Severe respiratory failure associated with influenza B virus infection

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Abstract
A 72-year-old man who had been diagnosed with type B influenza infection and high fever 4 days previously was admitted to our hospital. He presented with severe respiratory insufficiency; chest computed tomography (CT) revealed extensive ground-glass opacity in lung fields on both sides. Although peramivir and antibiotics were administered, reticular shadows on chest CT worsened and respiratory insufficiency deteriorated. The patient fulfilled the criteria for severe acute respiratory distress syndrome. Despite multimodal therapy, including non-invasive positive pressure ventilation, polymyxin B-immobilized fiber column hemoperfusion, and methylprednisolone infusion, his general condition gradually deteriorated. He died of respiratory failure on day 129. Pathology findings of the lungs during autopsy showed diffuse alveolar damage. To our knowledge, this is the first report of severe respiratory failure after type B influenza infection. Clinicians should be aware of the potential for fatal respiratory failure in cases of type B as well as type A influenza infections.

Introduction
Influenza virus infection sometimes causes critical illness that may lead to severe outcomes including acute respiratory distress syndrome (ARDS), sepsis, and death [1–3]; however, most cases of severe respiratory failure are associated with influenza A rather than influenza B virus infections. We report here a case of severe ARDS associated with influenza B virus infection.

Case Report
A 72-year-old man without relevant medical history presented with high-grade fever and was referred to a nearby clinic. His wife and two daughters had been diagnosed with influenza B virus infection several days prior. A rapid test using a nasal swab specimen was positive for influenza B antigens; he was therefore diagnosed with an influenza B virus infection. Oseltamivir was administered. Four days later, the patient returned to the clinic because of persistent fever and dyspnea at rest and was admitted to our hospital. At the time of hospitalization, his temperature was 38.7°C, blood pressure was 117/80 mmHg, heart rate was 76 beats/min, and oxygen saturation level was 88% on room air. Fine crackles were audible in lung fields on both sides. Laboratory findings were as follows: white blood cell count 7400/mm³, C-reactive protein 18.1 mg/dL, aspartate transaminase 91 IU/L, L-lactate dehydrogenase 362 IU/L, creatine kinase 793 IU/L, and Krebs von den Lungen-6 1772 U/mL. Arterial blood gas analysis demonstrated hypoxemia (PaO₂ = 72 Torr [partial pressure of oxygen], under the 5 L/min of nasal oxygen inhalation). Chest radiography showed ground-glass opacity in lung fields on both sides and chest computed tomography (CT) showed diffuse ground-glass opacity in lung fields on both sides (Fig. 1). Gram staining, Ziehl-Neelsen staining, periodic acid-Schiff
stain of sputum samples and sputum culture did not show any evidence of bacterial or fungal infection. There was no evidence of bacterial infection in blood cultures. On admission, the patient received high-flow nasal oxygen support and was treated with intravenous peramivir (600 mg/day) and antibiotics (initially piperacillin/tazobactam 13.5 g/day and levofloxacin 500 mg/day). However, the reticular shadow on chest CT worsened and the PaO2/FiO2 (ratio of arterial oxygen partial pressure to fractional inspired oxygen) ratio deteriorated to 83 on day 3. He was diagnosed with severe ARDS associated with influenza B virus infection. We proposed mechanical ventilation and high levels of positive end-expiratory pressure as a treatment of ARDS, however, the patient and the family refused to do intubation and we continued high-flow nasal oxygen support. Polymyxin B-immobilized fiber column hemoperfusion was performed on day 3 to eliminate the effect of inflammatory mediators and intravenous methylprednisolone 60 mg/day (1 mg/kg) was administered on day 6. However, the patient’s respiratory status did not improve and the reticular infiltrates on chest CT worsened. Despite noninvasive positive pressure ventilation support and the addition of immunosuppressant therapy (intravenous cyclophosphamide 500 mg biweekly), the patient’s condition gradually worsened and he died on day 129 after admission. An autopsy was performed with permission from the family. Pathological findings of lung specimens showed diffuse alveolar damage (DAD) with prominent hyaline membranes (Fig. 2). No specific abnormality was observed in other organs, including the heart, liver, and kidneys.

Discussion

The risk of severe outcomes, including respiratory failure, ARDS, and death, associated with influenza A virus infection are widely recognized [1–3], however, few studies have reported severe respiratory failure associated with influenza B virus infection. To our knowledge, this is the first case report of severe respiratory failure associated with influenza B virus infection with lung pathological findings of DAD.

Critical illnesses have recently been reported in patients with influenza B virus infections. Gutiérrez-Pizarra et al. compared the features of 50 hospitalized cases of influenza B and 80 cases of influenza A(H1N1)pdm09 infections with respiratory symptoms [4]. They reported that the proportion of patients with pneumonia and the rate of admission to the intensive care unit did not differ between cases of influenza B (10%) and influenza A (16.3%) infection. Notably, the mortality rates were almost identical between patients with influenza B (10%) and influenza A (16.3%) infection. In addition, Paddock et al. examined the pathological findings of the lung in autopsy cases of patients who died of influenza B virus infection and demonstrated that DAD patterns were found in 17.8% of cases [5]. These reports suggest that, similar with influenza A, influenza B infection can cause critical illness and respiratory failure. The present case also emphasizes the need to be aware of the potential for fatal respiratory failure in cases of influenza B virus infection.

In conclusion, we have described a case of fatal respiratory failure associated with influenza B virus infection. Influenza B virus infection is usually sporadic compared with the pandemic events common to influenza A infections, which may explain the relatively small number of reports on influenza B virus infection. Although influenza B virus infections are less frequent than influenza A infections, clinicians should pay careful attention to fatal respiratory failure in cases of influenza B virus infection.
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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