CASE FOR DIAGNOSIS

Progressive dyspnoea in a 40-yr-old female

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Case history

A 40-yr-old female presented with dyspnoea on minimal exertion and a paroxysmal dry cough, keeping her awake for long periods. The shortness of breath was reported to be progressive over the last 18 months. She had never smoked and was not on medication. There was no recent history of travelling and she only had a dog at home. Her medical history was marked with autosomal dominant polycystic kidney disease.

On clinical examination, the patient presented a moderate fever measured at 39°C and a regular pulse (90 beats·min⁻¹); blood pressure was 130/90 mmHg. Fine inspiratory crackles were heard on the left hemithorax and on the right base. A blood sample revealed an inflammatory syndrome with a

C-reactive protein (CRP) level of 97 mg·L⁻¹. Arterial blood gas analysis yielded a severe arterial hypoxaemia with an arterial oxygen tension (P_{a,O_2}) of 4.26 kPa (32 mmHg) and an oxygen saturation of 62%. The results of spirometry showed an important volume restriction: total lung capacity 2.55 L (normal 7.97 L); vital capacity 1.40 L (normal 6.09 L); forced expiratory volume in one second (FEV₁) 1.07 (normal 4.65 L). A chest radiograph (fig. 1) was performed, followed by a high-resolution computed tomography (HRCT) scan of the chest (fig. 2).

The patient was treated with inhaled steroids, inhaled bronchodilators, oxygen and antibiotics. Broad-spectrum antibiotics were given for 15 days with improvement of the inflammatory syndrome, but with no significant improvement of the dyspnoea. Due to lack of improvement with empiric therapy, surgical lung biopsy was performed on two different lobes (figs 3a and b) from the right lung.

Fig. 1. – Chest radiographical analysis.

Fig. 2. – High-resolution computed tomography (lung window setting) scan of the chest.

Fig. 3.—a) Lung biopsy at a low magnification, internal scale bar=1 mm. b) Lung biopsy at a higher magnification, internal scale bar=50 millimicrometres. Haematoxylin and eosin staining.

BEFORE TURNING THE PAGE, INTERPRET THE CHEST RADIOGRAPH, THE COMPUTED TOMOGRAPHY SCAN AND THE PHOTOMICROGRAPHS AND SUGGEST A DIAGNOSIS.

Interpretation

Chest radiography

The postero-anterior radiograph shows bilateral basal alveolo-interstitial opacities (fig. 1).

High-resolution computed tomography scan of the chest

Thin-section computed tomography (CT) of the chest HRCT (lung window setting) reveals geographical ground-glass opacities in association with interlobular septal thickening (curved arrows) in both the lower lobes, the right middle lobe and the lingula (fig. 2). The bronchi located in the lateral and postero-basal segment of the right lower lobe are slightly distorted and dilated (straight arrows), which is suggestive of fibrosis.

Pathology

Histological examination of the pulmonary parenchyma shows a uniform, diffuse alveolar septal thickening. Proliferating fibroblasts and chronic inflammatory cells, consisting mainly of lymphocytes and plasma cells, occupy the enlarged septa. In addition, the pneumocytes lining the alveolar septa were sometimes hyperplastic and alveolar macrophages accumulated in the alveoli, especially beneath the pleura (figs 3a and b).

Diagnosis: Nonspecific interstitial pneumonia with fibrosis

Clinical course

The patient completely recovered clinically and radiographically after a 7-month course of methylprednisolone and azathioprine. Therapy was tapered and finally stopped after 1 yr. Three months later, the respiratory condition deteriorated and from functional and radiological assessment it was concluded that there was a recurrence of nonspecific interstitial pneumonia (NSIP). The initial immunosuppressant therapy was resumed.

Discussion

NSIP is a relatively new clinicopathological entity that has been added to the current classification of idiopathic interstitial pneumonia (IIP). NSIP is seen most commonly in middle-aged adults, with a slight female predominance. Clinical symptoms are mainly dyspnoea and cough, and sometimes fever. The overall duration of the symptoms before biopsy is ~8 months [1, 2]. Radiographical and HRCT appearances of NSIP have been described [2–7]. Conventional chest radiographs commonly show bilateral interstitial infiltrates, but in some cases no abnormalities are present [1, 2]. Characteristic findings on HRCT are bilateral, patchy areas of ground-glass opacity with lower zone predominance often associated with bronchiectasis, as encountered in the present patient. Frequently, reticular abnormalities and areas of consolidation are also seen. Honeycombing was not seen in most of the series [3, 4, 6], but ranged to 30% in one study [7]. A "crazy-paving" pattern in a patient with NSIP was described by COCHE *et al.* [8]. This nonspecific appearance was characterised by ground-glass attenuation in a geographical distribution and smoothly thickened interlobular septae within areas of airspace disease. No bronchial dilatation was seen.

MACDONALD *et al.* [5] found that 21 patients with idiopathic NSIP were associated with more ground-glass attenuation and a finer reticular pattern at CT than patients with usual interstitial pneumonia (UIP). However, there seemed to be some overlap of the CT features between NSIP and UIP. Furthermore, the findings of FLAHERTY *et al.* [6] in a study of 109 patients, demonstrated more ground-glass opacity on HRCT in patients with UIP than patients with fibrotic NSIP. There was also a greater profusion of interstitial abnormality as shown by HRCT in patients with UIP. In addition, the article by MACDONALD *et al.* [5] reported higher sensitivity and specificity of thin-section CT in identifying NSIP than previously reported. The overlap of clinical and CT findings between UIP and NSIP suggests that surgical biopsy is mandatory for final diagnosis [1, 6]. The diagnostic yield of bronchoalveolar lavage (BAL) in interstitial lung disease is limited and it was felt that the results of BAL were unlikely to prove diagnostic in the present case. Furthermore, BAL was not attempted in the patient because gas exchange impairment made it relatively contraindicated.

Histologically, NSIP is usually characterised by a diffuse homogeneous interstitial thickening due to inflammation and fibroblast proliferation within the alveolar walls that does not fit with another IIP. The temporal uniformity of the parenchymal changes in NSIP contrasts sharply with the temporal heterogeneity of UIP [1, 2, 9–11]. NSIP is subdivided into a cellular and a fibrotic group. In cellular NSIP, alveolar septal thickening by inflammatory cells is predominant. Fibrotic NSIP is characterised by fibrosis with no or little inflammation [5, 11]. The area of ground-glass opacity may correspond to interstitial thickening caused by varying degrees of interstitial inflammation or active fibrosis. Bronchial dilatation or irregular linear opacity within ground-glass opacity may represent interstitial fibrosis rather than inflammation [3].

The prognosis is generally good with a beneficial response to steroids in most patients [1, 2]. The possibility of relapse of NSIP as observed in the present patient has been reported previously. For example, COTTIN *et al.* [12] found that four of their 12 patients with NSIP had recurrence while decreasing or after stopping therapy. Patients with a cellular pattern of NSIP appear to have better survival than those with a fibrotic pattern of NSIP [3, 10, 11]. The prognosis appears to depend on the extent of the fibrosis [1, 2]. The presence of a UIP pattern in any sample of the surgical lung biopsies confers a poor prognosis [6]. FLAHERTY *et al.* [6] showed that patients with a histological pattern of UIP in any lobe should be classified as having UIP. The lobar heterogeneity of patients with IIP was also demonstrated on radiography and HRCT. This highlights the value of obtaining a biopsy specimen of multiple lobes and the increased likelihood of obtaining biopsies from areas of active disease using the preoperative HRCT scan. Usually, the aetiology of NSIP is unknown, but connective-tissue diseases or potential sources of exposure may be aetiological [2, 9]. The importance of careful correlation of the clinical and pathological findings with the radiographical findings cannot be overemphasised when making the diagnosis of NSIP [1].

This case corresponds to the group 1 classification of KATZENSTEIN and FIORELLI [9], characterised by a cellular interstitial pneumonia with relatively little fibrosis.

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