Rapidly-progressive bronchiolitis obliterans organising pneumonia

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ABSTRACT

Bronchiolitis obliterans organising pneumonia is a clinicopathological syndrome characterised by indolent course of flu-like illness followed by cough, dyspnoea and fever, and responds well to steroid treatment. We describe a 76-year-old woman who presented with a short three-day history and progressed rapidly to respiratory failure. She was successfully treated with high-dose steroids.

Keywords: bronchiolitis obliterans organising pneumonia, corticosteroids, respiratory failure

Singapore Med J 2004 Vol 45(6):283-285

INTRODUCTION

Bronchiolitis obliterans with organising pneumonia (BOOP) is a distinct clinicopathological entity that was described by Epler et al in 1985[1]. Clinically, BOOP presents as a "flu-like" prodromal phase followed by progressive dyspnoea, cough, fever, weight loss, and crackles on chest auscultation. Radiographically, bilateral patchy alveolar infiltrates are present. Computed tomography (CT) shows bilateral areas of consolidation and ground-glass haziness[1,2]. BOOP has been causally related to collagen vascular diseases, various infections, toxic inhalations and certain drugs[2]. However, the most common cause is idiopathic BOOP[2], commonly known as cryptogenic organising pneumonia.

BOOP characteristically responds very well to steroids, with near-complete resolution in the majority of cases. A more aggressive variant of BOOP, termed rapidly-progressive BOOP, has been described recently. This variant follows a fulminant course, leading to respiratory failure, and is associated with high mortality[3]. We describe a case of rapidly-progressive BOOP that was managed aggressively with early lung biopsy to reach a diagnosis and successfully treated with pulse-dose steroids.

CASE REPORT

A 76-year-old woman presented to the Emergency Department with a three-day history of dyspnoea accompanied by productive cough and fever. She complained of severe right-sided pleuritic chest pain. She denied any arthralgia or rashes. She was a non-smoker with no other co-morbid factor. On physical examination, she was tachypnoeic and tachycardic, with a temperature of 39 degrees Celsius. Chest auscultation revealed diffuse bilateral crackles and bronchial breath sounds over the right lower chest. The remainder of the clinical examination was unremarkable.

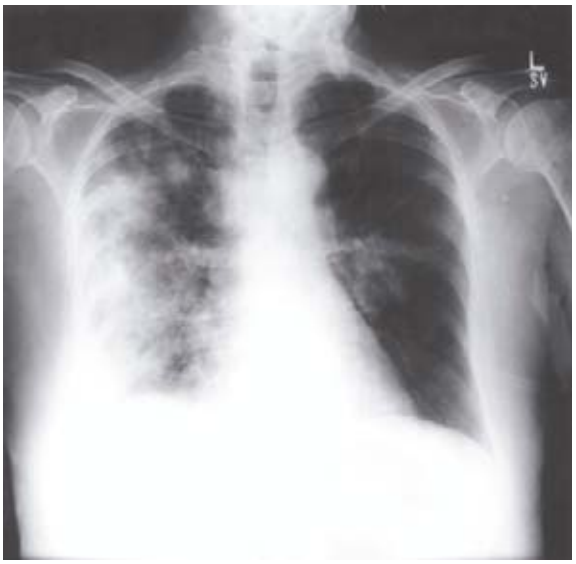

Fig. 1 Chest radiograph shows bilateral patchy alveolar opacities involving the middle and lower zones of the right lung and left perihilar area.

Diagnostic laboratory tests revealed an elevated leucocyte count of 16.6 x 10^3/mL with left-sided shift. Her autoimmune workup, including ANA, RA factor and cANCA, were all negative. Arterial blood gas values on room air revealed a pH of 7.472, $PaCO_2$ of 31.7mmHg, and PaO_2 of 57.7mmHg, with a SaO2 of 91.6%. Chest radiograph showed bilateral patchy alveolar opacities involving the middle and lower zones of the right lung and left perihilar area. There was no evidence of a pleural effusion (Fig. 1).

A diagnosis of community-acquired pneumonia was made, and antibiotic therapy was initiated with intravenous ceftriaxone and clarithromycin.

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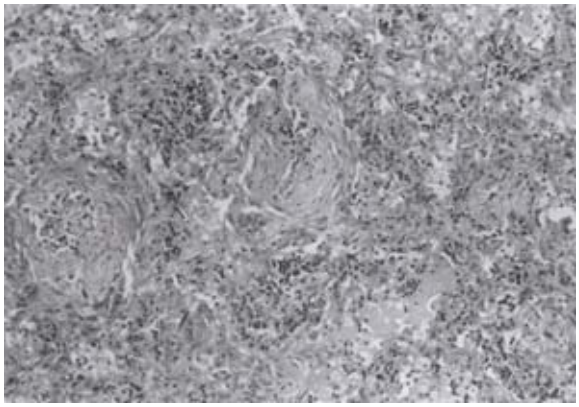

Fig. 2 Photomicrograph of lung tissue shows cellular mesenchymal proliferation filling the air spaces. Note the presence of spindle and stellate cells embedded in a pale staining matrix along with moderate degree of interstitial inflammation. Adjacent areas exhibit preserved alveolar spaces filled with acellular material and foam cells. (Haematoxylin & eosin, X40 magnification).

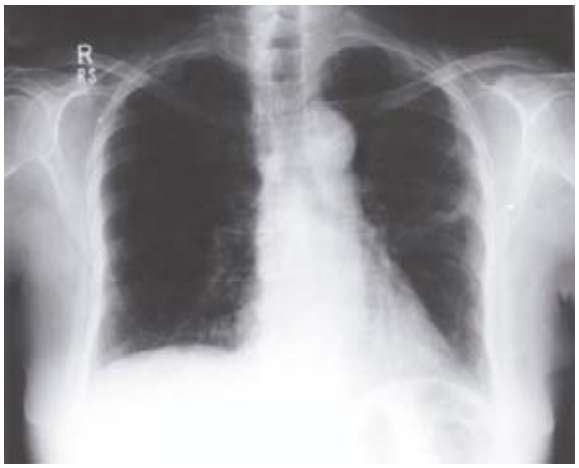

Fig. 3 Chest radiograph taken three months after discharge shows clearing of the bilateral opacities. Mild residual bilateral lower lobe interstitial infiltrates are visible.

Supplemental oxygen was given via a nasal cannula. On the third day of antibiotic treatment, the patient's condition deteriorated, requiring intubation and mechanical ventilation. Bronchoscopy with broncho-alveolar lavage was performed, and antibiotics were changed to intravenous piperacillin-tazobactam, clarithromycin and ciprofloxacin. The bronchoscopic specimens were negative on microbiological and cytological examination. The patient's condition continued to deteriorate, requiring higher oxygen concentrations and positive end-expiratory pressure (PEEP) to maintain oxygenation.

An open-lung biopsy was performed on the 9th day of treatment. Histopathological examination revealed preserved alveolar architecture, with obliteration of the alveolar spaces by plugs of connective tissue distributed within the terminal bronchioles, alveolar ducts and spaces. In scattered areas, foci of fibroblastic proliferation with mononuclear cell infiltrate and occasional foamy histiocytes were seen (Fig. 2). These findings were consistent with BOOP. No evidence of infection was found on tissue stains and cultures. Methylprednisolone, 250mg intravenously six hourly, was started on the 10th hospital day, and subsequently tapered after five days. The patient's condition started to improve and she was gradually weaned off mechanical ventilation on day 26. Oxygen was weaned and the patient was discharged in a stable condition on a regimen of a daily oral dose of prednisone (60mg).

Her three-month follow-up spirometry showed moderate restrictive impairment. At 12 months, her spirometry revealed significant improvement in forced vital capacity from 40% to 69% predicted, and forced expiratory volume in one second from 46% to 69% predicted. A follow-up chest radiograph three months after discharge showed clearing of the bilateral opacities with mild residual bilateral lower lobe interstitial infiltrates (Fig. 3). At the present time, 14 months after her initial presentation, she does not require supplemental oxygen and has been weaned off oral prednisone. She is now leading an independent life.

DISCUSSION

Idiopathic BOOP, which is synonymous with cryptogenic organising pneumonia, is a subacute disease with mild symptoms that may be progressive, leading to dyspnoea, cough and weight loss. It has a good prognosis and responds well to steroids[5]. Recently, a rapidly-progressive variant has been identified that responds poorly to standard steroid therapy and has a high mortality[3,4]. Cohen et al[3] reported a series of 10 patients with 70% mortality. Nizami et al[4] described five cases of progressive BOOP with 40% mortality, however, their series included two patients with subacute presentation.

In the series by Cohen et al[3], four out of 10 patients had concomitant connective tissue disease, raising the association of these two diseases. However, in the series by Nizami et al[4], no such connection could be verified. Our patient also did not have any evidence of an underlying connective tissue disease. In the previous two series, a very strong correlation to cigarette smoking was found. Our patient had been a lifetime non-smoker, with no history of active or passive exposure to cigarette smoke or tobacco products. Clinical features of dyspnoea, cough and fever associated with leukocytosis are consistent with the usual presentation of BOOP. However, the extremely acute presentation and rapid deterioration to respiratory failure is uncommon. The intense pleuritic chest pain has been reported in only one other patient[3]. The chest radiological presentation was consistent with the usual findings of bilateral ill-defined alveolar infiltrates with consolidation in BOOP.

The rapidity with which our patient progressed to respiratory failure raised the concern of an acute interstitial pneumonitis (Hamman-Rich syndrome). An early video-assisted thoracoscopic (VATS) biopsy helped in reaching the correct diagnosis. Histopathologically, the rapidly-progressive variant shows evidence of interstitial pneumonitis and alveolar septal inflammation, along with the usual findings of granulation tissue plugs within the lumen of small airways and their extension into alveolar ducts and alveoli, associated with BOOP. It has been suggested that BOOP can be a precursor of alveolar septal inflammation and honeycomb lung, and thus represents an early phase of the temporal spectrum of interstitial lung disease. It may lead to the development of end-stage fibrosis and honeycombing, if the process stays unchecked[3].

Contrary to cryptogenic organising pneumonia, the rapidly-proliferating variant has been reported to respond poorly to the usual doses of steroids (1mg/kg of prednisone), and pulse doses of steroid has been suggested[3]. Our patient did respond to pulse dose steroid therapy (methylprednisone 250mg intravenously every six hours for five days) followed by tapering of the dose, with a gradual resolution of the disease process. However, she had significant residual impairment in respiratory function which improved slowly. These findings are consistent with those of the other reported cases[2-4].

In conclusion, the rapidly-progressive variant of BOOP has a fulminant and rapid course, with considerable morbidity and mortality. Early diagnosis by lung biopsy (open lung or VATS) aids in a quick diagnosis. As described in our case, early institution of high-dose steroid therapy should be considered. Patients will likely have some residual impairment in respiratory function, which should improve over time.

ACKNOWLEDGEMENT

We thank Dr Suhail Muzaffar, Assistant Professor in Pathology, for providing support in reaching the diagnosis and subsequently providing the photographs for this article.

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