IDIOPATHIC BRONCHIOLITIS OBLITERANS WITH ORGANIZING PNEUMONIA IN SINGAPORE - FIRST CASE REPORT

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ABSTRACT

Idiopathic bronchiolitis obliterans organizing pneumonia (BOOP) has become accepted as a distinct disease entity. We report a patient who presented with the classical clinical, radiological and pathologic featues of this uncommon condition. To our knowledge, this is first case to be reported in Singapore. This case also illustrates the difficulty of making a definitive diagnosis and emphasizes its therapeutic importance.

Keyword : Bronchiolitis Obliterans Organizing Pneumonia

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INTRODUCTION

Idiopathic bronchiolitis obliterans organizing pneumonia (BOOP) is a clinico-pathological entity characterized by restrictive ventilatory defect, pulmonary infiltrates on chest X-ray, intra-alveolar aggregation of proliferative granulating tissues on histological examination and a favourable prognosis with steroid therapy.

This condition was first defined by Davison et al[1] in 1983. Subsequently Epler et al[2] published their study of 50 patients. To our knowledge, there have been no reports of idiopathic BOOP in Singapore. We report a case of a patient who demonstrated classical clinical, radiological and histological findings and therapeutic response to corticosteroids.

CASE REPORT

A 70-year old, Chinese male fish-monger presented in July 1988 with a history of lower limb weakness, vague abdominal discomfort and exertional dyspnoea for 2 days. He was found to be in oliguric acute renal failure. Chest radiograph revealed cardiomegaly, upper lobe diversion and pulmonary venous congestion and patchy consolidation of the right base. The cause of the renal failure was not established despite extensive investigations. The patient reponded to diuretics, with complete radiological clearance of his chest and improvement of his renal function. When he was reviewed in early August 1988, he was well with normal serum urea and chest radiograph.

In September 1988, he was admitted for a cough productive of mucoid sputum, malaise and exertional dyspnoea. He was febrile (39.5°C). Examination of the chest revealed bilateral basal dullness with reduced breath sounds and widespread crepitations. There was 3 cm hepatomegaly. Laboratory investigations revealed normochromic, normocytic anaemia of 8.9 g/dl, a total white cell count of 14,340/mm^3 with 82.4% polymorphs, 5.6% lymphocytes, 6.1% monocytes and 4% eosinophils. Chest X-ray showed bilateral confluent consolidation with peripheral predominance (Fig. 1a). With the patient breathing air arterial blood gas revealed hypoxaemia (pO_2) 68.3 mmHg, pCO_2 32.5mmHg, Std HCO_3 24.7mmol/l, O_2 sat 94.7%). Alkaline phosphatase and gamma glutamyl transferase were elevated to 580 U/L (normal 20-95) and 414 U/L (normal 5-80) respectively. The provisional diagnosis was bronchopneumonia and treatment was initiated with parenteral broad spectrum antibiotics.

Over the next few days, the fever subsided but the patient had persistent tachypnoea and tachycardia. Serial chest X-ray showed rapidly progressive extension of the alveolar infiltrates in both lungs. Spirometry demonstrated a restrictive type ventilatory defect (Table I). A search for pyogenic bacteria, legionella, mycobacterium, respiratory viruses and fungal organisms was negative. Cytological examination of the sputum did not reveal any malignant cells or pneumocystis carinii. Antibodies to human immunodeficiency virus was negative.

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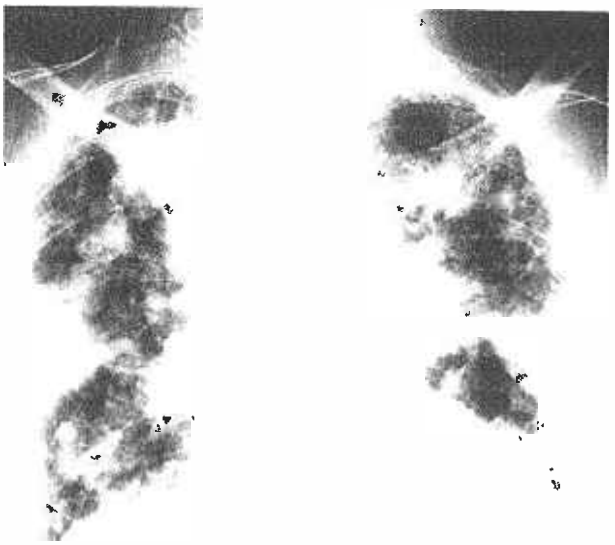
Table I
Serial measurements of spirometry, lung volumes and transfer factor before and after treatment with prednisolone

Parameter	Predicted	Pre-Treatment Oct 88	Post-Treatment Jan 89	Jul 89
FVC (L)	3.05	2.05	2.29	–
FEV_1 (L)	2.19	1.90	1.80	–
FEV_1/FVC	72%	93%	79%	–
VC (L)	2.87	2.06	2.36	2.44
TLC (L)	4.65	2.98	4.29	4.07
RV (L)	1.38	0.92	1.93	1.63
RV/TLC	35%	31%	45%	40%
DL_{co} (ml/min/mmHg)	14.0	11.5	16.4	16.7
DL_{co}/VA (L/min/mmHg)	3.68	3.29	4.10	4.29
Krogh's K (L/min)	3.16	2.84	3.54	3.71

Fig 1(a)
Chest radiograph of patient in September 1988 at presentation



His clinical condition and radiological findings continued to deteriorate. In the absence of a definitive diagnosis, an open lung biopsy through a left thoracotomy was performed 12 days after admission. At operation, diffuse induration interspersed with islands of normal lung tissue was noted. There was moderate amount of fibrinous, straw coloured pleural fluid at the costophrenic angle.

Histologic examination of the lung tissue revealed polypoidal masses of granulation tissue in the lumen of small terminal bronchioles and airways, composed predominantly of mononuclear cells, fibroblasts and smaller number of neutrophils (Fig 2). The alveolar walls were thickened by mild fibrosis, and cellular infiltrates, mainly lymphocytes and some plasma cells. There were focal areas of fibroblastic cellular proliferation, and fatty alveolar macrophages (Fig 3). In some parts of the lung, the cellular infiltrates filled some alveoli to form large nodules composed of loose connective tissue. All the

Fig 1(b)
5 days after commencement of steroid therapy

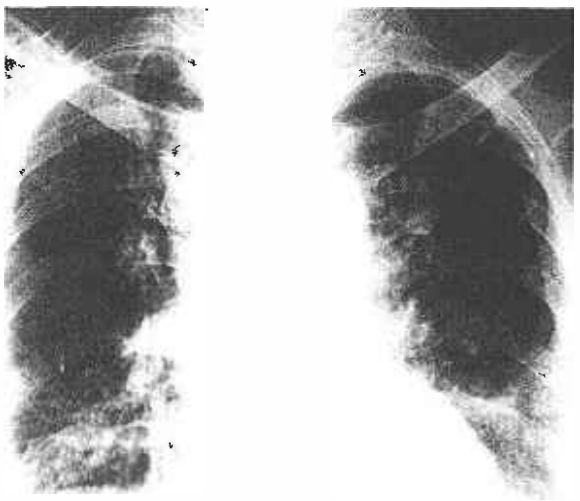
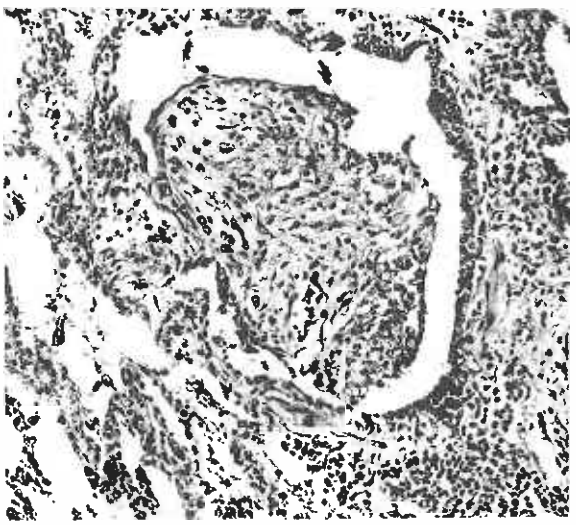


Fig 2
Lung biopsy: The bronchiole shows partial obliteration of the lumen by polypoidal granulation tissue composed predominantly of mononuclear cells. There is peribronchial inflammation. (Haematoxylin & Eosin x 125)



alveolar walls showed mild to moderate thickening by cellular infiltrates and collagenous tissue, but the fibrosis was patchy, with preservation of the background architecture. Special stains showed no organisms. No foci of eosinphils were seen. The picture was that of intraluminal organizing pneumonia.

At this point, the diagnosis of bronchiolitis obliterans with organizing pneumonia was made and prednisolone 30 mg daily was added to the treatment. He responded dramatically with clinical and radiological resolution within a week (Fig 1b). On subsequent reviews in the outpatient clinic, the patient remained well. Repeat tests of spirometry and transfer factor and serum liver enzymes were normal (Table I). Chest X-ray was normal except for minimal opacity at the thoracotomy site (Fig 5). To

Fig 3
Lung biopsy: The alveolar walls show infiltration by mononuclear cells and areas of fibroblastic cellular proliferation. Some of the alveolar lumen contain fatty macrophages.
(Haematoxylin & Eosin x 200)

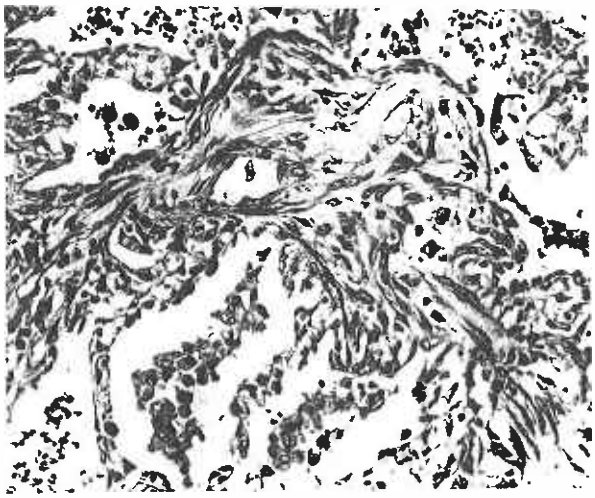
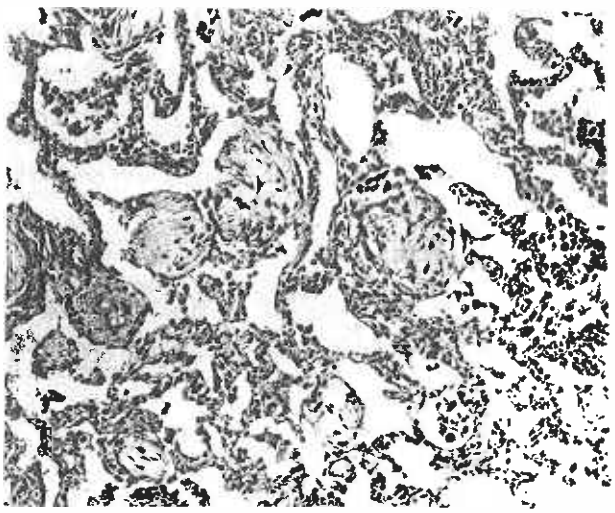


Fig 4
Lung biopsy: Patchy areas showing alveoli filled by nodules of loose connective tissue.
(Haematoxylin & Eosin x 100)

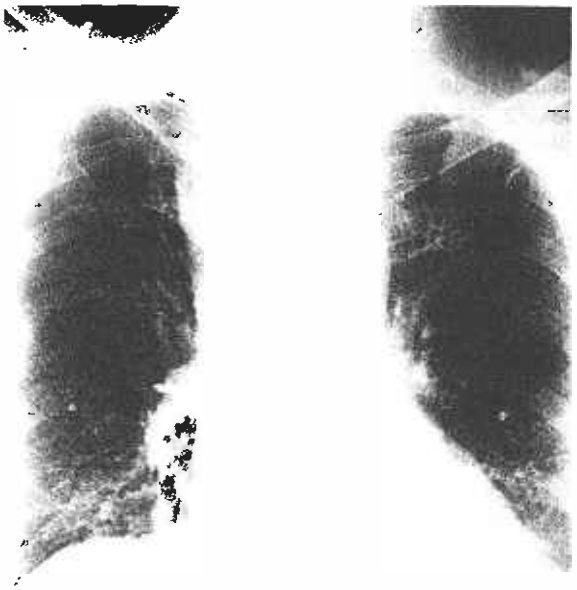


date, this clinical and radiological status was maintained with prednisolone 5 mg daily.

DISCUSSION

Our patient presented with a short history of severe dyspnoea, cough and malaise, bilateral changing radiographic shadowing, restrictive ventilatory defect, raised ESR and histologic evidence of organizing exudates within small airways and alveoli and a dramatic response to moderate doses of prednisolone. This picture

Fig 5
Chest radiograph after treatment with steroid for one month.



is typical of idiopathic bronchiolitis obliterans organizing pneumonia (BOOP).

The concept of organizing pneumonia is not new. In 1922, Floyd[3] first described characteristic findings of inflammation of distal lung structures (alveoli, alveolar ducts and bronchioles) which failed to resolve completely and underwent organization and fibrosis as a chronic sequela to unresolved bacterial lobar and tuberculous pneumonia. Since then, this type of organization had been reported to occur diffusely in the lungs of patients suffering from diverse disorders such as toxic fume inhalation[4], connective tissue disease[5-7], bone marrow transplantation[8], apparent drug reaction[9] and paraquat toxicity[10] and focally in interstitial organizing disorders such as hypersensitivity pneumonitis, chronic eosinophilic pneumonia[11] and usual interstitial pneumonia (UIP)[12].

In 1983, Davison et al[1] first defined a clinicopathological entity under the name of crytogenic organizing pneumonia. Epler et al later published a similar study of a large series of patients wih the same entity and coined the term bronchiolitis obliterans organizing pneumonia or BOOP by which this condition is widely known today. The idiopathic form of BOOP has now been widely recognized as a separate clinicopathologic entity.

Bronchiolitis obliterans organizing pneumonia is most commonly confused with usual interstitial pneumonia (UIP) or idiopathic pulmonary fibrosis and pure bronchiolitis obliterans (bronchiolitis fibrosa obliterans).

Several studies[2, 13, 14] have shown that BOOP may be distinguished from UIP. The predominant histological findings of UIP is diffuse fibrosis while that in BOOP is intraluminal granulation tissue plugs with general preservation of background architecture. The radiologic manifestations of idiopathic BOOP are characterized by predominantly peripheral alveolar opacities without significant lung volume loss while in UIP the radiograph shows bilaterally opacities with volume loss[13].

Idiopathic BOOP differs from bronchiolitis obliterans (bronchiolitis fibrosis obliterans). Idiopathic BOOP is characterized histologically by distal lung structure consolidation rather than proximal small airway obstruction. Functionally this is reflected in a restrictive ventilatory defect rather than an obstructive ventilatory defect of pure bronchiolitis fibrosa obliterans.

Several clinical reports[13-15] have fully justified the value of a definitive diagnosis of idiopathic BOOP. In our patient, despite extensive investigations, no obvious cause was found to account for the radiological appearance of diffuse lateralising pneumonic consolidation. The clinical relevance of the transient episode of acute renal failure without persistent renal dysfunction remained unclear but could conceivably be a predisposing factor for lung injury[16]. An open lung biopsy was thought to be justified. This method is diagnostically preferred to that of a transbronchial procedure although a recent report[15] suggested that transbronchial biopsy may be adequate to establish a working diagnosis. The subsequent dramatic and sustained response of our patient to steroid treatment further fully supported the effort made at a specific diagnosis.

This case illustrates the classical clinical, radiologic and pathologic features of idiopathic BOOP and underscores the therapeutic and prognostic value in identifying BOOP as a separate entity in patients with pulmonary fibrosis.

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