Restrictive Lung Disease

DDx

Extrathoracic
- NM Disease (refer)
- Thoracic Disease (refer)
- Pleural Disease (refer)

Intrathoracic
- Alveolar Disease (refer)
  - Alveolar Hemorrhage
  - Alveolar Proteinosis
  - Alveolar Edema
- Interstitial Lung Disease (ILD)
  - Mechanism: Insult to alveolar septal interstitium → fibrosis → decreased compliance and increased elasticity → decease in ALL lung volumes and decrease in diffusion → V/Q mismatch → vasoconstriction → dyspnea, non productive cough, fatigue, dry crackles/rales, pulmonary HTN → cor pulmonale, clubbing, cyanosis
  - Can be acute/subacute/chronic
  - Most ILDs are idiopathic but it is important to try to find a cause b/c it offers the best chance for Tx
  - Imaging: in general rarely diagnostic, 15% normal, CXR: interstitial changes (reticular/nodular/honeycombing vs HRCT: interstitial changes (ground-glass opacities), late findings include traction bronchiectasis
  - Transbronchial/Surgical Bx is often necessary to make Dx
- Idiopathic
  - Idiopathic Pulmonary Fibrosis (IPF), Interstitial Pulmonary Fibrosis (IPF), Usual Interstitial Pneumonitis (UIP)
    - Epidemiology: old male smokers
    - CXR: usually peripheral lower lobe dz, bibasal/subpleural opacities
    - S/S: insidious Sx, no extra-pulm involvement
    - Dx: DOB; biopsy (spatially and temporally heterogenous pattern of fibrosis interspersed w/ normal lung = “fibroblastic foot”). NB any end stage diffuse lung disease can look like IPF
    - Tx: distinctly poor response to Tx including steroids/immunosuppressants (consider IFN, NAC, Bosentan, imatinib) and prognosis compared to other ILDs w/ 50% mortality at 3yrs w/ only Tx being transplant
  - Cryptogenic Organizing Pneumonia (COP) aka Bronchiolitis Obliterans w/ Organizing Pneumonia (BOOP)
    - Epidemiology: old women
    - Mech: ILD that looks/acts just like an infectious pneumonia but no localized infection or response to antibiotics, 2/2 viral infection, medications, CTDs, radiation, inhalational toxins, etc but most are idiopathic (said to represent 25% of all chronic infiltrative lung diseases)
    - S/S: subacute ILD w/ significant systemic Sx
    - Dx: differentiate from IPF by the presence of neutrophils/lymphocytes on Bx/BAL, no diagnostic CXR/HRCT but often bilateral consolidation picture
    - Tx: spontaneous recovery or steroids
  - Lymphangioleiomyomatosis (LAM)
    - Mech: sporadic (or associated w/ tuberous sclerosis esp w/ renal angiomyolipomas) proliferation of smooth muscle cells
    - Epidemiology: young women
    - Complications: recurrent spontaneous PTX (often presenting Sx), hemoptysis, chyous effusions, atypical cp
    - CXR/CT: above but paradoxic hyperinflation and cysts
    - Tx: progesterone hormone but slowly progressive requiring lung transplant, b/c of recurrent PTX consider pleurodesis
  - Pulmonary Langerhan’s Cell Histiocytosis X
    - Mech: abnormal proliferation of abnormal Langerhan’s Cells aka Histioocytes and can be associated w/ systemic diseases (Letterer-Siwe Dz and Hand-Schuller-Christian Syndrome)
    - Epidemiology: young smoker
    - Complications: spontaneous PTX, lytic bone disease, diabetes insipidus
    - Dx: abnormal histiocytes containing intracellular Birbeck Granules on Bx
• CXR/CT: cysts/nodules in mid/upper zones, classically there is lack of disease at costophrenic angles
• Tx: variable course if severe steroids and lung transplant
  ▪ **Chronic Eosinophilic Pneumonia**
    • Mech: eosinophilic infiltration of interstitium + eosinophilia
    • Types
      o Primary (Simple aka Loeffler’s Syndrome from Ascaris lumbricoides, Acute, Chronic)
      o Secondary (Drugs, Parasite, Fungal, Vasculitis, ABPA, Asthma)
    • Tx: responds to steroids but relapses occur 75% of chronic cases
    • Complications: hypereosinophilic syndrome (peripheral eosinophilia infiltrates other organs esp heart causing damage)
  ▪ **Diffuse Aveolar Hemorrhage**
    • 2/2 Good Pastereur’s, Wegener’s, Churg-Straus, Idiopathic Pulmonary Hemosiderosis, CHF Hemorrhage
  ▪ **Pulmonary Alveolar Proteinosis**
    • Mech: rare accumulation of surfactant/phospholipids in alveoli and septum, primary or in association w/ hematologic malignancy or autoimmune dz
    • Epidemiology: adult males
    • CXR: bat-shaped alveolar infiltrates in middle zones
    • Dx: anti-GM-CSF
    • Tx: periodic lung lavage, granulocyte colony stimulating factor infusion, NO steroids b/c pts are at increased r/o infection
    • Complications: unusual infections w/ Nocardia, MAC, PCP
  ▪ **Nonspecific Interstitial Pneumonia (NSIP)**
    • similar to IPF but younger pts, better prognosis
    • Tx w/ steroids
  ▪ **Desquamative Interstitial Pneumonia (DIP) and Respiratory Bronchiolitis Associated Interstitial Lung Disease (RB-ILD)**
    • Seen in young male smokers
    • BAL shows pigmented macrophages
    • Tx: steroids
  ▪ **Acute Interstitial Pneumonia (AIP) aka Hamman-Rich Syndrome**
    • Acute dz that progresses to respiratory failure over 2wks
    • Systemic Sx + ILD then Sx that looks like ARDS
    • Tx: steroids but 75% die w/in 2mo
  ▪ **Lymphoid Interstitial Pneumonia (LIP)**
    • Very rare
    • Seen in women
    • ILD Sx w/ systemic Sx
    • BAL reveals lymphocytes looking like lymphoma
    • Associated w/ underlying autoimmune dz esp Sjogren’s or immunodeficiency esp HIV
  ▪ **Sarcoidosis**
    • Multisystem chronic non-caseating granulomatous disease of unknown etiology possibly infectious (NB transmission has occurred in heart/bone transplants)
      o Pulmonary (100%): ILD
      o MS (50%): arthralgia
      o General (30%): constitutional Sx
      o Derm (25%): erythema nodosum, apple butter plaques, subcutaneous nodules
      o Ophtho (25%): uveitis w/ blindness (most common cause of morbidity), conjunctivitis
      o GI (25%): infiltrative liver dz, parotid swelling
      o Heme (25%): cytopenias, palpable LNs
      o CV (5%): arrhythmias (most common cause of mortality)
      o CNS (5%): Bell’s Palsy, optic nerve dysfxn, papilledema, peripheral neuropathy
      o NB renal/GI/GU is rare
Exposure

- Chemicals
  - Cancer
    - Psuedolymphoma
    - Pulmonary Lymphoma
    - Lymphoid Granulomatosis
      - Lymphangitic Carcinomatosis
    - Other: Amyloid
  - Other: Inorganic Dusts (Pneumoconiosis)
    - Asbestos (used as a fire-retardant, exposure during mining/manufacturing, shipbuilding/repairing, building construction, etc., parietal pleural thickening w/ plaques at base w/ lower lobe ILD, r/o malignant lung cancer and mesothelioma, complication: bronchogenic carcinomas)
    - Silicosis (found in mining, stone cutting, glass manufacturing, etc, acute vs chronic disease, increased r/o TB (hence if pt also has a fever then check for TB), but no increased r/o cancer, localized upper lobe & peribronchial nodular fibrosis w/ eggshell calcifications of hilar LNs)
    - Beryllium (found in power plants, ceramic industry, etc, acute vs chronic disease similar to sarcoid)
    - Aluminum
    - Titanium
    - Cobalt
    - Coal
  - Organic Particles (Hypersensitivity Pneumonitis, acute flu-like illness vs chronic ILD, check serum precipitin Ab)
    - Fungi (Aspergillus, Actinomycetes, Alternaria, Cladosporium, Aureobasidium spp.) most common
    - Bacteria (Thermophilic spp. aka Farmer’s Lung, Humidifier Lung, Hot-Tub Lung, etc)
    - Mycobacteria (Atypical spp.)
    - Amoeba (Naegleria, Acanthamoeba spp.)
    - Animal/Insect Proteins
      - Avian Droppings/Feathers/Serum aka Bird Breeder’s Disease
      - Mammal Pelts/Urine/Serum aka Animal Handler’s Disease
  - Drugs
    - Chemo (Bleomycin, Busulfan, Methotrexate)

Cancer

- Psuedolymphoma
- Pulmonary Lymphoma
- Lymphoid Granulomatosis
- Lymphangitic Carcinomatosis
- Other: Amyloid

Autoimmune: SLE, RA, SS, Sjogrens, PM/DM, AS, Vasculitis

Sarcoidosis

- Epidemiology: young black & northern European females, smoking is protective, very unique clustering in certain occupations (nurses, firefighters, etc), first responders to World-Trade Center bombing resulted in a sarcoi-like illness
- Dx
  - Clinical
  - Bx (non-caseating granulomas and exclusion of other causes, in some cases you don’t need to do a Bx if S/S/imaging is clear)
  - CXR (Silzbach): Stage 0 (normal, seen in 10% of pts!!) → Stage 1 (bilateral hilar/mediastial LAD) → Stage 2 (bilateral hilar LAD + interstitial infiltrates, 50% of pts) → Stage 3 (interstitial infiltrates) → Stage 4 (fibrosis)
  - Skin Anergy (False Negative PPD 2/2 depressed T lymphocyte fxn)
  - High ACE Level (neither sensitive nor specific)
  - High VitD Levels
  - BAL (lymphocytosis)
  - Lymphopenia/Eosinophilia
  - Always check a CXR, PPD, Ophtho exam, PFTs
- Tx: most resolve spontaneously in 2yrs and thus require no Tx but if symptomatic OR critical organ involvement (CV, CNS, Eye, Hypercalcemia/uria, Stage 2/3 CXR) then Tx w/ systemic corticosteroids (30mg/d x2mo then taper over the next 10mo), hydroxychloroquine, methotrexate, anti-TNF, etc
  - Autoimmune: SLE, RA, SS, Sjogrens, PM/DM, AS, Vasculitis
  - Cancer
    - Psuedolymphoma
    - Pulmonary Lymphoma
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    - Animal/Insect Proteins
      - Avian Droppings/Feathers/Serum aka Bird Breeder’s Disease
      - Mammal Pelts/Urine/Serum aka Animal Handler’s Disease
    - Chemical
      - Isocyanates
      - Trimellitic Anhydride
      - Copper Sulfate
    - Drugs
      - Chemo (Bleomycin, Busulfan, Methotrexate)
- Abx (Nitrofurantoin, Sulfa)
- CV (Amio, Hydralazine)
- NSAIDs (Gold, Penicillamine)
- Recreational (Cocaine)
- Radiation