Rheumatoid Arthritis and the Lung

Lung disease is a well-recognised and important extra-articular manifestation of rheumatoid arthritis. A study in New Zealand of patients recently diagnosed with rheumatoid arthritis found that 30% of patients reported respiratory symptoms (dyspnoea, cough, wheeze), 20% of patients had physiological evidence of airflow obstruction and 40% had reduced gas transfer. The prevalence of abnormalities found with high-resolution CT was decreased attenuation in 67%, bronchiectasis in 35%, bronchial wall thickening in 50%, ground glass opacification in 18% and reticular changes in 12% of patients [1].

The range of pulmonary problems associated with rheumatoid arthritis includes [2]:

- **Rheumatoid nodules:**
  - The only pulmonary manifestation specific to rheumatoid arthritis.
  - They are typically benign but can lead to pleural effusion, pneumothorax, haemoptysis, secondary infection, and bronchopulmonary fistula.

- **Caplan’s syndrome** [3]:
  - See also separate Caplan’s Syndrome article.
  - In 1953, Caplan described a characteristic radiographic pattern in coal miners with rheumatoid arthritis that was distinct from the typical progressive massive fibrosis pattern of coalworkers’ pneumoconiosis.
  - CXRs show multiple well-defined rounded nodules, which are about 0.5-2 cm in diameter, distributed throughout the lungs but predominantly at the lung periphery.

- **Interstitial lung disease (ILD)** [4]:
  - ILD and airways disease are the most common forms of rheumatoid arthritis-related lung disease [5].
  - ILD can be present in most types of connective tissue disease, including rheumatoid arthritis, scleroderma, systemic lupus erythematosus, polymyositis or dermatomyositis, Sjögren's syndrome and mixed connective tissue disease [6].
  - ILD most often occurs in middle-aged men. It is usually associated with severe arthritis and high serum levels of rheumatoid factor.
  - It presents with insidious onset of dyspnoea with occasional dry cough.
  - Associated pulmonary vasculitis may cause pulmonary hypertension.

- **Bronchiolitis:**
  - **Bronchiolitis obliterans with organising pneumonia**: clinical features include cough, shortness of breath, and bilateral crackles. The vital capacity is slightly decreased and the diffusing capacity is moderately to severely decreased. High-resolution chest CT scan shows bilateral ground-glass opacities with air bronchograms and triangular, pleura-based opacities. Steroids are the best treatment option. The prognosis is generally good, with resolution and cure for most patients [7].
  - **Obliterative bronchiolitis**: a rare, usually fatal condition. Associated with penicillamine, gold, and sulfasalazine treatment. Presents with rapid-onset dyspnoea and dry cough. Fever is uncommon.

- **Bronchiectasis** [8]:
  - See also separate Bronchiectasis article.
  - Bronchiectasis co-existing with rheumatoid arthritis differs from the other types of bronchiectasis.
  - Patients with rheumatoid arthritis and bronchiectasis have worse obstructive airways disease, increased susceptibility to recurrent lower respiratory tract infections, faster lung function decline and higher mortality compared with subjects with bronchiectasis alone.

- **Arteritis:**
  - Arteritis of the pulmonary artery and lung is rare; signs of systemic vasculitis are usually present.

- **Infection:**
  - Respiratory infections account for 15-20% of deaths in rheumatoid patients.

- **Drug toxicity:**
  - Acute interstitial pneumonitis may occur in 1-5% of patients treated with methotrexate (see 'Methotrexate-associated lung disease in rheumatoid arthritis', below).
  - Penicillamine and gold may also cause pulmonary complications [9].

- **Pleural effusions:**
  - See separate Pleural Effusion article.
  - Pleural effusions in rheumatoid arthritis are usually small, unilateral and asymptomatic.
  - Occasionally, an empyema may develop
- **Lung cancer**: is more common in patients with rheumatoid arthritis than in normal control subjects.
- **Other diseases**: 
  - Rheumatoid arthritis patients can get apical fibro-bullous disease (apical fibrotic cavity lesions similar to ankylosing spondylitis).
  - Thoracic cage immobility causing restrictive lung disease.
  - Primary pulmonary hypertension (rare); secondary pulmonary hypertension (due to ILD) is more common.

**Epidemiology**

Rheumatoid arthritis is often associated with pleural disease (20-40%), interstitial pneumonitis (5-10%), nodules (1%), interstitial fibrosis, bronchiolitis obliterans organising pneumonia, and pulmonary vasculitis.

**Differential diagnosis**

The association of rheumatoid arthritis with lung disease may be due to:

- Rheumatoid-associated lung disease.
- Drug-related lung disease secondary to drugs used to treat rheumatoid arthritis.
- Infection secondary to immunosuppression.
- Co-existent medical conditions - eg, chronic obstructive pulmonary disease.

**Investigations**

- Blood tests for evaluation of rheumatoid arthritis, including serology.
- Respiratory function tests, including spirometry.
- CXR.
- Aspiration of pleural fluid.
- CT or MRI scan.
- Lung biopsy.
Management

There are several management guidelines, including those from the National Institute for Health and Care Excellence (NICE)[10, 11, 12, 13]. These are important guidelines for improvement of the management of rheumatoid arthritis. They do not include details of the management of lung disease in rheumatoid arthritis.

ILD caused by rheumatoid arthritis is usually treated with a corticosteroid or a combination of a corticosteroid and azathioprine or cyclophosphamide. Methotrexate is also being increasingly used.

Prognosis

- ILD associated with rheumatoid arthritis causes significant morbidity and mortality.
- Mortality is high in patients who develop ILD and pulmonary hypertension.
- The median survival of all patients with ILD associated with rheumatoid arthritis has been reported to be approximately five years.

Methotrexate-associated lung disease in rheumatoid arthritis

- Methotrexate pneumonitis is an unpredictable and life-threatening side-effect of methotrexate therapy.
- Presentation is often subacute with symptoms often present for several weeks or months before diagnosis.
- It presents most often with cough, dyspnoea and fever. It may progress rapidly to respiratory failure.
- Early diagnosis, cessation of methotrexate, and treatment with corticosteroids and/or cyclophosphamide are important in management.
- There is a high rate of recurrence of lung injury after re-challenge with methotrexate.

Further reading & references

9. British National Formulary (BNF); NICE Evidence Services (UK access only).
10. Guideline for the management of rheumatoid arthritis (first 2 years); British Society for Rheumatology (July 2006).
11. BSR and BHPR guideline for the management of rheumatoid arthritis (after the first 2 years); British Society for Rheumatology and British Health Professionals in Rheumatology (January 2009).

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Author: Dr Colin Tidy  Peer Reviewer: Dr John Cox

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