Severe acute asthma caused by *Chlamydophila pneumoniae* infection

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Abstract
Asthma exacerbation is associated with respiratory infections, including those by viruses and atypical bacteria. We herein report a case of severe acute asthma in an adult caused by *Chlamydophila pneumoniae* (*C. pneumoniae*) infection. A 39-year-old woman without a history of asthma reported to the emergency department with progressive worsening of cough, shortness of breath, and wheezing with low oxygen saturation. A computed tomography (CT) scan revealed patchy ground-glass opacity and bronchial wall thickening. She was treated with systemic corticosteroids, inhaled short-acting β2 agonists, aminophylline, doripenem, and levofloxacin. Through successful treatment in the intensive care unit (ICU), her condition and the chest X-ray and CT findings improved. *Chlamydophila pneumoniae* infection was confirmed by elevated paired serum *C. pneumoniae*-specific IgA antibodies. *Chlamydophila pneumoniae* infection is an important cause of severe acute asthma. On CT, findings typical of *C. pneumoniae* pneumonia were noted.

Introduction
Asthma exacerbation is a significant issue in the management of bronchial asthma for both adults and children. Exacerbation has been associated with respiratory infections, including those from viruses and atypical bacteria. A previous review suggested that *Mycoplasma pneumoniae* (*M. pneumoniae*) and *Chlamydophila pneumoniae* (*C. pneumoniae*), in contrast to viruses, may be involved more with asthma persistence rather than exacerbation [1]. Exacerbations may occur in patients with a pre-existing diagnosis of asthma or, occasionally, as the first presentation of asthma. We herein describe a case of severe acute asthma in an adult caused by *C. pneumoniae* infection; computed tomography (CT) findings showed patchy ground-glass opacity, which resolved with successful intensive care unit (ICU) treatment.

Case Report
The patient was a 39-year-old woman with seasonal allergic rhinitis but no history of asthma. She was a current smoker (19 pack years) and owned hamsters. Over the previous 2 months, she suffered from cough, especially at night. When she visited her family doctor due to complaints of coughing and wheezing, she was diagnosed as having atypical pneumonia and was administered azithromycin (2 g extended release suspension, orally, once). Two days later, her symptoms did not resolve and worsened with the development of dyspnoea; she was unable to speak at all. She was admitted to the emergency department of our hospital. A physical examination revealed a body temperature of 37.1°C, oxygen saturation of 75% (room air), and a respiratory rate of 44 breaths/min. The chest X-ray and CT scan showed right infiltrates and patchy ground-glass opacity with bronchial wall thickening, respectively (Fig. 1). Laboratory tests revealed a white blood cell count of 22,800/μL, serum C-reactive protein of 3.93 mg/dL, and total serum IgE of 110 IU/mL. Specific IgE was positive for Japanese cedar and Japanese cypress but negative for hamster epithelium. On admission to the ICU, she was diagnosed with severe acute asthma with atypical pneumonia. Subsequently, she was treated with systemic corticosteroids, inhaled short-acting β2 agonists, aminophylline, doripenem, and levofloxacin with oxygen...
therapy (mask, 15 L/min). The treatment was successful; her condition improved and she was discharged on the 14th day. Chest X-ray and CT findings improved after 4 weeks (Fig. 2). The titres for IgA- and IgG-type antibodies to *C. pneumoniae* were measured using a commercial ELISA kit (Hitazyme *C. pneumoniae* antibody-IgA and IgG kits, Hitachi Chemical Co Ltd, Tokyo, Japan) [2]. Acute *C. pneumoniae* infection was confirmed by an elevated paired serum *C. pneumoniae*-specific IgA antibody index (enzyme immunoassay): IgA, 1.1–2.7 (positive, index rise ≥ 1.00) and IgG, 1.7–1.4 (positive, index rise ≥ 1.35) [2]. There was no change in *M. pneumoniae*-specific antibody. No other microorganism was detected. There was no epidemic of influenza, respiratory syncytial virus, or human metapneumovirus. At discharge, pulmonary function tests revealed a forced vital capacity (FVC) of 2.94 L (90.7% of predicted), a forced expiratory volume in 1 second (FEV₁) of 2.77 L (100.7% of predicted), and FEV₁/FVC of 94.2%. At long-term follow-up, the diurnal variability of peak expiratory flow rate (morning/evening, L/min) ranged from 300/400 (28.6%) to 430/450 (4.5%). She quit smoking and keeping pets. Her asthma is now totally controlled with regular treatment of an inhaled fluticasone/vilanterol combination and oral montelukast at the outpatient clinic of our hospital.

**Discussion**

This is a clear case of *C. pneumoniae* initiated or infectious asthma as the onset of asthma was coincident with *C. pneumoniae* lung infection leading to the observed pathology and diagnosis of asthma. This has been previously demonstrated in prospective studies [3].

Generally, it is difficult to diagnose acute *Chlamydia pneumoniae* infection in clinical practice because of the lack of definitive diagnostic methods. Diagnostic methods include nasopharyngeal swab culture, antibody tests, direct antigen detection, and polymerase chain reaction. Serologic tests are common but are not standardized methods, and there is some variability as under any assay condition.
Establishment of definitive diagnostic methods for C. pneumoniae is needed. In Japan, the enzyme-linked immunosorbent assay (ELISA)-based detection of C. pneumoniae-specific IgA and IgG is usually used to identify this pathogen [2]. The sensitivity and specificity of the ELISA have been verified by comparison with titres measured by a microimmunofluorescence test.

Miyashita et al. confirmed C. pneumoniae infection in 168 Japanese adults with acute asthma exacerbation using three different methods, including isolation in cell culture, polymerase chain reaction, and serum-specific antibodies by microimmunofluorescence test and found significantly higher frequency (1.2–8.9%) compared to 108 control subjects who were matched for age, sex, and smoking status (0–2.8% positive) [4]. Although we confirmed acute C. pneumoniae infection in this case, there may be more undiagnosed cases of acute asthma or asthma exacerbation.

CT findings of C. pneumoniae infection have been reported previously [5]. Of 24 total patients with C. pneumoniae pneumonia, 20 had consolidation, 17 had bronchovascular bundle thickening, 15 had reticular or linear opacity, and 13 had ground-glass opacity. Bronchial wall thickening was also noted. These findings indicate that the CT findings in our case were typical. In fact, the CT findings were an aid for diagnosing C. pneumonia-induced pneumonia.

It seems that a delay in diagnosing asthma was the reason for the development of severe acute asthma in this patient. Proactive follow-up is needed to prevent recurrence of severe acute asthma.

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

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