Interstitial Lung Disease

SS Visser , Lung Unit, UP.

ILD - Definition

Heterogenous group of diseases with involvement of alveolar walls and peri- alveolar tissue -non-malignant, non-infective.

± 180 diseases known to have interstitial involvement as the primary disease or as part of a multiorgan process eg the collagen vascular diseases.

An acute phase may occur but onset is usually insidious, leading to chronic progressive disease.

Symptoms, clinical manifestations, radiographic and physiologic changes and histology are very similar

ILD -Pathology

- **Intraluminal and mural alveolitis→blood vessel and interstitial involvement →scarring and distortion(fibrosis) →impaired gas exchange and ventilation**
- **Aetiology: these diseases are classified according to aetiology: I Known / Unknown and pathology: II Without granulomas/ With granulomas.**
- **Aetiology may differ but immunopathogenesis is basically the same.**

Markers of Activity 1

- **Bronchoalveolar lavage**
- **S-angiotensin converting enzyme**
- **Gallium scan**
- **CT scan (high resolution)**

Markers of Activity

Bronchoalveolar lavage produces a fluid with typical characteristics: Normal :

- **Macrophages** **80%**
- **Lymphocytes** **10%**
- **Plasma cells** **1-5%**
- **Neutrophils** **1-8%**
- **Eosinophils** **1%**
- **CD_4/CD_8 T lymphocytes** **1,5%**

Bronchoalveolar Lavage (BAL)

- **ILD involves inflammatory cells and result in a different BAL cell pattern**
- **This technique is of diagnostic importance as well as an index of disease activity.**

Idiopathic Pulmonary Fibrosis

- **It is the prototype ILD**
- **clinically : non-productive cough and progressive dyspnea on effort**
- **Radiology: reticulonodular/reticular veiling of lower lung zones on XR chest**
- **Physiology: restrictive lung function**

Clinical Manifestations

- **Average age at presentation ± 50y(range infancy → old age)**
- **Familial clusters- genetic factors increase susceptibility**
- **Work and environmental history important (pneumoconiosis and hypersensitivity lung disease)**
- **↑ number of patients associate awareness of dyspnea with the aftermath of a viral respiratory illness**
- **Exertional dyspnea progresses over months -years to dyspnea at rest**
- **Constitutional Symtoms: fever, arthralgia, anorexia, weight loss**

Physical Signs

- **Initially ±no abnormality → later:**
- **Clubbing, cyanosis, tachypnea**
- **Late inspiratory, high tone crepitations over the basal lung zones, inaudible in front of the open mouth and unchanged after coughing**
- **Pulmonary hypertension**
- **Right ventricular failure**

Diagnosis 1

- **Clinical**

- **Radiography:1. XR chest: diffuse reticular or reticulonodular veiling in the lower lung zones ± small lung volumes ± honey combing (cystic spaces)**

  2.CT Scan: High resolution

Diagnosis 2

- **CT scan: a. A very sensitive and specific procedure to differentiate tissue infiltration, pleural involvement, cystic and bronchiectatic changes**

  b.Can distinguish between early cellular phase (ground glass appearance) and fibrosis (interlobular and intralobar septal thickening)

  c. Peripheral distribution of fibrotic changes is indicative of Idiopathic pulmonary fibrosis or collagen vascular disease

Diagnosis 3

- **Lung function: Restrictive with decreased static lung volumes (TLC, FVC and RV reduced)**

  FeV1/FVC is normal or increased

  Compliance is decreased, diffusion is decreased

  Exertional or resting hypoxemia present (blood gas)

- **Histology: Transbronchial biopsy can dx ILD in 25% but in sarcoidosis in 80%**

  Open lung biopsy =gold standard for diagnosis and for assessment of disease activity

- **Histology, microbiology, immuno-fluorescence and electron microscopy have to be done**

Treatment -A. Specific

- **Prednisone 1mg/kg/day for 8-12 weeks. If response good→wean to maintenance of 0,25 mg/kg/day**
- **No response or deterioration: Cyclophosphamide 1mg/kg/day + prednisone 0,25 mg/kg/day - endpoint is to halve WBC (minimum 1000/ml blood)**
- **Pulse steroid therapy not superior to daily steroids**
- **Alternatives: Penisillamine, Cyclosporin, Colchicine**

Treatment -B:General

- **Stop smoking**
- **Oxygen for PaO_2<55 mmHg or SaO_2<89%**
- **Cor pulmonale - diuretics +O_2**
- **Infection - antibiotics**
- **Vaccination - influenza and pneumococcus**
- **Bronchodilators if airway obstruction is also present (mixed disease)**
- **Single lung transplant**

HYPERSENSITIVITY PNEUMONITIS

DEFINITION

- **Immune induced inflammation of lung parenchyma = alveolar walls and terminal airways.**

  The cause is inhalation of organic and other dusts on a regular basis, by a susceptible host.

- **Diagnosis is based on a constellation of clinical, radiologic, physiologic and immunologic criteria which are separately non-pathognomonic.**

AETIOLOGY

1. **Thermophile actinomycetes (cane sugar, mouldy hay, mushroom compost, grain + silage).**
2. **Aspergillus (compost, mouldy tobacco, oats).**
3. **Penicillium (mouldy cheese, oakwood).**
4. **Animal protein (birds, fishmeal, rat urine, poultry, furs, pituitary snuff).**
5. **Isocyanates (varnish, polyurethane foam).**
6. **Aerobasidium pullulans (contaminated H20 in air conditioning systems, saunas).**

PATHOGENESIS

- **- In symptomatic as well as asymptomatic patients.**
- **<u>Acute phase</u>: Increase PMN's in alveoli + small airways.**
- **<u>Chronic phase</u>: Mononuclear cell infiltrate → granulomas = delayed hypersensitivity reaction.**
- **<u>BAL</u> (= bronchoalveolar lavage)**
- **Increased T cells (CD4) + PMN's ± mast cells.**
- **Later: CD8 T cells. T cells modulate granuloma formation.**

CLINICAL MANIFESTATIONS

= Interstitial pneumonitis: acute, subacute, chronic.

1. **<u>Acute form</u>: Cough, fever, malaise, dyspnoea 6-8 hours after AG exposure – clears within days if exposure is terminated.**
2. **<u>Subacute form</u>: Cough + dyspnoea gradually over weeks → cyanosis, sometimes requiring hospitalization. Clears within days, weeks or months when exposure is discontinued.**
3. **<u>Chronic form</u>: Continuous exposure results in cough + exertional dyspnoea. With low dose exposure over a prolonged time the acute and sub-acute manifestions may not occur.**

DIAGNOSIS 1

1. **Non-specific neutrophilia, lymphopenia, raised ESR and CRP, RF and Immunoglobulins.**

2. **Serum precipitins against AG-indicative of adequate exposure to cause an immune response.**

3. **XR Chest: May be normal even in severely symptomatic patients. Usually focal, diffuse or nodular infiltrates in the acute and subacute forms. Honeycombing and diffuse reticulonodular infiltrates in the chronic form.**

DIAGNOSIS 2

1. **Lung function: Restriction, decreased diffusion and exercise induced hypoxaemia.**

2. **BAL.**

3. **Lung biopsy – mononuclear brongiolitis, interstitial infiltrates of lymphocytes and plasma cells and single, non-caseating granulomas in the parenchyma without vascular involvement.**

THERAPY

1. **Avoid AG.**
2. **Acute form: Spontaneous recovery.**
3. **Subacute form + severe symptoms: Prednisone 1mg/kg/day for 7-14 days. Reduce and wean in 2-6 weeks.**
4. **Chronic form: Prednisone 1mg/kg/day for 2-4 weeks with weaning to lowest dose required to maintain functional status.**

   With termination of exposure long term steroids may not be necessary.

SARCOIDOSIS

Definition:

- A chronic multisystem disease of unknown cause.
- Accumulation of T helper lymphocytes and mononuclear phagocytes leading to granuloma formation (non-caseating) with distortion of tissue architecture.
- Cutaneous anergy and impaired cellular immunity.
- Skin, lung, eyes, lymph gland involvement occur commonly.

PREVALENCE

- Prevalence:

- All sexes, races, ages but slightly more common in women and ages 20-40 years (75%).

CLINICAL MANIFESTATIONS

A systemic disease – thus: general + organ specific symptoms and signs.

1. **Asymptomatic – diagnosis on routine CXR (10-20%).**

2. **Acute/subacute form (20-40%). Symptoms develop over a few weeks: Fever, malaise, fatigue, anorexia, weight loss.**

   Respiratory: Cough, dyspnoea, chest discomfort.

CLINICAL MANIFESTATIONS

2 Syndromes:

a) Löfgren – **Erythema nodosum, arthralgia and bilateral hilar adenopathy on CXR.**

b) Heerfordt – **fever, parotid enlargement, anterior uveitis and NVII paralysis.**

CLINICAL MANIFESTATIONS

3. **Chronic form (40-70%).**

Symptoms develop over months – usually respiratory symptoms + constitutional complaints (10% have symptoms of extrapulmonary involvement). This form leads to permanent damage to the lungs and other organs.

CLINICAL MANIFESTATIONS

Pulmonary involvement

90% have abnormal CXR

50% develop permanent lung damage

5-15% develop progressive fibrosis

Symptoms: **Exertional dyspnoea. Non-productive cough.**

Physical signs: **Late inspiratory basilar crepitations. Pleural involvement rate (1-5% unilateral pleural effusion).**

CLINICAL MANIFESTATIONS

Complications:

1. **Respiratory failure, bullae + mycetoma → haemoptysis.**
2. **Eyes → blindbess.**
3. **CNS + heart → sudden death.**

DIAGNOSIS 1

1. **Clinical – Löfgren, Heerfordt.**

2. **Radiology: (Pulm Sarcoidosis).**

   Stage I bilateral hilar adenopathy (BHA)

   Stage II BHA + interstitial infiltrate.

3. **Stage III interstitial infiltrate without BHA.**

4. **Stage IV Extensive fibrosis with bullae.**

DIAGNOSIS 2

3. **Histology**
   - **lymph gland**
   - **skin**
   - **liver**
   - **transbronchial lung**
   - **open lung**

   Tissue has to be cultured for TB as well.

4. **Biochemistry**

   S-ACE, hypercalcuria, hypercalcaemia, hyper-gamma globulinaemia.

5. **Historical – Kveim skin test.**

6. **PPD (+8 AG) → cutaneous anergy.**

ASSESSMENT OF DISEASE ACTIVITY

1. **ESR, S-ACE**
2. **Gallium scan**
3. **Lung function**
4. **Broncho-alveolar lavage (T helpers elevated)**
5. **High resolution CT scan.**

TREATMENT 1

Cellular + granulomatous component indicates active disease with good response to treatment.

Fibrosis indicates irreversible disease with no response to treatment.

TREATMENT 2

1. **Asymptomatic with Stage I lung disease with/without Erythema nodosum but without extrapulmonary disease → observe.**
2. **Stage II without symptoms→** observe, with **symptoms → Rx with Corticosteroids (CS).**
3. **Stage III without symptoms and slight lung function impairment → observe.**

   If lung functions deteriorates over 3-6 months → Rx with CS.

TREATMENT 3

4. **Stage II, asymptomatic but with severe lung function impairment → Rx with CS.**

5. **Stage III (usually have symptoms) → Rx.**

6. **Stage IV → poor response to Rx.**

DOSE OF CORTICOSTEROIDS

1. **30-40mg Prednisone/day for 6-12 weeks. Wean gradually over 6 months to 10-15mg/day.**

   NB: Cardiac, occular and CNS

   Sarcoidosis: 60-80mg/day.

   50% Relapse after discontinuation of Rx.

2. **With relapse – Prednisone 60-80mg/day.**

3. **If no response ? Chloroquine**

   ? Methotrexate

INTERSTITIAL LUNG DISEASE (ILD) + COLLAGEN VASCULAR DISEASE (CVD)

Other pulmonary structures are also involved eg pleura + blood vessels (vasculitis)

1. **Systemic Lupus Erythematosis (SLE)**:

   Pleuritis, pleural effusion, acute pneumonits; ILD rare; pulmonary infection needs to be eliminated; alveolar haemorrhage; "vanishing lung" – small lung volume due to diaphragm weakness (myopathy).

ILD – COLLAGEN VASC DIS

2. **Rheumatoid arthritis (RA)**:

   Pleural effusion, subpleural nodules, lymphocytic alveolitis, ILD.

   Methotrexate (used for Rx of RA) → hypersensitivity pneumonitis.

   Penisillamine → bronchiolitis obliterans.

   ILD in males may be the presenting feature of RA (before onset of arthritis).

INTERSTITIAL LUNG DISEASE (ILD) + COLLAGEN VASCULAR DISEASE (CVD)

3. **Ancylosing Spondylitis**

   Bilateral upper lobe fibrosis with cavitation.

4. **Systemic sclerosis**:

   Distal esophageal motility disturbance → GE reflux → chronic aspiration.

   Cutaneous scleroderma → chest wall involvement → restrictive lung function.

   Pulmonary vasculitis → pulmonary hypertension.