Causes and investigation of increasing dyspnoea in rheumatoid arthritis

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Rheumatoid arthritis (RA) is the most common inflammatory arthropathy in the United Kingdom. The exact level of thoracic involvement in this systemic disorder is unknown but postmortem studies show pleural involvement in up to 40% of cases.¹ While the disease as a whole is more common in women, pleural and pulmonary involvement tend to affect males more frequently. There are many different manifestations of thoracic involvement (table) and when dyspnoea is the presenting problem the differential diagnosis is wide.

We present two cases in which high resolution computed tomography (HRCT) proved extremely useful in the diagnosis of the cause of shortness of breath, and discuss other thoracic manifestations of rheumatoid arthritis.

PATIENT 1

Clinical history

A 61 year old man presented with increasing shortness of breath. He had a four year history of seropositive, nodular rheumatoid arthritis (RA) controlled on sulphasalazine and diclofenac. On examination he was dyspnoeic at rest and had bilateral basal crackles. There was no evidence of digital clubbing. Pulmonary function tests revealed a restrictive defect with no obstructive element. Both total lung capacity (TLC) and the transfer coefficient (Kco) were reduced.

Thoracic manifestations of rheumatoid arthritis

<i>Skeletal</i>	
Superior rib notching	
<i>Pleural</i>	
Effusion	
Pneumothorax	
Empyema	
<i>Pulmonary</i>	
Diffuse	Fibrosis
	Obliterative bronchiolitis
	Vasculitis
	Secondary to drug therapy
Focal	Necrobiotic nodules
	Caplan's syndrome
<i>Cardiac</i>	
Pericarditis	
Myocarditis	
Cardiac nodules	
Coronary vasculitis	Myocardial
	Valvular
<i>Miscellaneous</i>	Primary
	Atherosclerotic
<i>Miscellaneous</i>	
Mediastinal lymphadenopathy	

Radiological findings

Chest radiography demonstrated a hazy opacification at both lung bases. Figure 1 shows an HRCT image demonstrating abnormalities in both lower lobes consisting mainly of a ground glass change in a predominantly subpleural distribution. This is associated with some thickening of the interlobular septa producing fine lines tangential to the pleura in the lung periphery.

Diagnosis

The radiological diagnosis is of early fibrosing alveolitis associated with rheumatoid arthritis.

PATIENT 2

Clinical history

A 56 year old lady presented with increasing shortness of breath. She had a three year history of seropositive RA controlled on first line medication. She had not received penicillamine and had no history of asthma or other chronic lung disease. Her chest was hyperinflated, with bilateral basal crackles and occasional mid-inspiratory squeaks. Pulmonary function tests demonstrated a low FEV₁:FVC ratio. TLC and residual volume were increased, giving the picture of an obstructive defect.

Radiological findings

The chest radiograph showed clear but hyperinflated lungs. Figure 2 shows an HRCT image demonstrating no evidence of emphysema, but there are geographic areas of decreased attenuation which become more marked on expiration. This is indicative of air trapping occurring at a bronchiolar level.

Diagnosis

The radiological diagnosis is of bronchiolitis obliterans (or obliterative bronchiolitis) secondary to the rheumatoid arthritis.

Discussion

Fibrosing alveolitis and bronchiolitis obliterans are two of the diffuse pulmonary manifestations of connective tissue disorders which, particularly in their early stages, are difficult to

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Figure 1 Patient 1: HRCT image through the chest demonstrating peripheral, ground glass opacification with focal thickening of the interlobular septa (arrow).

Figure 2 Patient 2: Expiratory HRCT image through the chest demonstrating geographical areas of decreased attenuation (darker lung) as a result of trapped air.

Figure 3 HRCT image demonstrating marked, basal, fibrotic, honeycombing in a patient with severe, extensive lung fibrosis.

diagnose from the clinical findings or from the chest radiograph.

Conventional CT improves demonstration of the pulmonary parenchyma, but usually images a 10 mm thick slice which blurs the fine detail of the lung. In HRCT a 1–2 mm slice is analysed and the resultant data manipulated with a high resolution algorithm. This computer manipulation results in an increase in both spatial resolution and sharpness, and the images provided supply exquisite detail of the pulmonary parenchyma. Many radiological studies have demonstrated the increased sensitivity and specificity of HRCT over plain films and conventional CT with regard to diffuse lung disease.^{2–4}

PULMONARY FIBROSIS

Interstitial fibrosis is the most common diffuse pulmonary involvement caused by the connective tissue disorders and is most frequently seen in systemic sclerosis and rheumatoid arthritis. Radiologically, the appearances are almost identical to those of cryptogenic fibrosing alveolitis, though there is some evidence that in RA the pattern is less symmetrical.⁵ The changes usually occur in a peripheral, subpleural location.

Histological examination reveals alveoli partly filled with inflammatory and desquamated type II epithelial cells and the interstitium thickened by a mononuclear cell infiltrate.¹ These changes result in a ground glass pattern on HRCT—a finding which usually indicates an active alveolitis. As fibrosis occurs with progression of the disease, there is increased thickening of the interstitium.⁶ This results in a reticular pattern on HRCT. Subsequently, coarse fibrotic scars are formed and, with further disorganisation of the lungs, cystic spaces appear, giving rise to a honeycomb appearance (fig 3).

BRONCHIOLITIS OBLITERANS

Bronchiolitis obliterans in RA is usually associated with penicillamine therapy, but may occur without this association.⁷

Histological examination reveals inflammation of the respiratory bronchioles and alveolar ducts leading to their plugging by granulation tissue and eventual obliteration by fibrosis.⁸ The distal alveoli are normal and remain aerated by means of collateral air drift via the pores of Kohn and canals of Lambert. The areas of decreased attenuation on HRCT, which are most evident on scans performed in expiration, are caused by trapped air in the alveoli distal to the blocked or narrowed bronchioles. It is likely that reflex vasoconstriction, secondary to local hypoxia around the stagnant air, further contributes to the decreased attenuation.⁹ Other features which may be present (though not in the case presented) are small branching opacities in the lung periphery attributable to bronchiolar plugging and dilatation of the more proximal airways as a result of the secondary development of bronchiectasis.⁹

OTHER THORACIC MANIFESTATIONS

A variety of pleural, pulmonary and cardiac abnormalities directly attributable to RA may cause dyspnoea. Pleural involvement is present in up to 40% of cases of RA coming to postmortem examination. Pleural effusions are the most common manifestation, but the collections are rarely large enough to cause dyspnoea and only 5% of patients will show plain film evidence of effusions during the course of their disease.⁶ Pleural involvement may also lead to pneumothoraces and empyemata.

As discussed above, diffuse pulmonary fibrosis is the most frequent pulmonary abnormality. The HRCT changes are characteristic, but are identical to those seen with cryptogenic fibrosing alveolitis. Other pulmonary causes of dyspnoea include vasculitis and changes secondary to drug therapy. Diffuse pulmonary vasculitis is rare in RA, being more commonly seen in systemic lupus erythematosus. A necrotising arteritis may cause pulmonary haemorrhage, which produces patchy areas of pulmonary consolidation or ground glass opacification on HRCT and the condition is characterised by an increase in the transfer factor (TLCO) on pulmonary function tests. Patients occasionally present with haemoptysis. Another manifestation of pulmonary vasculitis is pulmonary hypertension secondary to an obliterative arteritis but pulmonary hypertension is more usually secondary to diffuse pulmonary involvement. The chest radiograph reveals clear lungs and enlarged central pulmonary vessels.

Changes resulting from drug therapy are relatively frequently seen during the treatment of rheumatoid arthritis. Penicillamine may cause an obliterative bronchiolitis with HRCT changes identical to those described in patient 2. Methotrexate can cause a pneumonitis which produces a patchy ground glass change on HRCT, and gold can produce both consolidation and fibrosis.¹⁰ Resolution of these changes usually occurs after discontinuation of the drugs. Rheumatoid nodules cause focal pulmonary involvement. All areas of the lung may be involved, though the lesions are typically subpleural in location. Clinical features are uncommon.

Pericarditis is the most common cardiac abnormality, though there is clinical evidence of pericardial fluid in only 2% of patients with RA. Progression to tamponade or constrictive pericarditis can occur.¹¹ Myocarditis is extremely rare but, if severe, can lead to cardiac failure. Rheumatoid nodules may develop within the myocardium and can cause conduc-

tion disturbances ranging from first degree to complete heart block, depending on the site. Nodules can also develop in the valvular structures, usually on the left, and more frequently the mitral rather than the aortic valve is involved.¹¹ This can lead to valvular regurgitation. Atherosclerotic coronary vessel disease is more frequently seen in patients with RA than in the general population, probably secondary to steroid therapy, and direct coronary artery vasculitis can also occur, leading to myocardial ischaemia. The most common radiographic manifestations of cardiac involvement are cardiomegaly and pulmonary oedema secondary to left heart failure.

Summary

Fibrosing alveolitis and bronchiolitis obliterans are two of the many pulmonary manifestations of the connective tissue disorders. When shortness of breath is the main complaint, it is often difficult to diagnose the individual causative lesion from the clinical examination, lung function tests, and chest radiographic findings. In such cases high resolution computed tomography, with its increased sensitivity and specificity for analysis of the pulmonary parenchyma, provides an excellent diagnostic tool for determining the presence and type of pulmonary abnormality.

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