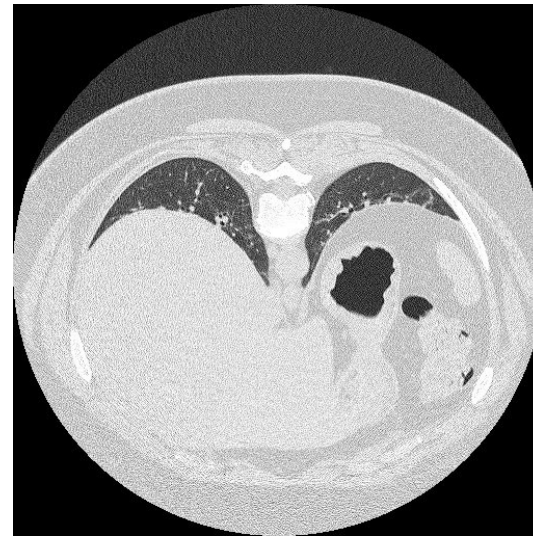


Expiratory

High Resolution CT Chest



Supine

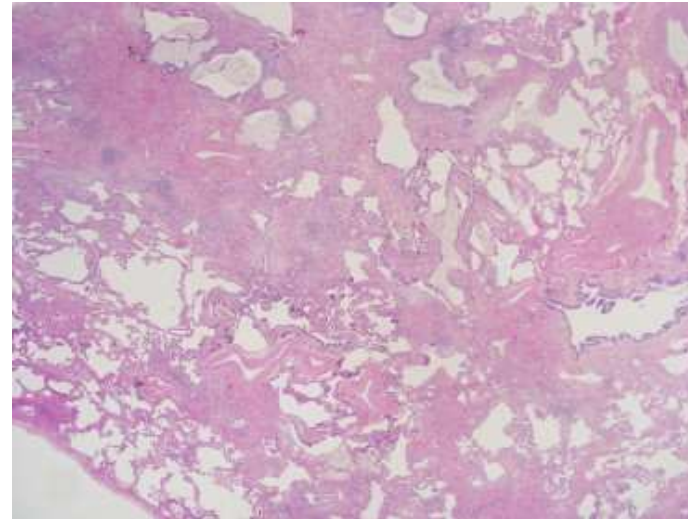


Prone

HRCT Patterns



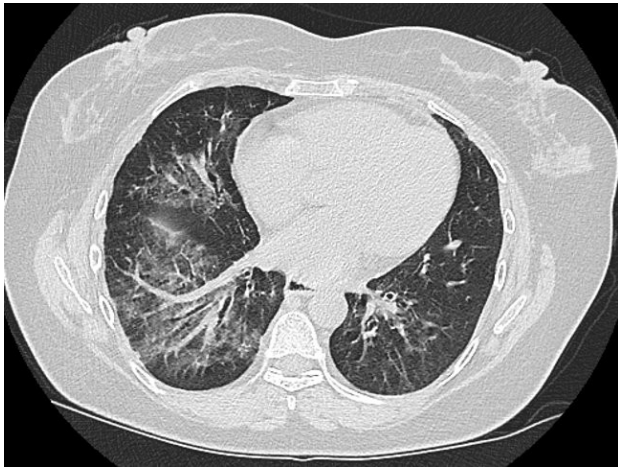
UIP Pattern on HRCT



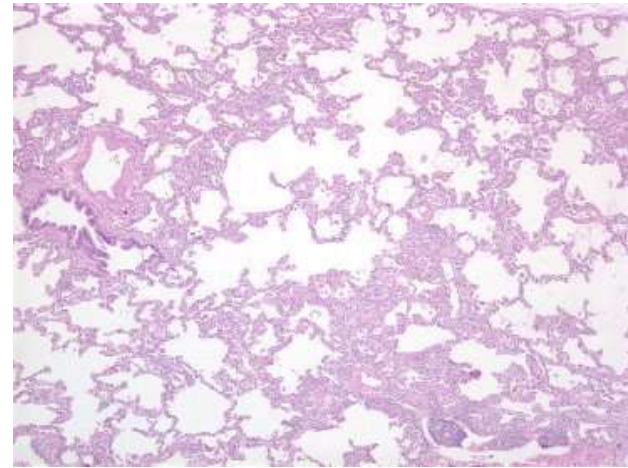
UIP Pattern on Histology

Myers, JL. *Semin Diagn Pathol*
2007;24:183-7

HRCT Patterns



NSIP Pattern on
HRCT



NSIP Pattern on
Histology

Myers, JL. *Semin Diagn Pathol* 2007;24:183-7

Case

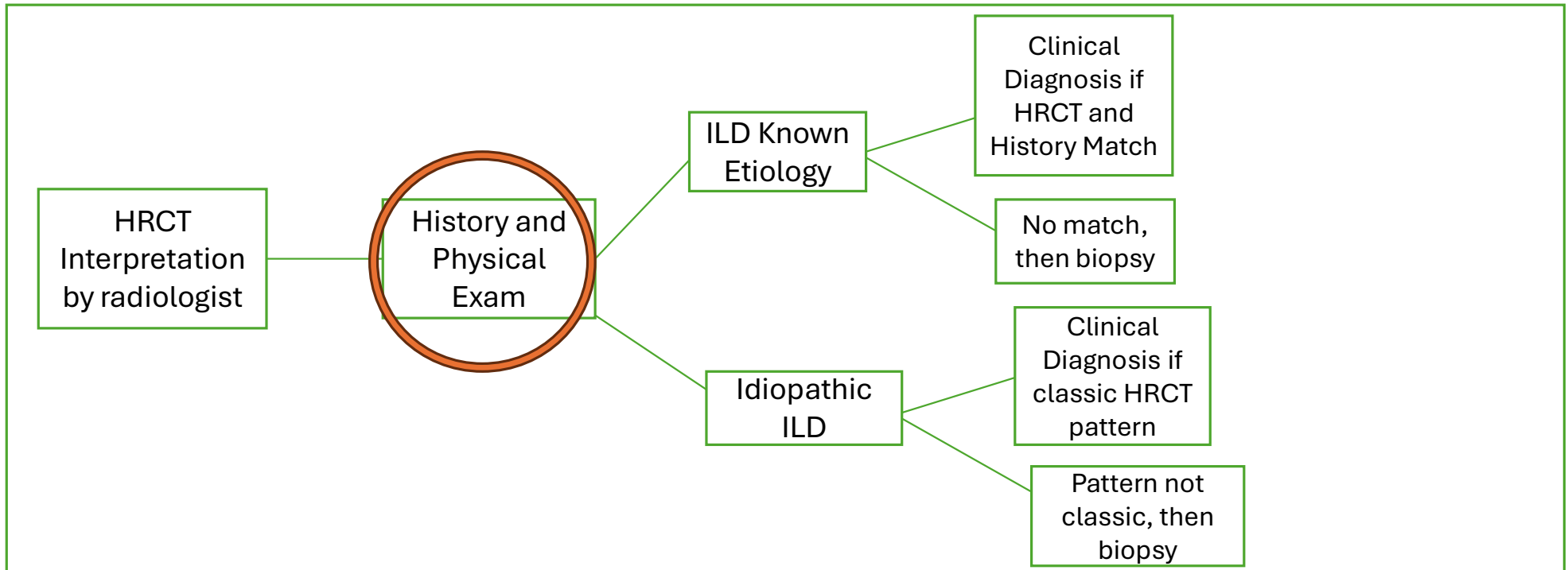
High resolution CT chest completed and radiology interpretation states

“Basilar predominant peripheral reticulation, traction bronchiectasis, and honeycombing consistent with a UIP pattern.”

Is UIP the diagnosis?

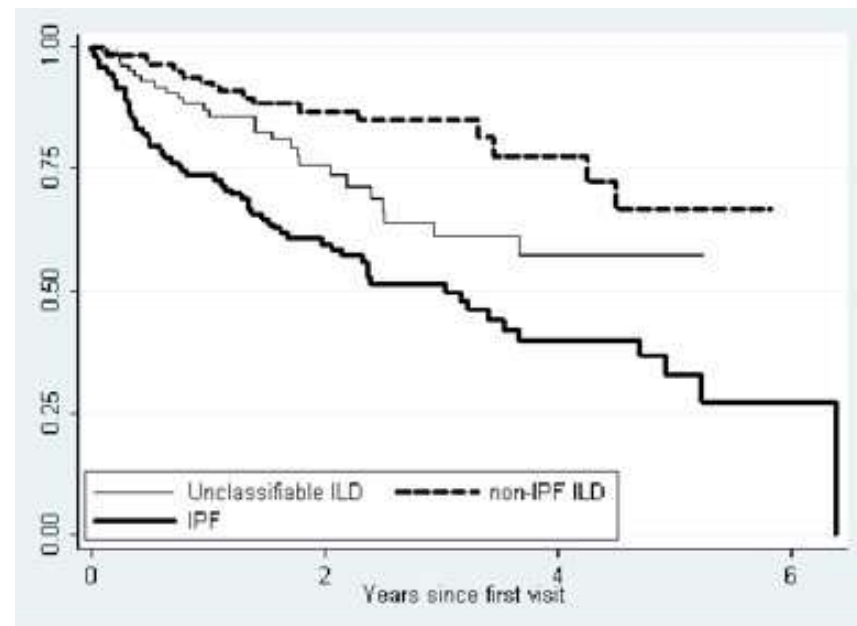
What is the next step?

Evaluation of Interstitial Lung Disease



Importance of History and Physical Exam

Prognosis Varies by Etiology



Hyldgaard C, et al, Unclassifiable interstitial lung diseases: Clinical characteristics and survival. *Respiology* 2017;22:494-500

History

Systemic Disease:

- Personal history of sarcoidosis or autoimmune disease
- Family history of sarcoidosis or autoimmune disease
- Review of Systems:
 - Constitutional: fever, chills, weight loss, night sweats, arthralgias, myalgias
 - Skin: rashes, oral ulcers, photosensitivity, alopecia, skin tightening, skin thickening
 - Musculoskeletal: arthritis, muscle weakness, prolonged morning stiffness (greater than 30 minutes)
 - GI: abdominal pain, bloating, blood in stool, jaundice, dysphagia, reflux
 - Other: Raynaud's, dry mouth, dry eyes, focal neurological symptoms, confusion, spontaneous abortion, hematuria

History

Connective Tissue Disease ILD

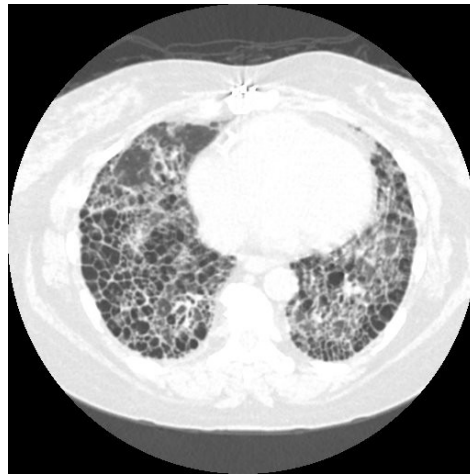
- Women more commonly affected
- Younger age of onset
- Underlying disease presents before the onset of lung involvement in 80-85% of cases
- **Rheumatoid Arthritis:**
 - ILD, pulmonary nodules, pleural effusion, bronchiectasis
- **Scleroderma:**
 - ILD, pulmonary hypertension
- **Myositis:**
 - ILD, neuromuscular weakness
- **Systemic Lupus Erythematosus:**
 - ILD, pleural effusion, shrinking lung syndrome

History

Variable HRCT patterns in Connective Tissue Disease ILD



Pleuroparenchymal
Fibroelastosis
pattern on HRCT



UIP pattern on HRCT



NSIP pattern on
HRCT

History

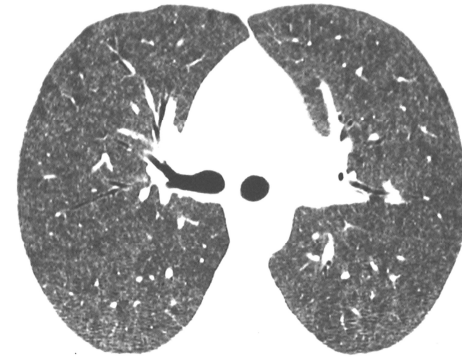
Occupational and Environmental Exposure:

- Complete work history: industry, job title, job duties, and materials used
- Home Environment:
 - Bioaerosol: water damage, visible mold/mildew, humidifiers, pools, hot tubs, saunas, birds, feather pillows, farming, composte heap
- Hobbies: wood working, metal making, and ceramics

History

Hypersensitivity Pneumonitis

- Granulomatous Disease of the lung
- Complex pulmonary syndrome mediated by the immune system (exaggerated T cell response) and caused by the inhalation of antigens (bacteria, fungi, animals)
- Imaging with upper lobe predominant centrilobular ground glass nodules or fibrosis
 - Mosaicism and air trapping also present
- Bronchoscopy or surgical lung biopsy may be required for diagnosis
- Treatment involves exposure removal



Raghu, G, et al. Diagnosis of Hypersensitivity Pneumonitis in Adults. An Official ATS/JRS/ALAT Clinical Practice Guideline. Am J Respir Critical Care Med. 2020, 202(3), 10.1164

History

Occupational

- Fibrotic diseases caused by the inhalation of fibrogenic dust/particles
- Main agents are asbestos, coal, and silica
- Clinical Features:
 - Linear Dose Response
 - Long latency between exposure and onset of disease (decades)
 - Symptoms limited to the respiratory system
 - Treatment involves removal from exposure
 - Slow progression
- Diagnosis:
 - Significant exposure
 - Latency
 - Compatible clinical picture
 - Compatible radiographic images

History

Occupational

Disease	Occupational exposure	Types of industries exposed	CT features	Histological features
Asbestosis	Asbestos	Carpenters, boiler room workers, construction workers, ship-yard workers, maintenance and insulation workers, vehicle brake mechanics, asbestos cement workers, tiles, shingles and textiles workers, certified asbestos handlers	Parenchymal bands, traction bronchiectasis, rounded atelectasis, honeycombing, intralobular thickening, subpleural curvilinear lines, GGO	Diffuse interstitial fibrosis, asbestos bodies, asbestos fibres
Silicosis	Respirable crystalline silica	Construction and quarry work, tunnelling, stonemasonry, mining, ceramic and pottery industry, kitchen worktop fitters, stone-washing	vary depending on type of silicosis (acute, chronic, accelerated); includes upper lobe predominant small pulmonary nodules in perilymphatic distribution and hilar and mediastinal lymphadenopathy with or without calcification	Small fibroblastic nodules and histiocytes becoming increasingly hyalinised over time; silicotic nodule; occasionally granulomas
Chronic beryllium disease	Beryllium	Electronics, aerospace, telecommunication, nuclear industry	Pulmonary nodules with upper lobe fibrosis, traction bronchiectasis and interlobular septal thickening; mediastinal lymphadenopathy may be present	Peri-bronchial non-necrotising granuloma
Hard metal lung disease	Tungsten carbide/cobalt	Tool manufacturing, hard metal tool use, diamond polishing, dental technician	Multifocal consolidation, GGO, upper zone predominant reticulation and interlobular septal thickenings, pulmonary nodules	Giant cell interstitial pneumonitis; airspace filling with alveolar macrophages and cannibalistic multinucleated giant cells
Metal dust-induced granulomatosis	Aluminium	Aluminium plants, welding, grinding, polishing, smelting, foundries, automotive industry	GGO, patchy consolidation, reticulation, traction bronchiectasis, pulmonary nodules	Non-caseating granulomas with birefringent material on polarised light; granulomatous pneumonitis or fibrosis
	Titanium	Milling, grinding, paint production		
	Zirconium	Aircraft, aerospace, nuclear industries		

Feary, J., et al. Occupational lung disease: when should I think of it and why is it important? *Breathe*, 2023, 19(2), 10.1183

History

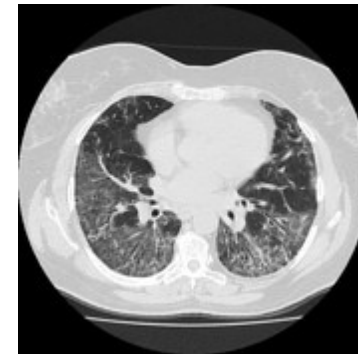
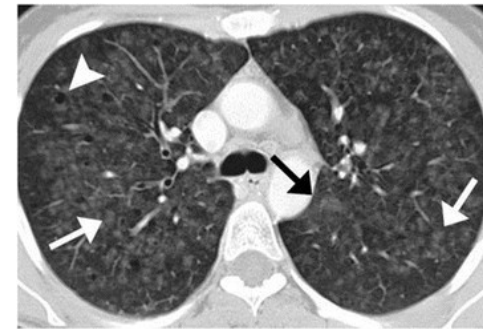
■ Drugs

- Occurs with a large number of medications as well as herbal preparations
- Affects people of either gender and at any age
- Initiation of a new medication does not necessarily have to be present
- Can have extrapulmonary manifestations including eosinophilia, rashes, and renal involvement but these are rare
- The most common medications are in the following three categories: antibiotics, chemotherapy, and anti-arrhythmics
 - Antibiotics: nitrofurantoin and trimethoprim/sulfamethoxazole
 - Anti-arrhythmics: amiodarone
 - Oncology: chemotherapy and checkpoint inhibitors

History

Smoking Related ILD

- Respiratory Bronchiolitis ILD and Desquamative Interstitial Pneumonia
 - Affect cigarette smokers between the third and sixth decade of life



History

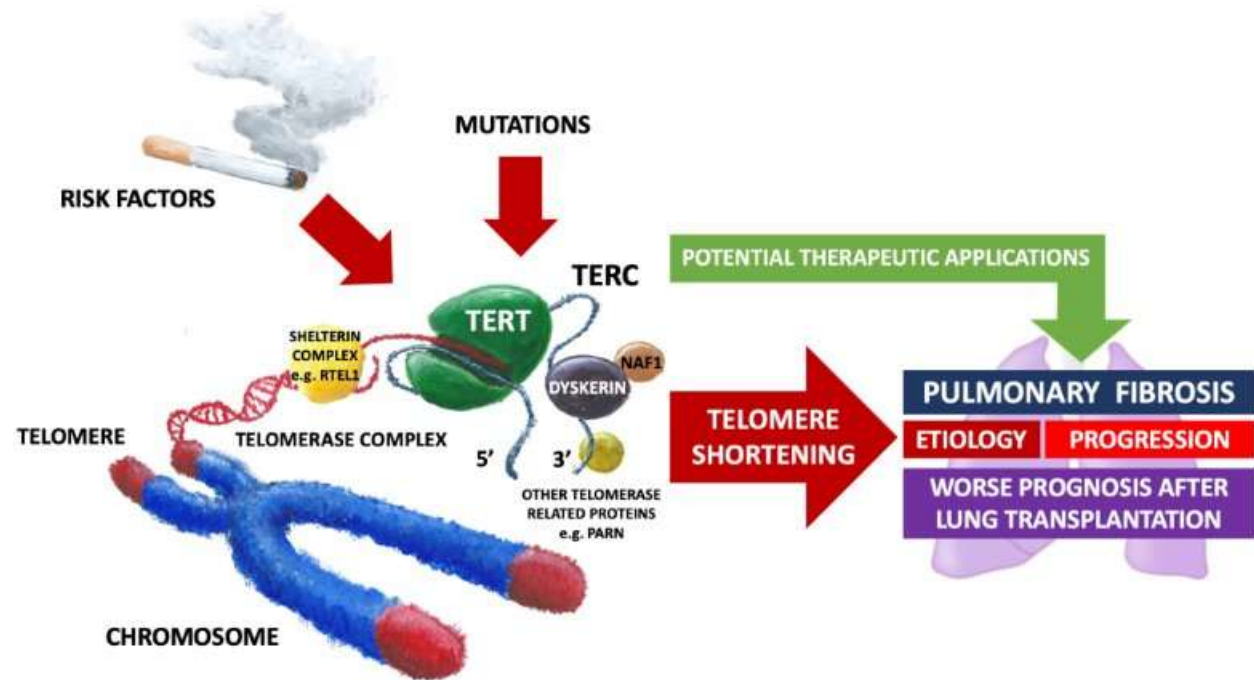
Familial

- Telomeres are important for stability of the chromosome and allow for complete replication of the ends
- Telomere length homeostasis is required for proper cellular function
- Abnormalities involving telomeres and their proteome play a role in the pathobiology of idiopathic pulmonary fibrosis
 - Incomplete DNA replication leads to the loss of sequences which form telomeres
 - Telomerase compensates for this loss by adding de novo TTAGGG repeats
 - Telomerase consists of telomerase reverse transcriptase, regulatory subunits and telomerase RNA component
 - Both subunits have been linked with lung fibrosis pathogenesis
- In addition to activating DNA damage pathways, short telomeres contribute to fibrosis when exposed to an injury by impairing tissue repair

Bilgili H, Bialas AJ. Telomere abnormalities in the pathobiology of IPF. *J Clin Med* 2019;8:1232

History

Familial

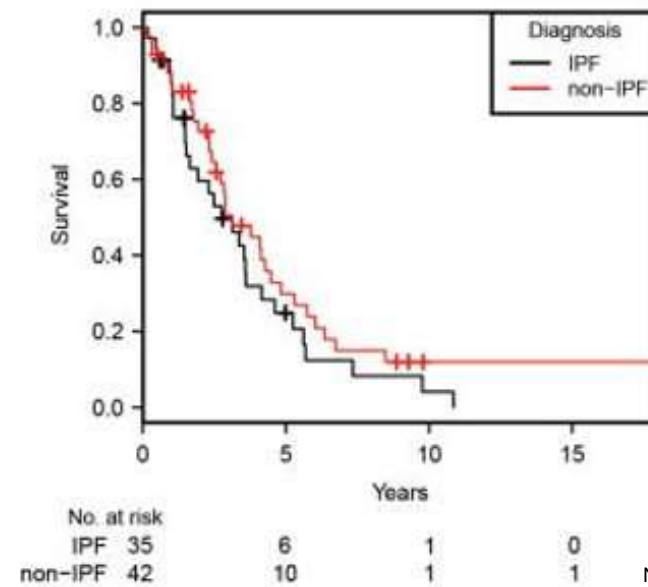


Bilgili H, Bialas AJ. Telomere abnormalities in the pathobiology of IPF. *J Clin Med* 2019;8:1232

History

- Short telomeres are not specific for idiopathic pulmonary fibrosis and this pathology was described in other interstitial lung diseases

C

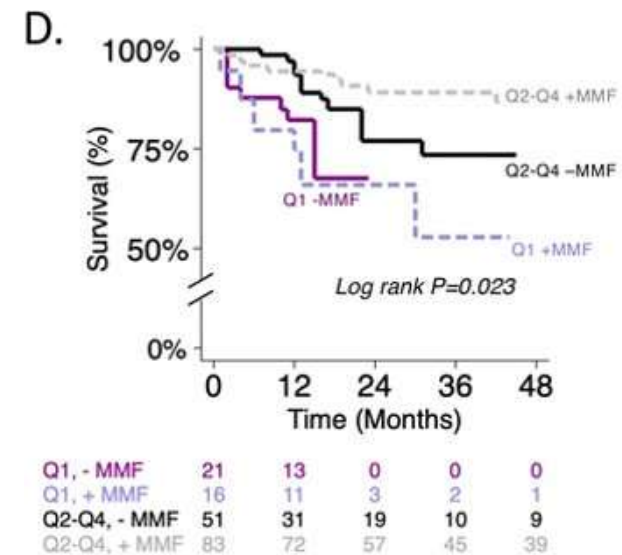


Newton CA, et al. Telomere-related lung fibrosis is diagnostically heterogeneous but uniformly progressive. *ERJ* 2016;48:1710-20

History

Short Telomeres and Immunosuppression

- Study of patient with chronic hypersensitivity pneumonitis and short telomeres showed that treatment with Cellcept was not associated with improved survival or lung function
 - Findings were similar to the association in IPF which suggests a final common pathology in the pathophysiological process of advanced fibrosis in these conditions

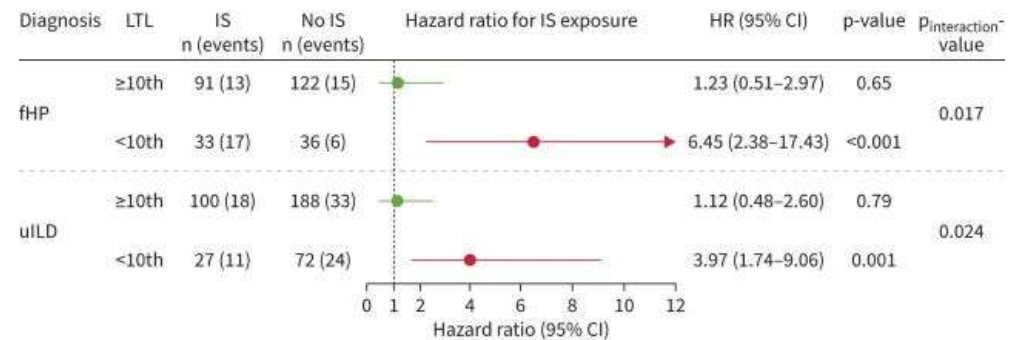


Adegunsoye A, et al. Leukocyte telomere length and mycophenolate therapy in chronic hypersensitivity pneumonitis. *ERJ* 2021;57:2002872

History

Short Telomeres and Immunosuppression

- Study of patients with fibrotic hypersensitivity pneumonitis, unclassifiable ILD, and connective tissue disease ILD and short telomeres
 - Reduced survival was seen in patients with fibrotic hypersensitivity pneumonitis and unclassifiable ILD and short telomeres when exposed to immunosuppression
 - Not powered for association with connective tissue disease ILD



Zhang, D., et al. Telomere length and immunosuppression in non-idiopathic pulmonary fibrosis interstitial lung disease. *ERJ* 2023; 62(5):2300441

Physical Exam

- Crackles
 - Velcro crackles
 - Less common with granulomatous diseases
- Cyanosis
 - Late finding but exercise induced desaturation is common
- Clubbing
 - Especially in IPF and asbestosis
- Evidence of right heart strain
 - Prominent P2, JVD, RV lift, lower extremity edema
- Signs that indicate an etiology other than idiopathic:
 - Inspiratory squeaks
 - Seen with bronchiolar involvement
 - Hypersensitivity pneumonitis and autoimmune disease
 - Evidence of Pleural Disease
 - Decreased breath sounds, dullness to percussion
 - Evidence of Connective Tissue Disease
 - Raynaud's, sclerodactyly, synovitis

Case

A 65 year old male presents to his primary care physician with a dry cough that has been present for the past year and a half. He has also noticed dyspnea on exertion for the last nine months that has been progressive.

- Review of systems was only positive for occasional heartburn

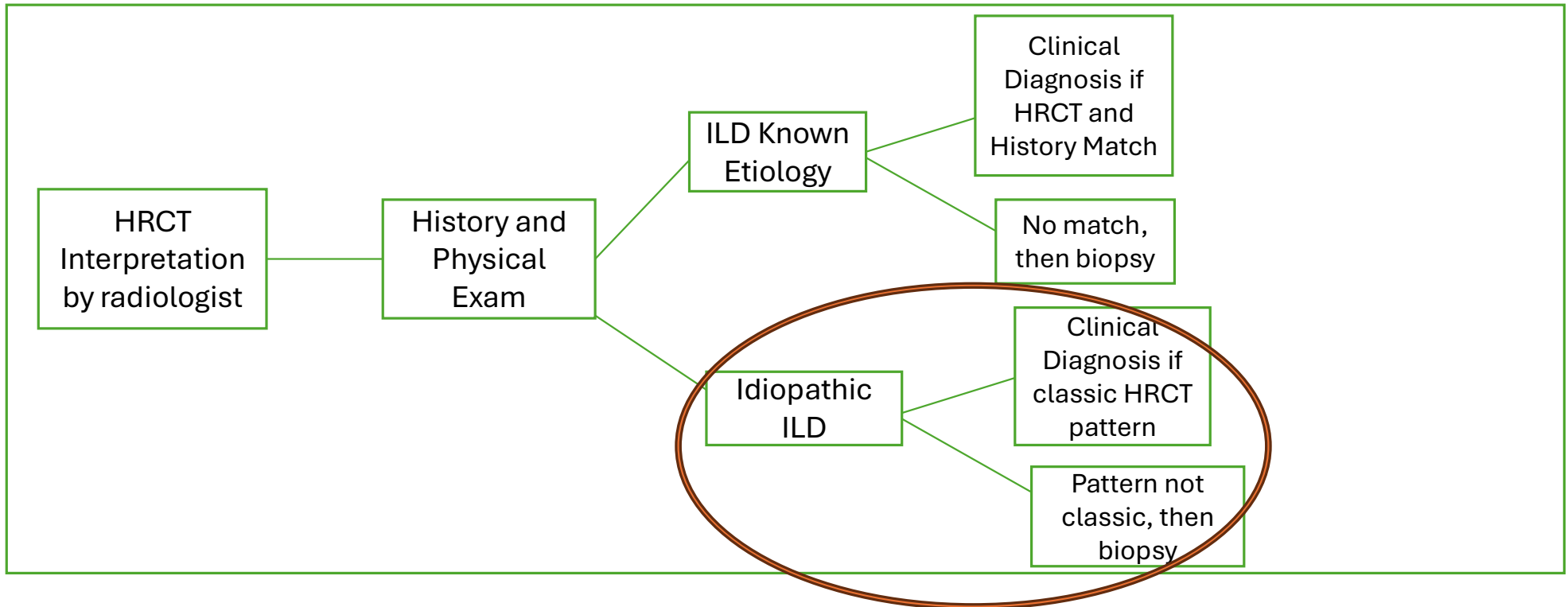
Case

- Past Medical History: hypertension and hyperlipidemia
- Past Surgical History: appendectomy
- Family History: mother had breast cancer and father has coronary artery disease
- Social History: denies current or prior tobacco use
- Medications: atorvastatin and Tums PRN
- Occupation: attorney
- Environmental History: currently lives in a house without any water damage. Does not own any birds.

Case

- Physical Exam: pertinent for inspiratory crackles predominately in the bases and clubbing
- Pulmonary Function Testing: FVC 60%, TLC 54%, and DLCO 47%
- Autoimmune Serologies: negative

Evaluation of Interstitial Lung Disease



Idiopathic Clinical Diagnosis

HRCT and/or Pathology Pattern	Diagnosis if Idiopathic
Usual Interstitial Pneumonia (UIP)	Idiopathic Pulmonary Fibrosis
Nonspecific Interstitial Pneumonia (NSIP)	Idiopathic NSIP

Surgical Lung Biopsy

- Indicated when history and imaging are not completely diagnostic
- 1-2% mortality from the procedure

Case

Diagnosis

Idiopathic Pulmonary Fibrosis

Treatment

Antifibrotics

Antifibrotic	Indication	Mechanism of Action	Adverse Effects
Nintedanib	IPF and PPF	Tyrosine Kinase Inhibitor	Diarrhea, bleeding, hepatotoxicity, rare bowel perforation
Pirfenidone	IPF	Unclear	Diarrhea, photosensitivity, hepatotoxicity, TID dosing
Nerandomilast	IPF and PPF	Phosphodiesterase 4B inhibitor	Diarrhea, upper respiratory infection

All slow the progression of fibrosis

*PPF: progressive pulmonary fibrosis

Conclusion

- Evaluation of a patient with interstitial lung disease requires a high resolution CT chest as well as a thorough history to evaluate for a known etiology
- If an unknown etiology is present then idiopathic designation made based on imaging with or without pathology
- Antifibrotics include nintedanib, pirfenidone, and nerandomilast

Acknowledgements

- Interstitial lung disease group
 - Traci Adams, MD
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