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Case Report

## Legionella pneumonia appeared during hospitalization in a patient with hematological malignancy confirmed by sputum culture after negative urine antigen test

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#### ABSTRACT

Legionella pneumophila is recognized as a common causative organism for community-acquired pneumonia, but it is rarely a causative organism for hospital-acquired pneumonia, except in cases of hospital outbreak. Recently, most of the Legionella cases have been diagnosed using the urine antigen test. However, this test can reliably detect only L. pneumophila serogroup 1. Here we report a 63-year-old male patient who was recently diagnosed with acute leukemia and treated with chemotherapy and who developed pneumonia on hospital day 8 during the nadir phase. He was later diagnosed with Legionella pneumonia by culture despite a negative urine antigen test. This case suggests that Legionella pneumonia is an important differential diagnosis for pneumonia in inpatients in the early phase of hospitalization and that when Legionella infection is clinically suspected, culture using selective media or molecular tests should be performed even if the urine antigen test is negative.

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#### 1. Introduction

Legionella pneumophila is recognized as a common causative organism for community-acquired pneumonia, but it is rarely a causative organism of hospital-acquired pneumonia [1]. The urine antigen test is a useful diagnostic tool with high sensitivity, but it can reliably detect only L. pneumophila serogroup 1 [2]. Here we report on a 63-year-old male patient who was recently diagnosed with acute leukemia and treated with chemotherapy and who developed pneumonia on hospital day 8 during the nadir phase. He was later diagnosed with Legionella pneumonia by sputum culture despite a negative urine antigen test.

#### 2. Case report

The patient was a 63-year-old man without a significant medical history. He presented with 2 months' general malaise and was

\* Corresponding author. E-mail address: ryota510@hotmail.com (R. Hase). diagnosed with acute leukemia. He was admitted to Japanese Red Cross Narita Hospital and chemotherapy with idarubicin and cytarabine was started on hospital day 1. Cefepime was also started after two sets of blood cultures were performed. He became neutropenic on hospital day 6 and had new fever. Cefepime was switched to meropenem as an initial therapy for neutropenic fever, and vancomycin was also administered on hospital day 9. He had dry cough and hypoxia on hospital day 12, and both his chest X-ray and CT revealed new infiltration in both lungs (Fig. 1). His fever persisted and hypoxia deteriorated, but his consciousness was clear. He was intubated and supported by mechanical ventilation in ICU on hospital day 16. He was referred to our infectious disease service team for the management of nosocomial pneumonia on hospital day 17. Upon examination, he was unconscious with sedation. His vital signs were blood pressure of 117/60 mmHg, heart rate of 112 beats/min with norepinephrine support, body temperature of 38.6 °C, respiratory rate of 15 breaths/min, and oxygen saturation on ventilator (FiO2 0.8, PEEP 12) of 96%. Physical examination revealed coarse crackles in both lungs. Laboratory tests showed neutropenia, with a WBC count of 100/µL, anemia with

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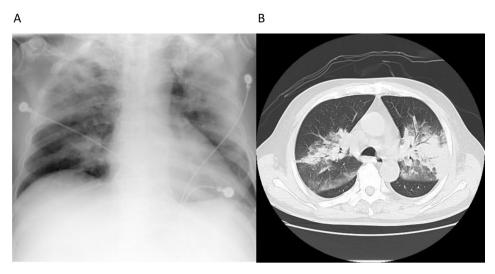


Fig. 1. A. Chest X-ray performed on hospital day 12 revealed bilateral lung infiltration. B. Chest CT performed on hospital day 12 revealed bilateral lung consolidations.

hemoglobin level of 8.0 g/dL, thrombocytopenia with platelet count of 5,000 cells/L, and elevated inflammatory marker with elevated C-reactive protein levels of 20.47 mg/L. His liver function enzyme, lactate dehydrogenase, and serum sodium levels were within the normal range. We administered sulfamethoxazole-trimethoprim for Stenotrophomonas maltophilia detected by the previous sputum culture and ciprofloxacin for empirical coverage of L. pneumophila because his history revealed that he might have been occupationally exposed to outdoor air conditioner units. The urine antigen test for Legionella using BinaxNOW® Legionella (Alere Medical, Tokyo, Japan) was performed with a negative result. We asked the laboratory to perform sputum culture for L. pneumophila with the selective media. Wadowsky-Yee-Okuda medium was used, later revealing a yield colony that resembled L. pneumophila (Fig. 2). The colony was identified as L. pneumophila using the MALDI Biotyper (Bruker Daltonics, MA, USA) with a score of 2.172 and later confirmed as serogroup 9 by the immune serum agglutination test (Denka Seiken, Tokyo, Japan). The patient was treated for Legionella pneumonia for 4 weeks. His symptoms improved and he was

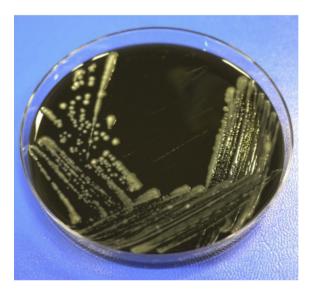


Fig. 2. The sputum culture revealed the growth of colonies on Wadowsky-Yee-Okuda medium.

extubated once, but he died of exacerbation of acute leukemia on hospital day 55 (see Fig. 3).

#### 3. Discussion

We identified two important clinical issues: (1) *L. pneumophila* should be considered as a causative organism for pneumonia in inpatients, particularly in the early phase of hospitalization and (2) a negative urine antigen test cannot rule out the possibility of *Legionella* pneumonia.

L. pneumophila should be considered as a causative organism for new-onset pneumonia in inpatients in the early phase of hospitalization. Moreover, it should be considered as a causative organism not only in the setting of hospital-acquired pneumonia but also in the setting of late-onset, community-acquired pneumonia. Two explanations are possible in the present case. First, L. pneumophila may have been acquired by inhalation in the hospital environment. Cases of nosocomially-acquired Legionella disease have been reported in many countries and have been related to possible exposure to Legionella in the hospital environment [3]. Our infection control team surveyed the possible contamination of L. pneumophila in the ward's water supply and the presence of other patients with L. pneumophila infection; however, no evidence of contamination or of a hospital outbreak of L. pneumophila infection was detected. Second, L. pneumophila may have been acquired in the community, with clinical symptoms appearing during hospitalization after the incubation period. Diagnosis of this type of pneumonia is particularly confusing when the incubation period is long, but it should not be categorized as hospital-acquired pneumonia according to the definition of the Infectious Diseases Society of America/American Thoracic Society: "pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission [4]." The incubation period of Legionella diseases is reported to be 2–14 days [1]. This fact suggests that community-acquired L. pneumophila should be considered as the causative organism for pneumonia among inpatients if the clinical symptoms appear within the first 2 weeks of hospitalization. We first suspected Legionella pneumonia because of the patient's occupation as an electric engineering technician working on the maintenance of air-conditioning units, with possible exposure to Legionella. However, additional history obtained from his family revealed that he had been away from his work for approximately a

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