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A Case of Afebrile Pneumonia Caused by Non-Toxigenic
Corynebacterium diphtheriae

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Afebrile pneumonia is a relatively unusual disease and may be caused by certain pathogens such as Chlamydia trachomatis, Ureaplasma urealyticum, respiratory syncytial virus, and Pneumocystis jirovecii (1,2). However, the specific causative agents of afebrile pneumonia have not yet been fully identified to date. Non-toxigenic Corynebacterium diphtheriae and toxigenic C. diphtheriae are partly responsible for respiratory infections including pneumonia, although the incidence of these infections may be very low (3,4). Here, we describe a case of afebrile pneumonia caused by non-toxigenic C. diphtheriae.

A 60-year-old Japanese female had been diagnosed with amyotrophic lateral sclerosis (ALS) at the age of 47 years. Two years after onset, she underwent tracheotomy and was provided with a mechanical ventilator. Aside from an occa-
sional history of urinary tract or respiratory infections, she had no previous history of chronic or other infectious diseases. On May 9, 2007 (hospital day 1), she presented with respiratory distress due to elevated airway intrapressure, and purulent sputum (non-bloody, white-yellow color) was aspirated using a respiratory catheter, but no fever was noted (36°C). Chest radiography showed many spots of consolidations in the bilateral lung, pleural effusion in the left intrathoracic space, and infiltrations with partial atelectasis in the left lower lobe of the lung (Fig. 1A). On the day of radiologic examination, her clinical data were as follows: leukocyte count, 1.06 × 10⁴/μL (reference values, 3.5 to 9.0 × 10⁴/μL); platelet count, 1.87 × 10⁵/μL (reference values, 1.5 to 3.0 × 10⁵/μL); and C-reactive protein level, 1.8 mg/dL (reference values, <0.3 mg/dL). On the basis of these findings, she was diagnosed with afebrile pneumonia and was treated with levofloxacin (200 mg/day, day 1), panipenem/betamipron (500 mg/day, days 2 to 10), and intravenous fluids for 12 days. The lung lesion improved after hospital day 5 and the patient was afebrile during the clinical course.

Aspirated sputum samples were collected and examined by bacterial culture using 5% sheep blood agar. Many small and optically identical colonies (diameter, 0.5 to 1 mm) grew on the blood agar. Gram and Neisser staining of the colonies suggested Corynebacterium (Fig. 1B). In addition, phagocytosis of bacteria was clearly observed in the sputum smear (data not shown). Confirmation of the bacterial pathogen Corynebacterium was performed using the RapID CB Plus kit (Kyokuto Pharmaceutical, Tokyo, Japan). We also amplified the diphtheria toxin gene using a PCR technique (5,6); however, the gene was not detected (Fig. 1C). Moreover, the nucleotide sequence of the 16S rRNA gene of the present strain completely matched that of the C. diphtheriae prototype strain (7). The results confirmed the pathogen to be non-toxigenic C. diphtheriae (biotype: mitis). C. diphtheriae was no longer detected after hospital day 3. The isolate was susceptible to erythromycin, clarithromycin, clindamycin, benzylpenicillin, sulbactam/amoxicillin, cefazolin, cefmetazole, cefpirome, imipenem, meropenem, vancomycin, teicoplanin, and minocycline, while the isolate was resistant to levofloxacin, ciprofloxacin, and fosfomycin. The pathogen’s infection route could not be precisely elucidated in the present case.

It has been suggested that non-toxigenic C. diphtheriae may be associated with various infections such as pharyngitis, myocarditis, polyneuritis, and pneumonia (3,4). The present patient with ALS was confirmed to have afebrile pneumonia caused by this pathogen. In general, high fever is an important clinical sign in patients with pneumonia; however, few patients are diagnosed with afebrile pneumonia (1,2). The epidemiology of non-toxigenic C. diphtheriae in many countries, including Japan, remains poorly understood, despite the fact that this infection seems to be increasingly reported and has been found to occur in vaccinated individuals in other countries (3). ALS is a rare progressive neurodegenerative disease with an incidence of about 1/50,000, and it is known that respiratory complications in ALS patients may involve respiratory failure, pneumonia, and pulmonary embolism (8,9). Various bacteria may be associated with ALS in ALS patients, and this disease may be life-threatening (8,9). Here, we encountered a single case of afebrile pneumonia associated with ALS. From this case alone, we could not definitively determine whether C. diphtheriae easily causes afebrile pneumonia or not in ALS patients. However, it is possible that non-toxigenic C. diphtheriae is an etiologic pathogen of afebrile pneumonia, although it may be rare.

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