Singapore Med J 2002 Vol 43(6) : 314-317

An Unusual Case of Nonspecific Interstitial Pneumonia Treated Initially with Surgical Resection

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ABSTRACT

Nonspecific interstitial pneumonia (NSIP) has been recently described as a distinct clinicopathologic entity. We describe an unusual case of a middle-aged man who presented with exertional dyspnoea, cough, radiographic airspace opacities in the left lung and previous history of right thoracotomy for suspected right lower lobe neoplasm. Histology at that time revealed "chronic inflammation". A course of high-dose steroids was given after failure of the airspace opacities to respond to a trial of antituberculous therapy. Improvement in symptoms and radiological appearance was noted subsequently. A diagnosis of nonspecific interstitial pneumonia was made on review of the initial open lung biopsy specimen. Seven months after tailing down to maintenance low-dose steroids, the NSIP relapsed. The NSIP subsequently responded again to high-dose steroids. This case illustrates that NSIP is a difficult diagnosis, may present as a focal lung opacity initially, and may relapse after steroid dose is tailed down.

Keywords: nonspecific interstitial pneumonia, focal opacity, steroids, relapse

Singapore Med J 2002 Vol 43(6):314-317

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INTRODUCTION

First described in 1994, nonspecific interstitial pneumonia (NSIP) has been recently identified as a distinct form of idiopathic interstitial pneumonia[1,2]. Bilateral patchy infiltrates are major radiological findings[3-5]. We report an unusual case of NSIP presenting initially as a focal lung opacity mimicking neoplasm.

CASE REPORT

A 53-year-old man first presented to us on 10 April 1997 with exertional dyspnoea for two months. This was associated with occasional cough. However he had no fever, chest pain, haemoptysis, loss of weight or loss of appetite. He was a smoker of 30 pack-years. He had a past history of having a right thoracotomy in 1993 for chronic cough of three months' duration and a persistent right lower lobe solitary nodular opacity. The biopsy of the lung was then initially reported as "chronic inflammation". He was not known to have pulmonary tuberculosis before. He was only on atenolol 50 mg once a day for essential hypertension. He used to work in a shipyard, piping lines for over 20 years. He did not keep any pets.

Physical examination was unremarkable except for presence of right thoracotomy scar. He was afebrile and there were no clinical features of connective tissue disorders such as systemic lupus erythematosus, rheumatoid arthritis or scleroderma. In addition, there was no clubbing and lungs were clear clinically.

Full blood count showed haemoglobin 13.8 g/dl, white cell count 9.8 x 10^9/I (polymorphs 79%, lymphocytes 10%, monocytes 10%, eosinophils 0%). The erythrocyte sedimentation rate was 44 mm in the first hour. Connective tissue screen (antinuclear antibody, rheumatoid factor) and ANCA were negative. Chest radiographs showed airspace shadows in the left upper and middle zones. There were also features of right-sided thoracotomy (Fig. 1). CT scan of the thorax showed patchy alveolar infiltrates in the left lung which were amorphous and groundglass in appearance (Fig. 2). Bronchoscopy did not reveal any endobronchial lesion. Bronchoalveolar ravage (BAL) showed no malignant cells and cultures for tuberculosis and fungus were negative. Transbronchial lung biopsy showed chronic inflammation with no evidence of malignancy.

Empiric antituberculous treatment was started on 26 August 1997 with no improvement. Oral prednisolone 30 mg daily was started on 13 January 1998 for presumptive bronchiolitis obliterans organising pneumonia (BOOP) with subsequent gradual clearing of chest radiographic opacities over the next few months. The previous histology from open lung biopsy in 1993 was subsequently reviewed (Fig. 3). This showed diffuse thickening of the alveolar walls by a moderate interstitial infiltrate of lymphocytes and plasma cells and deposition of collagen within the pulmonary interstitium. Occasional lymphoid follicles with germinal centres were seen as well. The diagnosis of nonspecific interstitial pneumonia was made based on the temporal homogeneity

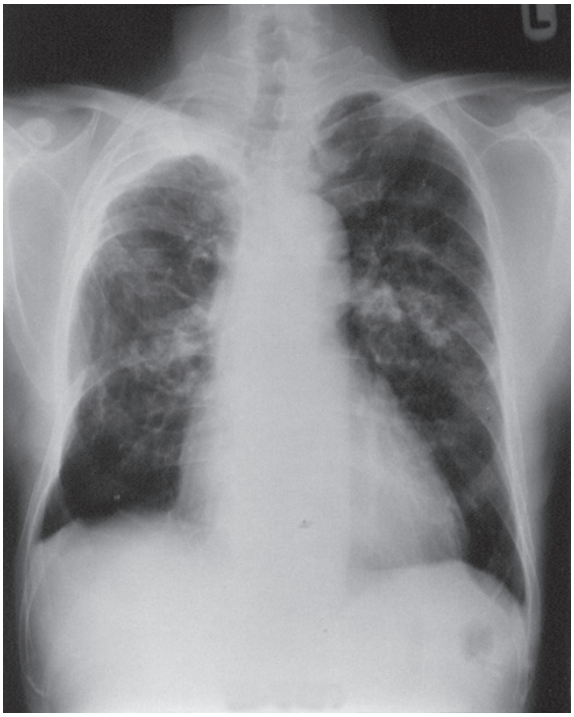

Fig. 1 Chest radiograph on initial presentation, four years after a right thoracotomy for a right lower lobe opacity. This demonstrates small areas of patchy consolidation at the left upper zone and at the left midzone. There are features of right sided thoracotomy with partial resection of the right sixth rib, reduction of lung volume, scarring at the periphery of the midzone and marked apical pleural thickening.

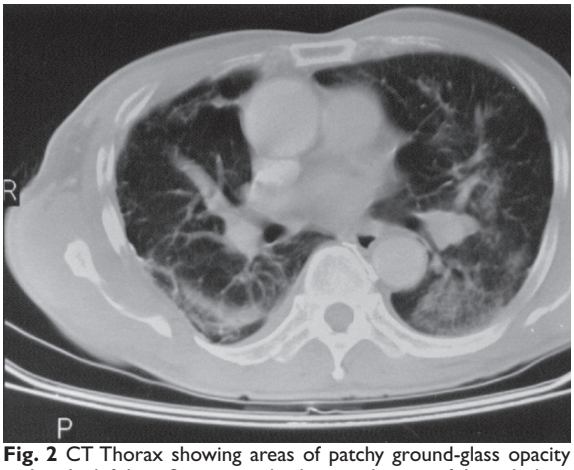

Fig. 2 CT Thorax showing areas of patchy ground-glass opacity within the left lung. Scarring and volume reduction of the right lung is related to the previous surgery.

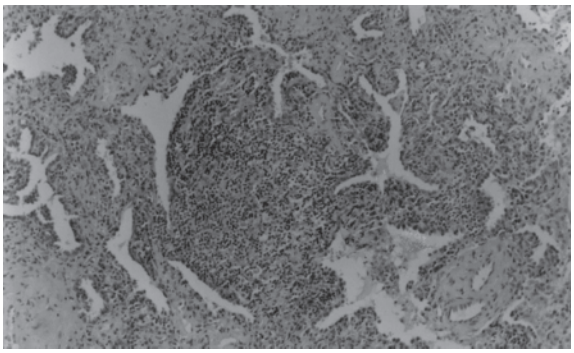

Fig. 3 Open lung biopsy showing interstitial fibrosis and chronic inflammation. Lymphocytes form aggregate (hemotoxylin-eosin stain; magnification: X 200).

of the lesion with uniform distribution of histologic changes which distinguished it from the histologic variability and patchiness of usual interstitial pneumonia (UIP). The histologic specimen also lacked honeycomb changes. Diffuse intra-alveolar accummulation of macrophages characteristic of desquamative interstitial pneumonia (DIP) was absent. The presence of prominent alveolar septal inflammation and fibrosis as well as the lack of hyaline membranes are unusual in acute interstitial pneumonia (AIP)[2,6,8].

Pulmonary function tests showed restrictive pattern with FEV1/FVC ratio of 91% and reduced DLCO (54% of predicted) (Table I).

With stabilisation of the chest radiographic findings (Fig. 4), our patient was maintained on low dose prednisolone at 5 mg once a day since 12 January 1999. He was later admitted on 17 August 1999 for acute cholecystitis. During this admission, he complained of increased shortness of breath for the last two weeks. The repeat chest radiograph showed increased opacities over the left midzone (Fig. 5). High resolution CT (HRCT) scans of the thorax on 26 August 1999 showed increased areas of consolidation and opacities in the left lower lobe (Figs. 6a and 6b). Repeat bronchoscopy revealed chronic inflammation on transbronchial lung biopsy. Bronchoalveolar lavage for acid-fast bacilli smears and cultures as well as aerobic cultures were negative. Relapse of nonspecific interstitial pneumonia was diagnosed and the dose of prednisolone was increased to 15 mg thrice a day with improvement in serial chest radiographs (Fig. 7) and lung function tests (Table I).

DISCUSSION

The classification of interstitial pneumonias[2,7,8] has undergone modifications in recent years, with emphasis on pathologic, therapeutic and prognostic differences. Recently, Katzenstein et al[2] described four histologic forms of idiopathic interstitial pneumonia with nonspecific interstitial pneumonia as a separate entity, distinct from usual interstitial pneumonia (UIP), desquamative interstitial pneumonia (DIP)/respiratory bronchiolitis interstitial lung disease (RBILD) and acute interstitial pneumonia (AIP).

In contrast to UIP, which is synonymous with cryptogenic fibrosing alveolitis or idiopathic pulmonary fibrosis, NSIP responds better to steroids and carries a better prognosis[2,9-11]. While relapses in UIP and BOOP have been reported[12,13], our patient is the first documented case of a relapse in NSIP with the tailing down of steroids after improvement with corticosteroid therapy.

Nonspecific interstitial pneumonia has been classified into cellular and fibrotic forms[1,6]. The inflammatory and fibrotic processes present in NSIP are temporally homogeneous histologically, unlike UIP which is characterised by variegated appearance and fibroplastic foci[2]. However, the differences between NSIP and

Table 1. Serial lung function tests.

	4 May 1999	26 August 1999	15 November 1999
FEV1 (l)	2.33 (87% predicted)	1.76 (66% predicted)	2.38 (90% predicted)
FVC (l)	2.55 (80% predicted)	2.03 (64% predicted)	2.59 (82% predicted)
FEC1/FVC (%)	91	87	92
TLC (l)	4.25 (86% predicted)	3.35 (68% predicted)	4.24 (86% predicted)
DLCO (mmol/min/kPa)	4.75 (54% predicted)	3.87 (44% predicted)	5.3 (60% predicted)
KCO (mmol/min/kPa/l)	1.33 (67% predicted)	1.36 (68.6% predicted)	1.41 (72% predicted)

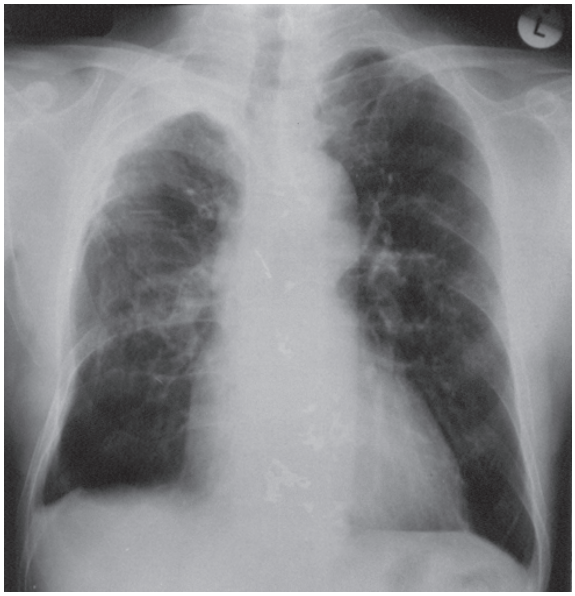

Fig. 4 Chest radiograph showing clearing of left infiltrates, six months after commencement of steroids.

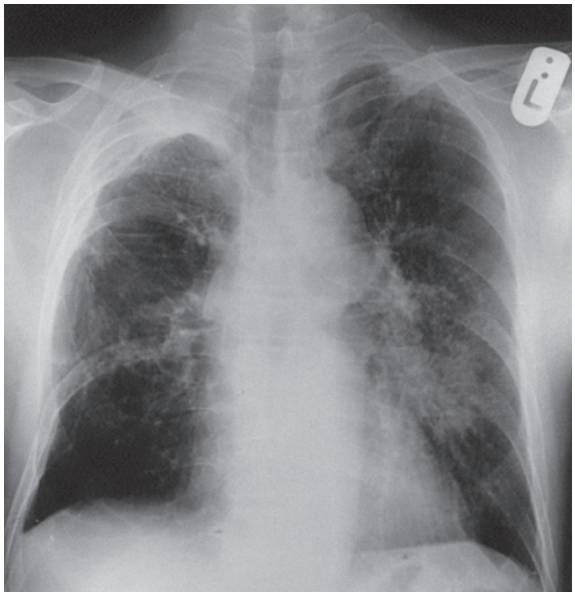

Fig. 5 Worsening of chest radiograph when steroids were tailed down to a lower dose. This demonstrates the appearance of ill defined patchy consolidation at the central portion of the left midzone.

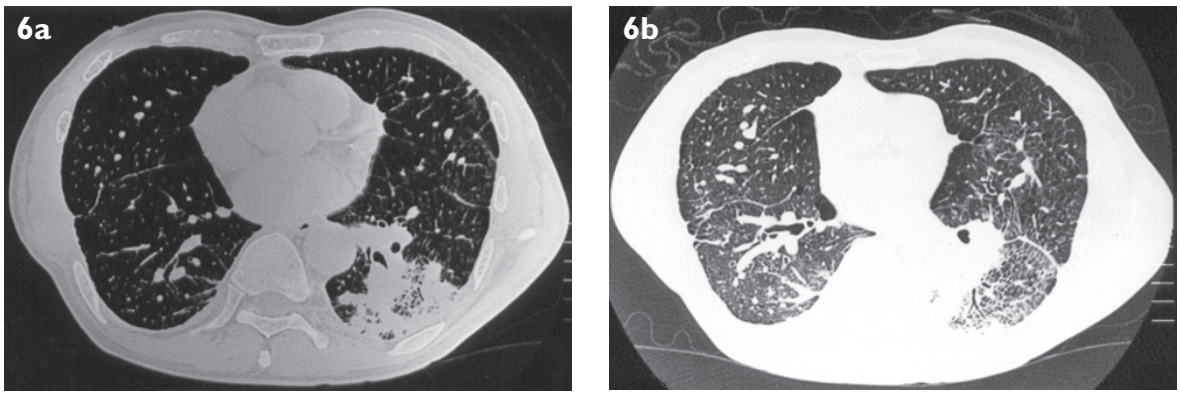

Fig. 6 High-resolution CT scan of thorax showing (a) patchy consolidation at the apical segment of the left lower lobe, predominantly subpleural in location. (b) Areas of ground-glass density associated with interlobular septal thickening is seen more superiorly.

BOOP were not readily apparent either on chest radiographs or on the basis of BAL fluid cell findings. Bilateral patchy infiltrates were major findings in NSIP and BOOP (24/31, 77.4% versus 13/16, 81.3%) as compared with UIP (26/64, 40.6%). Reticular and nodular shadows were found in 22.5% of patients with NSIP and in 59.4% of those with UIP whereas no difference was found between BOOP and NSIP cases[3]. BAL lymphocytosis was characteristic of both NSIP and BOOP[3].

Since NSIP was only described as recently as 1994 by Katzenstein et al, radiological descriptions are limited. The chest radiograph is abnormal in about 90% of patients with NSIP. Abnormalities are usually bilateral with a basal predominance. They may be consolidative and patchy, reticulonodular, or mixed. Other described features are reduced lung volume, pleural effusion (5%), hilar nodes (6%) and normality (6%)[14].

A number of HRCT features have been described in NSIP, which may occur in isolation or in

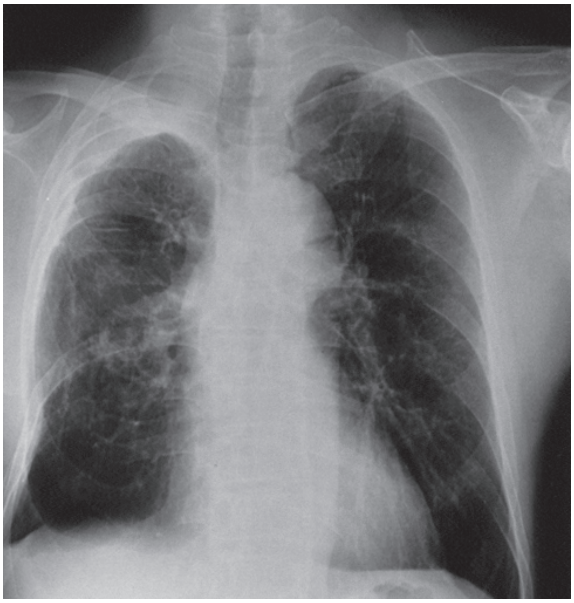

Fig. 7 Chest radiograph obtained four months after increase of the steroid dosage shows complete resolution of the left midzone consolidation with mild residual scarring.

combination. The most common finding is that of bilateral patchy areas of ground-glass attenuation, which may be symmetric or asymmetric, diffusely distributed in all zones or with a basal predominance. The subpleural region is most commonly affected. Consolidation is seen in 16-35% of patients almost always in combination with ground-glass opacity. It is bilateral, basal and subpleurally predominant. Honeycombing was present in 28-30% of patients. Dilated airways (38-71%) are seen in areas of consolidation and ground-glass opacity. Thickened bronchovascular bundles have been described in 65% of cases. In one series, irregular linear opacities were seen in 46% and were bilateral and symmetric in 87%[14].

Less common HRCT findings are poorly defined nodular opacities (centrilobular, subpleural and lower zone predominance), pleural effusion (4%) and enlarged hilar/mediastinal lymph nodes (5%)[14]. Hartman et al showed that NSIP has a variable appearance on HRCT with features showing overlap with that of other interstitial pneumonias and pulmonary diseases. Several patients with pathologically proven NSIP in this series had HRCT findings suggesting alternative diagnoses. Usual interstitial pneumonia, extrinsic allergic alveolitis and BOOP were the most common alternative diagnoses while diffuse alveolar damage, lymphocytic interstitial pneumonia, alveolar proteinosis, and respiratory bronchiolitis associated interstitial lung disease were less common differential diagnoses[15]. Although focal opacity mimicking neoplasm has been described in BOOP[16], that of our patient presenting as such with NSIP has not been reported before.

The diagnosis in our patient was secured from open lung biopsy. It has been emphasised that diagnosing the various entities of interstitial pneumonias requires a wedge of lung that can only be supplied by thoracoscopy or thoracotomy, and that small biopsy specimens such as percutaneous needle and transbronchial biopsies cannot provide sufficient tissue[2].

In conclusion, NSIP, like BOOP, may present as a focal opacity mimicking lung neoplasm. While it is steroid-responsive, relapses may occur with the tailing down of steroids. The value of open lung biopsy in securing diagnosis is evident.

ACKNOWLEDGEMENT

We wish to thank A/Prof Wang Yee Tang (Head, Department of Respiratory Medicine, Tan Tock Seng Hospital) for vetting the manuscript.

REFERENCES

1. Katzenstein AA, Fiorelli RF. Nonspecific interstitial pneumonia/ fibrosis: histologic patterns and clinical significance. Am J Surg Pathology 1994; 18:136-47.
2. Katzenstein AA, Myers JL. Idiopathic pulmonary fibrosis: clinical relevance of pathologic classification. Am J Respir Crit Care Med 1998; 157:1301-15.
3. Nagai S, Kitaichi M, Itoh H, Nishimura K, Izumi T, Colby TV. Idiopathic nonspecific interstitial pneumonia/fibrosis: comparison with idiopathic pulmonary fibrosis and BOOP. Eur Respir J 1998; 12:1010-9.
4. Kim TS, Lee KS, Chung MP, et al. Nonspecific interstitial pneumonia with fibrosis: high-resolution CT and pathologic findings. AJR 1998; 171:1645-50.
5. Park JS, Lee KS, Kim JS, et al. Nonspecific interstitial pneumonia with fibrosis: radiographic and CT findings in seven patients. Radiology 1995; 195:645-8.
6. Travis WD, Matsui K, Moss J, Ferrans VJ. Idiopathic nonspecific interstitial pneumonia: prognostic significance of cellular and fibrosing patterns: survival comparison with usual interstitial pneumonia and desquamative interstitial pneumonia. Am J Surg Pathol 2000; 24(1):19-33.
7. Liebow AA. Definition and classification of interstitial pneumonias in human pathology. Prog Respir Res 1975; 8:1-31.
8. Katzenstein AA, Myers JL. Nonspecific interstitial pneumonia and the other idiopathic interstitial pneumonias: classification and diagnostic criteria (Editorial). Am J Surg Pathol 2000; 24(1):1-3.
9. Ryu JH, Colby TV, Hartman TE. Idiopathic pulmonary fibrosis: current concepts. Mayo Clinic Proc 1998; 73:1085- 101.
10. Bjoraker JA, Ryu JH, Edwin MK, et al. Prognostic significance of histopathologic subsets in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 1998; 157:199-203.
11. Cottin V, Donsbeck AV, Revel D, Loire R, Cordier JF. Nonspecific interstitial pneumonia individualization of a clinicopathologic entity in a series of 12 patients. Am J Respir Crit Care Med 1998; 158:1286-93.
12. King TE Jr. BOOP: an important cause of migratory pulmonary infiltrates? (Editorial) Eur Resp J 1995; 8:193-5.
13. Masanor A, Satoru Y, Mitsunori S. Bronchiolitis Obliterans Organizing Pneumonia manifesting as multiple large nodules or masses. AJR 1998; 170:291-5.
14. Wilson AG, Hansell DM. Immunologic diseases of the lungs. In: Armstrong P, Wilson AG, Dee P, Hansell DM, editors. Imaging of diseases of the chest. Mosby 2000; 536-7.
15. Hartman TE, Swensen SJ, Hansell DM, Colby TV, Myers JL, Tazelaar HD, et al. Nonspecific interstitial pneumonia: variable appearance at high-resolution chest CT. Radiology 2000; 217:701-5.
16. Tazelaar HD. Pathology of chronic obstructive pulmonary disease, asthma, and bronchiolitis obliterans organising pneumonia. In: The ACCP Pulmonary Board Review, 1998-1999; 58.