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Influenza B/Streptococcal co-infection complicated by organizing pneumonia

Wang C. Kwok[1], Sonia H. Y. Lam[2], Maria P. Wong[3], Mary S. M. Ip[1] & David C. L. Lam[1]

[1]Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China.
[2]Department of Diagnostic Radiology, Queen Mary Hospital, Hong Kong SAR, China.
[3]Department of Pathology, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China.

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Correspondence
David Chi Leung Lam, Department of Medicine, HKU, Queen Mary Hospital, 102 Pokfulam Road, Pokfulam, Hong Kong SAR, China. E-mail: dcllam@hku.hk

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Abstract

Organizing pneumonia is a rare complication of influenza infection that has substantial morbidity. We report the first case of organizing pneumonia associated with influenza B and *Streptococcus pneumoniae* coinfection that had significant improvement with corticosteroid treatment. The clinical and radiological features of organizing pneumonia associated with this coinfection are similar to those after influenza A infection. Timely use of systemic glucocorticosteroids would be of benefit in promoting resolution for influenza-associated organizing pneumonia.

Introduction

We describe in this report a patient with influenza B and streptococcal infection followed by development of organizing pneumonia. From our observation and the literature, systemic steroids may be beneficial in treating post-influenza organizing pneumonia. Further research on this disease particularly focusing on the prognostic factors, optimal regime of corticosteroid, and the long-term outcome are important.

Case Report

A 45-year-old female non-smoker with good past health was admitted to hospital with fever, dyspnoea, and productive cough. She had not received influenza or pneumococcal vaccinations in the past. Nasopharyngeal swab was positive for influenza B by antigen detection. Urine pneumococcal antigen was positive, and sputum bacterial culture yielded *Streptococcus pneumoniae*. Chest X-ray (CXR) showed diffuse lung infiltrates. She deteriorated rapidly with respiratory failure, requiring mechanical ventilation. Antimicrobial treatment included piperacillin with tazobactam, clarithromycin, and oseltamivir. There was initial improvement, but she deteriorated again five days later, with worsening hypoxemia. Computer tomography of thorax with contrast revealed multiple pulmonary emboli, and enoxaparin was started. Extensive ground-glass opacities with interstitial thickening and multiple lung cysts bilaterally were also found. Bronchoalveolar lavage did not show any specific micro-organisms. She continued to deteriorate, and extracorporeal membrane oxygenation (ECMO) was started. She gradually improved and was finally weaned off from ventilator support after eight days and ECMO after 12 days. However, she had persistent dyspnea, and CXR showed persistent lung infiltrates. High-resolution computed tomography (HRCT) of thorax on day 28 revealed extensive ground-glass opacities and multiple lung cysts bilaterally (Fig. 1A). Bronchoscopy with transbronchial lung biopsy showed patchy paraseptal fibroblastic proliferation with edematous stroma compatible with organizing pneumonia (Fig. 2). Lung function test showed restrictive pattern with reduced diffusing capacity for carbon monoxide (Table 1). Prednisolone 30 mg daily was started on day 44. She showed significant improvement in the level of dyspnoea and exercise tolerance, and a two-month tapering steroid regime was given. Reassessment HRCT of thorax three months after initiation of steroid showed that the ground-glass opacities and lung cysts almost completely resolved with some residual fibrosis (Fig. 1B). Lung

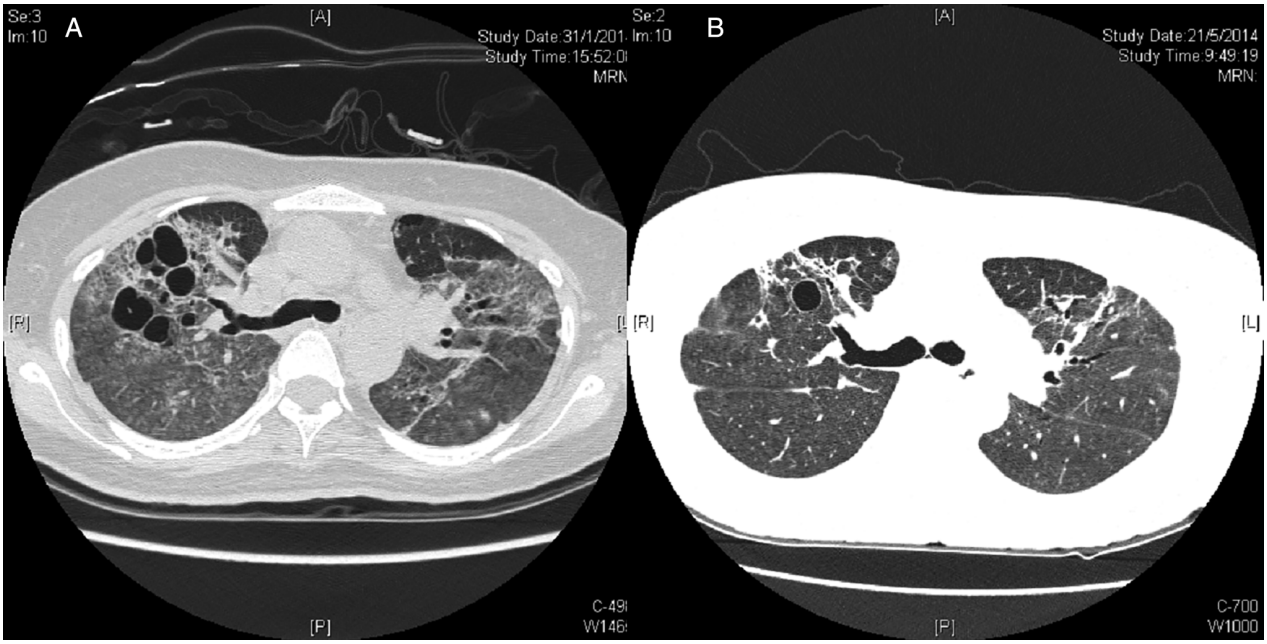

Figure 1. (A) High-resolution computed tomography (HRCT) of thorax on day 28 revealed that both lungs were filled with ground-glass opacities with relative apical sparing and multiple lung cysts. (B) HRCT of thorax done three months later, after two months of steroid treatment, showed that the previous ground-glass opacities and lung cysts have almost completely resolved, but there was residual fibrosis with traction bronchiectasis at apices and anterior segments of bilateral upper lobes, medial segment of the right middle and lingular lobes.

function test about one year later showed that forced vital capacity had recovered substantially (Table 1). She was essentially asymptomatic despite some degree of lung function impairment.

Discussion

To date, six cases of post-influenza organizing pneumonia have been reported in the literature; all had influenza A infection, and most were infected by H1N1 strain [1–3]. The usual presenting features included refractory respiratory failure during the infective episodes and incomplete recovery after antiviral therapy. The reported cases have variable degrees of respiratory failure and received corticosteroid treatment [1–3].

To our knowledge, this patient is the first reported case of organizing pneumonia associated with influenza B and streptococcal co-infection. This co-infection was reported to cause severe infection in healthy young adults [4]. Six cases of severe infection have been reported that resulted in multi-organ failure, with three deaths. The patient also had a stormy course that was complicated by organizing pneumonia. The reason that this complication has not been reported is likely related to the rarity of this co-infection. The clinical and radiological features of organizing

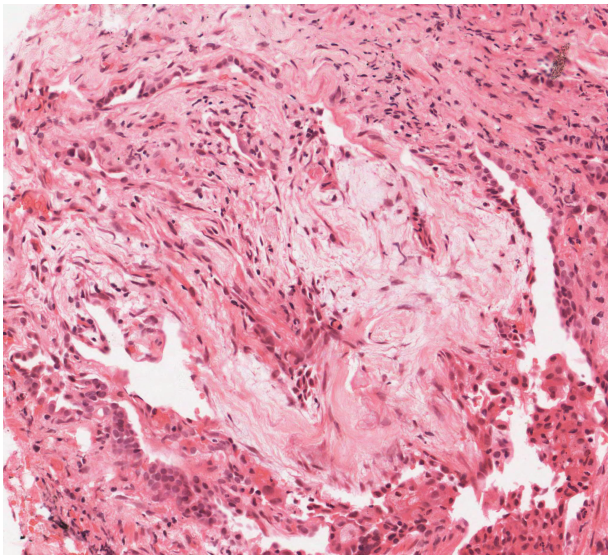

Figure 2. The transbronchial biopsy section (haematoxylin and eosin stain) showed a piece of normal bronchial mucosa and a piece of peribronchial parenchyma. The latter showed patchy paraseptal fibroblastic proliferation with edematous stroma. Neutrophilic consolidation or granulomas were not observed, and interstitial lymphocytes were scanty. While there were no characteristic intra-alveolar fibroblastic tufts, the features suggested reparative changes, compatible with organizing pneumonia.

Table 1. Lung function tests at diagnosis of organizing pneumonia and after steroid treatment.

Age	45
Gender	Female
Underlying infection	Influenza B/*Steptococcal pneumonia*
Smoking status	Non-smoker
Lung function at diagnosis of post-flu organizing pneumonia	
FEV_1, L	0.86 (39% predicted)
FVC, L	1.03 (39% predicted)
FEV_1/FVC, %	84
DLCO	27% predicted
Lung function after recovery	
Time after diagnosis of OP	13 months
FEV_1, L	1.69 (78% predicted)
FVC, L	1.97 (76% predicted)
FEV_1/FVC, %	86
DLCO	56% predicted
KCO	90% predicted
Time from onset of infection to steroid treatment	44 days
Duration of steroid treatment	2 months
Long-term sequelae	Asymptomatic; HRCT showed scattered areas of fibrosis

DLCO, diffusing capacity for carbon monoxide; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; HRCT, high-resolution computed tomography; KCO, diffusing capacity for carbon monoxide adjust for alveolar volume.

pneumonia after influenza B and Streptococcus coinfection are similar to that after influenza A infection.

This patient has another interesting radiological feature, the presence of multiple lung cysts that completely resolved after steroid treatment. These changes probably reflected resolution of obstructive bronchiolitis, which led to the bullous appearance. Corticosteroid treatment promptly improved the symptoms, and the patient was subsequently asymptomatic despite some residual radiological and lung function impairment.

The patient in our report was young and healthy and had a complicated course of influenza infection. In the latest World Health Organization (WHO) recommendations, young and healthy subjects are not the priority groups for seasonal influenza vaccination [5]. Whether it is beneficial and cost-effective to extend the indications of influenza vaccination to them are controversial, but the potential benefits of being vaccinated, especially during epidemics, may outweigh the risks and costs. Our patient demonstrated the potential severity of influenza B and pneumococcal co-infection. This would give support to the current WHO recommendations from 2013 onwards, that is, whenever it is possible to consider quadrivalent vaccines that cover two strains of influenza B viruses, compared to the past WHO recommendations before 2013 that suggested the use of trivalent vaccines that contain one influenza B virus only [5].

The evolution of acute viral pneumonia into post-viral organizing pneumonia is probably indistinct in the majority of patients. In general, persistence or relapse of compatible radiological infiltrates after initial clearing of viral pneumonic phase, together with clinical deterioration, should prompt the possibility of the development of organizing pneumonia. Other causes of hypoxemia have to be considered, such as pulmonary embolism, as found in our patient. Secondary or persistent infections should be excluded before use of corticosteroids. We have another patient with organizing pneumonia complicating influenza A infection, who also had severe infection and required ECMO support. That patient had steroids started later, 84 days after the initial infection. Despite improvement with corticosteroids, she suffered from extensive lung fibrosis and residual dyspnoea. The disease course in this patient suggested that timely diagnosis of organizing pneumonia and commencement of systemic glucocorticosteroid could effectively control the post-viral inflammatory process and may prevent irreversible fibrosis. In conclusion, we propose that all patients with clinical suspicion of influenza-associated organizing pneumonia should have imaging and histological proof as early as possible. For those with persistent or progressive clinical and/or radiological features, timely commencement of corticosteroid should be considered to prevent long-term complications.

Disclosure Statements

No conflict of interest declared.
Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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