Diffuse Parenchymal Lung Disease

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- Diffuse parenchymal lung diseases (DPLDs) are a group of disorders based on similar clinical, radiographic, physiologic, and pathologic changes that affect the alveolar walls and often the related small airways and distal pulmonary vasculature.

- Like other lung diseases, these disorders present primarily with shortness of breath.

- Imaging studies will typically demonstrate bilateral rather than unilateral lung disease.

Classification and Epidemiology

- Although there are hundreds of disorders that can present with diffuse parenchymal lung disease, they are typically divided into those with a known cause or those which are idiopathic.

- DPLD is uncommon, compared to other pulmonary diseases such as asthma or COPD.

- The true prevalence of DPLDs is unknown; however, the literature estimates the prevalence at approximately 70 per 100,000 persons, with idiopathic cause accounting for 30% to 40% of disease in these patients.

Known causes:

- Drug induced; examples: amiodarone, methotrexate, nitrofurantoin and chemotherapeutic agents.

- Smoking-related: "Smokers"' respiratory bronchiolitis characterized by gradual onset of persistent cough and dyspnea. Radiograph shows ground-glass opacities and thickened interstitium. Smoking cessation improves prognosis. Desquamative interstitial pneumonitis and pulmonary Langerhans cell histiocytosis are other histopathologic patterns associated with smoking and DPLD .

- Radiation : may occur 6 weeks to months following radiation therapy.

- Chronic aspiration : Aspiration is often subclinical and may exacerbate other forms of DPLD.

- Pneumoconiosis: Asbestosis, silicosis , berylliosis

- Connective tissue disease.

- Hypersensitivity pneumonitis.

Unknown Causes

Idiopathic interstitial pneumonia

- Idiopathic pulmonary fibrosis

- Acute interstitial pneumonia : dense bilateral acute lung injury similar to acute respiratory distress syndrome; 50% mortality rate.

- Cryptogenic organizing pneumonia: may be preceded by flu-like illness, radiograph shows focal areas of consolidation that may mimic infectious pneumonia or may migrate from one location to another.

Sarcoidosis : variable clinical presentation, ranging from asymptomatic to multi-organ involvement.

Diagnostic Approach and Evaluation

- Nonproductive cough and dyspnea are the most common presenting symptoms of a DPLD.
- Dyspnea that comes on suddenly and is of short duration is more likely due to respiratory infection, asthma, pulmonary embolism, or heart failure than DPLD.
- In contrast, patients presenting with subacute or chronic dyspnea lasting weeks to months without response to treatment should be evaluated for DPLD.
- As opposed to the typical nonproductive cough of DPLD, a long history of cough with sputum production can suggest an underlying chronic infection, airways inflammation such as chronic bronchitis, or bronchiectasis.

- When DPLD is suspected, questions should focus on determining the onset of symptoms, the disease course (improving or worsening), medications, and exposures.

- The most common identifiable etiologies of DPLDs are those associated with exposures, and the history should include a thorough review of occupations, home environment, hobbies, and other activities.

- Medication review should include current medications as well as those taken before the onset of symptoms.

- Connective tissue diseases can lead to the development of DPLD; therefore, the review of systems should assess for symptoms of arthralgia, myalgia, arthritis, tenosynovitis, dry eyes, dry mouth, dysphagia, gastroesophageal reflux, and unexplained rash.

- A family history of DPLD due to connective tissue disease should substantially increase clinical suspicion.

- Physical examination findings differ depending on the underlying cause of DPLD.
- In patients with connective tissue disorders, findings may include Raynaud phenomenon, skin thickening, sclerodactyly, malar rash, inflammatory arthritis, or tenosynovitis.
- Lung examination findings are variable and may be normal. This is more likely early in disease or in those with imaging findings of ground-glass opacity or micronodules.
- Decreased breath sounds and dullness to percussion may suggest a pleural effusion, which is atypical for many DPLDs.
- Wheezes may suggest small airways disease, while inspiratory dry "Velcro" crackles are more suggestive of fibrosis.

- The physical examination should include resting and exertional pulse oximetry. It is common for patients with DPLD to have normal resting pulse oximetry.

- individuals with DPLD will often demonstrate desaturation when ambulating. Desaturation of greater than 4 % while ambulating is consistent with a diffusion limitation, which is a hallmark of interstitial lung disease.

- Patients with a clinical suspicion of DPLD should undergo full pulmonary function testing, including lung volumes and DLCo.

- The vast majority of DPLDs have restrictive physiology.

- Plain chest radiography is an appropriate initial test for the evaluation of dyspnea and cough in patients suspected of having DPLD.

- Chest radiography may show various findings in patients with DPLD, including diffuse reticular and reticulonodular patterns, increased septal line thickening, consolidation, pleural effusions with or without pleural calcification, bronchiectasis, and hilar or mediastinal lymphadenopathy.

- Chest radiograph can be normal in patients with minimal disease, and a normal chest radiograph does not rule out DPLD.

- High-resolution CT (HRCT) scan of the chest (slice thickness 1-2 mm) is the best imaging study to identify abnormalities that can help diagnose the underlying disease.

- The findings on HRCT highly correlate with the histopathology identified on open lung biopsy.

- The diagnosis of idiopathic pulmonary fibrosis can be made without lung biopsy based on the results of HRCT.

- Serologic testing for diffuse parenchymal lung disease is most appropriate in young patients, those with symptoms of rheumatologic disease, or those with a family history of rheumatologic conditions.

Hypersensitivity Pneumonitis

- Repetitive inhalation of antigens in a sensitized patient can result in hypersensitivity pneumonitis (HP).
- It is an immunologic response that results in noncaseating granulomas and peribroncial mononuclear cell infiltration with giant cells.
- The antigens are typically complex proteins, which can come from several sources, including agricultural dusts, thermophilic fungi, and bacteria.

There are three form of HP, and they each present differently.

- The **ACUTE** form, which is most easily identified, results after a large exposure to an inciting antigen.

- The patient will develop fevers, cough, and fatigue, typically within 12 hours of exposure.

- Physical examination will reveal inspiratory crackles.

- Chest radiography can demonstrate diffuse micronodular disease but may be normal.

- HRCT will demonstrate diffuse centrilobular micronodules and ground-glass opacity.

- After removal from the offending antigen, symptoms will resolve withen approximately 48 hours.

- Subacute and chronic forms of HP likely occur after more prolonged lower level antigen exposure.

- Bird fanciers disease is an example of a chronic disorder. These patients have a chronic low-level exposure to avian antigens within the home and will ultimately experience cough, fatigue, weight loss, and shortness of breath. Similar to the acute form, the HRCT will show micronodules and ground-glass opacities, but there is also evidence of septal line thickening and fibrosis.

- In its most severe and chronic form, significant traction bronchiectasis and honeycomb changes will be evident.

- Removal of exposure to the offending antigen is essential in the treatment of HP.

- Glucocorticoids are often used for those with more severe symptoms. Response to this therapy is variable.

Idiopathic Pulmonary Fibrosis

- Idiopathic Pulmonary Fibrosis (IPF) is the most common idiopathic form of DPLD.
- It typically presents in patients between 50 and 70 years of age who have a greater than 6-month duration of a dry cough and dyspnea on exertion.
- History will reveal no potential cause for the development of fibrosis.
- Lung examination is noticeable for Velcro inspiratory crackles that are predominant at the bases and may be subtle in early disease.
- Clubbing is present in up to 50% of patients.

- The diagnosis of IPF is challenging because it is uncommon and indolent.
- The best diagnostic test is HRCT, which may show abnormalities , such as bilateral, peripheral, and basal predominant septal line thickening with honeycomb changes.
- IPF is progressive, with a median survival of 3 to 5 years after diagnosis.
- FDA-approved therapy with nintedanib and pirfenidone decreases the rate of progression of idiopathic pulmonary fibrosis but is not curative.

Asbestos-Related Lung Disease

- Asbestos includes a group of minerals that, when crushed, will break into fibers. These fibers are chemically heterogeneous hydrated silicates that are used in industry because of their high tensile strength, heat resistance, and acid resistance.

- In the past, asbestos fibers were widely used in insulation, brake linings, flooring, cement paint, and textiles.

- Asbestos-associated diseases have a prolonged latency period (15 to 35 years).

- Duration and extent of exposure are key risk factors for the development of disease.

- The most common symptom is exertional dyspnea.

- Findings of parietal pleural calcifications or plaques on chest radiograph should alert the clinician to the possibility of asbestos exposure.

- Most patients with pleural plaques are asymptomatic.

- Asbestos exposure increases the risk for development of lung cancer regardless of smoking status, but the risks are substantially higher in smokers.

Silicosis

- Silicosis is a fibrotic lung disease caused by the inhalation of silica dust.
- There are four main types of silicosis: acute silicosis , chronic simple silicosis, chronic complicated silicosis and accelerated silicosis.
- It is associated with altered cell immunity and macrophage function. Patients with silicosis are at increased risk for the development of mycobacterial infection and connective tissue disease.
- Once fibrosis develops in silicosis, there is little evidence that any therapies alter disease course.
- If individuals have continued exposure, removal from the environment will prevent further lung injury.

- Silica exposure is associated with increased risk of lung cancer, particularly for smokers.

- Smoking cessation remains an essential intervention.

Thank you.