CASE FIVE

Short case number: 3_10_5
Category: Respiratory System
Discipline: Medicine
Setting: General Practice
Topic: Interstitial lung disease and sarcoidosis

Case

Lisa Miller, aged 50 years, presents to your general practice following discharge from hospital. You had referred her to a specialist two weeks ago because of progressive shortness of breath. She advises that she was admitted to hospital by the specialist and investigated. She has been told she has interstitial lung disease but they are still awaiting results to determine the exact cause. She is worried because no one told her what this means and more importantly, she had not been given any treatment to cure the shortness of breath.

Questions

1. Define interstitial lung disease and list the conditions which can mimic it.
2. Summarise the general approach to the diagnosis of interstitial lung disease in terms of history, examination and investigations.
3. Using a flow chart explain how the diffuse parenchymal lung diseases are classified.
4. Draw an algorithm for the investigation of patients with interstitial lung disease following initial clinical and chest x-ray examination.
5. Define sarcoidosis and summarise in a table its typical clinical presentation.
6. What role does the general practitioner have in assisting patient to obtain information about their care by another doctor, specialist or hospital and what strategies exist to support this communication (PPD to answer)

Suggested reading:

- Colledge NR, Walker BR, Ralston SH, Penman ID, editors. Davidson's Principles and Practice of Medicine. 22nd edition. Edinburgh: Churchill Livingstone; 2014. Chapter 19.

ANSWERS

Interstitial lung disease and sarcoidosis

1. Define interstitial lung disease and list the conditions which can mimic it.

The diffuse parenchymal lung diseases (DPLDs) are a heterogeneous group of conditions associated with diffuse thickening of the alveolar walls with inflammatory cells and exudates (e.g. the acute respiratory distress syndrome-ARDS), granulomas (e.g. sarcoidosis), alveolar haemorrhage (e.g. Goodpasture's syndrome, p. 503), and/or fibrosis (e.g. fibrosing alveolitis). Lung disease may occur in isolation, or as part of a systemic connective tissue disorder - for example, in rheumatoid arthritis and systemic lupus erythematosus. The DPLDs are rare and poorly understood. However, although the presentation and natural history differ, they are frequently considered collectively as they share similar symptoms, physical signs, radiological changes and disturbances of pulmonary function.

Conditions which can mimic it include:
Infection

- Viral pneumonia
- *Pneumocystis jirovecii*
- *Mycoplasma pneumoniae*
- TB
- Parasites, e.g. filariasis
- Fungal infection

Malignancy

- Leukaemia and lymphoma
- Lymphatic carcinomatosis
- Multiple metastases
- Bronchoalveolar carcinoma

Pulmonary oedema
Aspiration pneumonitis

2. Summarise the general approach to the diagnosis of interstitial lung disease in terms of history, examination and investigations.
Establishing a diagnosis is important because:

- Firstly, there are prognostic implications; e.g. sarcoidosis is frequently self-limiting, whereas idiopathic pulmonary fibrosis (IPF) is most often fatal.
- Secondly, establishing a specific diagnosis will avoid inappropriate treatment (e.g. powerful immunosuppressive regimens)
- Thirdly, some DPLDs can be expected to respond better than others to treatment, e.g. a good symptomatic response to corticosteroids could be predicted in sarcoidosis
- Finally, a lung biopsy taken when the patient is already established on empirical immunosuppressive therapy is not only associated with a higher morbidity and mortality, but the

interpretation of the tissue obtained is more difficult. It is desirable, therefore, to be confident about the diagnosis before starting any therapy.

History:

Gradually progressive shortness of breath on exertion may be the only symptom, and hence the patient may not present clinically until there is extensive lung pathology. History-taking should include a thorough and comprehensive search for exposure to organic and inorganic dusts. A 'lifetime' occupational history is essential and should include hobbies that may involve similar exposures. Contact with birds at home or in the working environment is the cause of the most common form of hypersensitivity pneumonitis (HP). The smoking status should be recorded and a drug history that includes over-the-counter prescriptions should be obtained. A history of rashes, joint pains or renal disease may suggest an underlying connective tissue disorder or vasculitis. The presence of any co morbid disease should be ascertained such as collagen vascular disease, immunodeficiency, HIV or malignancy. In exceptional cases there is a family history of DPLD.

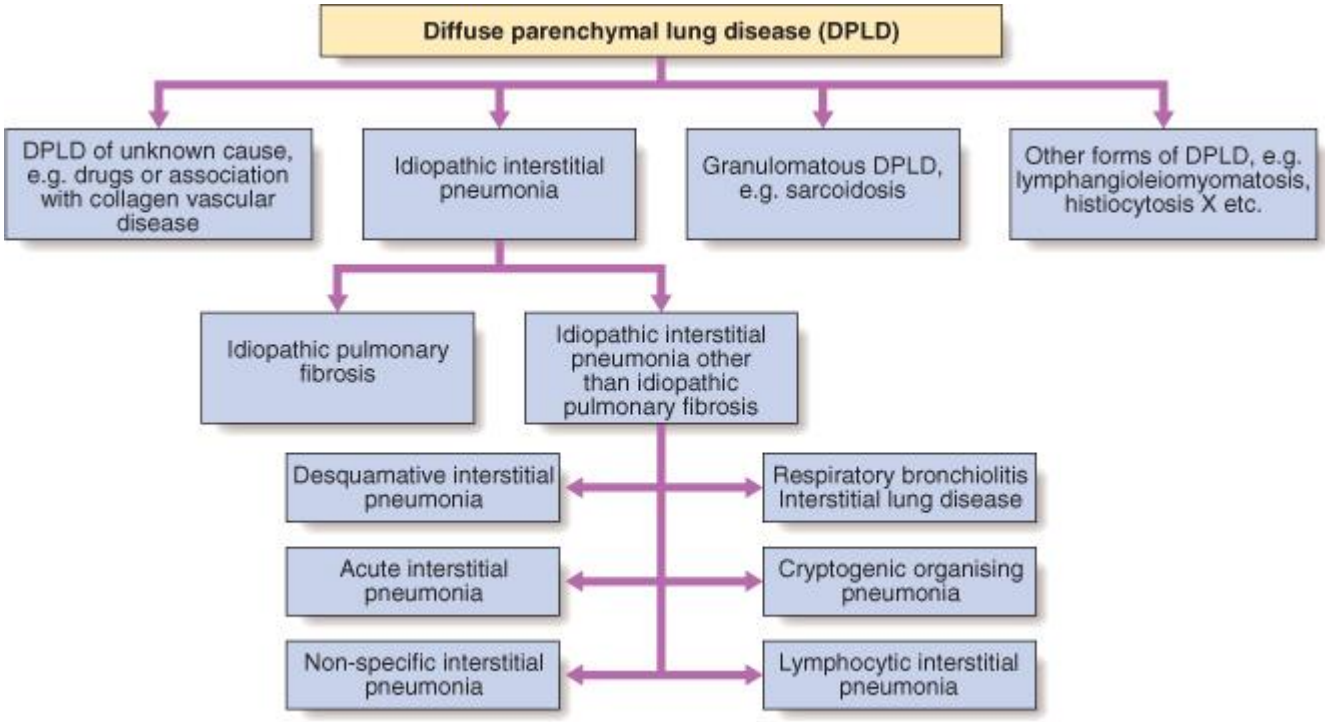
Examination:

In many early cases, there are few, if any, physical signs. In advanced disease, tachypnoea and cyanosis may be evident at rest and there may be signs of pulmonary hypertension and right heart failure. Finger clubbing may be prominent, particularly in IPF or asbestosis. There may be restriction of lung expansion and showers of end-inspiratory crackles posteriorly and laterally. Extrapulmonary signs, including lymphadenopathy or uveitis, may be present in sarcoidosis and arthropathies or rashes may occur when a DPLD is a manifestation of a connective tissue disorder.

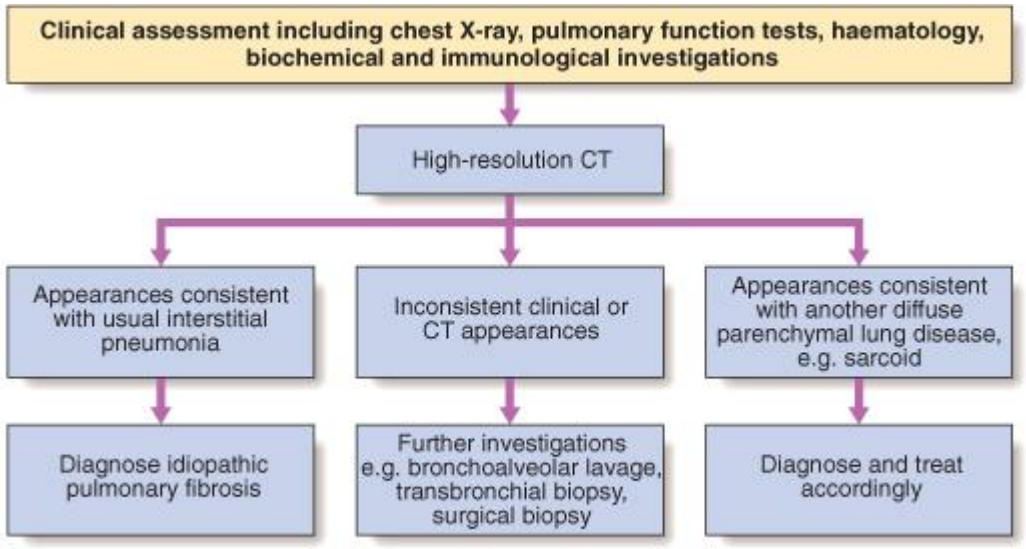
Investigations:

Some blood tests may be useful in indicating systemic disease or providing crude indices of disease activity (FBC, Ca^{2+}, LDH, ACE, ESR, CRP). Pulmonary function tests typically show a restrictive pattern with diminished lung volumes and a reduced gas transfer, although an elevated gas transfer may be seen in cases of alveolar haemorrhage. The chest X-ray typically shows a fine reticular, reticulonodular or even nodular pattern of infiltration at the bases and periphery with cystic areas and honeycombing in advanced disease. However, plain radiography is insensitive and may not appear abnormal until disease is advanced. HRCT is more sensitive and specific and has become extremely valuable in detecting early interstitial lung disease, assessing the extent and type of involvement and guiding further investigations and management. Bronchoscopy is useful in certain circumstances. Increased numbers of lymphocytes in the bronchoalveolar lavage (BAL) may suggest either sarcoid or hypersensitivity pneumonitis, whereas a neutrophilia is more suggestive of IPF. Analysis of BAL may suggest important differential diagnoses such as infection or malignancy, and in rare instances may be diagnostic when iron-laden macrophages are seen in pulmonary haemosiderosis. Transbronchial biopsies may establish the diagnosis in sarcoidosis and in some conditions which mimic ILDs, such as lymphatic carcinomatosis and certain infections. However, it is less specific in heterogeneous disorders such as IPF where video-assisted thoracoscopy (VATS), or a limited thoracotomy, may be required to obtain a more representative sample.

3. Using a flow chart explain how the diffuse parenchymal lung diseases are classified.



4. Draw an algorithm for the investigation of patients with interstitial lung disease following initial clinical and chest X-ray examination.



5. Define sarcoidosis and summarise in a table its typical clinical presentation.

Sarcoidosis is a multisystem granulomatous disorder. The condition is more commonly seen in colder parts of Northern Europe where the incidence is approximately 40/10 000. The aetiology remains uncertain. Links with atypical mycobacteria and viruses remain speculative; there is some evidence of familial clustering and genetic factors are undoubtedly important. Sarcoidosis appears less commonly in smokers.

The mediastinal and superficial lymph glands, lungs, liver, spleen, skin, eyes, parotid glands and phalangeal bones are most frequently affected, but all tissues may be involved. The characteristic histological feature is a non-caseating epithelioid granuloma; fibrosis is seen in up to 20% of cases of pulmonary sarcoidosis. Disturbances in calcium metabolism reflect increased formation of calcitrol (1,25-dihydroxyvitamin D_3) by alveolar macrophages and may lead to hypercalciuria, hypercalcaemia and, rarely, nephrocalcinosis.

Typical clinical presentations:

- Asymptomatic-abnormal routine chest X-ray (c. 30%) or abnormal liver function tests
- Respiratory and constitutional symptoms (20-30%)
- Erythema nodosum and arthralgia (20-30%)
- Ocular symptoms (5-10%)
- Skin sarcoid (including lupus pernio) (5%)
- Superficial lymphadenopathy (5%)
- Other (1%), e.g. hypercalcaemia, diabetes insipidus, cranial nerve palsies, cardiac arrhythmias, nephrocalcinosis

6. What role does the general practitioner have in assisting patient to obtain information about their care by another doctor, specialist or hospital and what strategies exist to support this communication (PPD to answer)