

# Nosocomial pneumonia caused by water-born *Legionella pneumophila* in a pediatric hematopoietic stem cell transplantation recipient for thalassemia major

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## ABSTRACT

**Background.** Nosocomial pneumonia caused by *Legionella pneumophila* serogroup 2-14 occurred in a 7-year-old patient following allogeneic hematopoietic stem cell transplantation for thalassemia major.

**Case.** The patient was diagnosed with nosocomial *Legionella pneumophila* by polymerase chain reaction (PCR) examination of the bronchoalveolar lavage and culturing *Legionella pneumophila* serogroup 2-14 from the patient's room faucet water. *Legionella pneumophila* was eradicated from our hospital's water distribution system by superheating and chemical eradication methods (hyper-chlorination and hydrogen peroxide). We did not detect any other case after this event.

**Conclusion.** Early recognition of contamination of the hospital water system with *Legionella* proves the importance of prevention in new cases.

**Key words:** Hematopoietic stem cell transplantation, *Legionella pneumophila*, pneumonia.

*Legionella pneumophila* is an intracellular gram-negative bacillus that requires special microbiological culture media. It seems that the risk of *L. pneumophila* pneumonia may be increasing in immunocompromised patients.<sup>1,2</sup> Patients who receive bone marrow transplantation are sensitive to *Legionella* infection due to prolonged intervals of neutropenia and abnormalities in cell-mediated immunity. Therefore, *Legionella* infections in an immunocompromised patient can easily be severe and cause high mortality.<sup>3</sup> Nosocomial *Legionella* infections are often transmitted via contaminated aerosol or aspiration of contaminated water. Relevant aerosol sources for hospital-acquired legionellosis include therapeutic devices and water distribution

system outlets.<sup>4-6</sup> Some practices for eradicating *Legionella* from the hospital water distribution system are superheating, hyper-chlorination, ultraviolet light, and the addition of copper and silver electrodes to the water.<sup>3,5</sup> Herein, we report the management of an immunocompromised child with nosocomial *Legionella pneumophila* pneumonia acquired from the contaminated hospital water system.

## Case Report

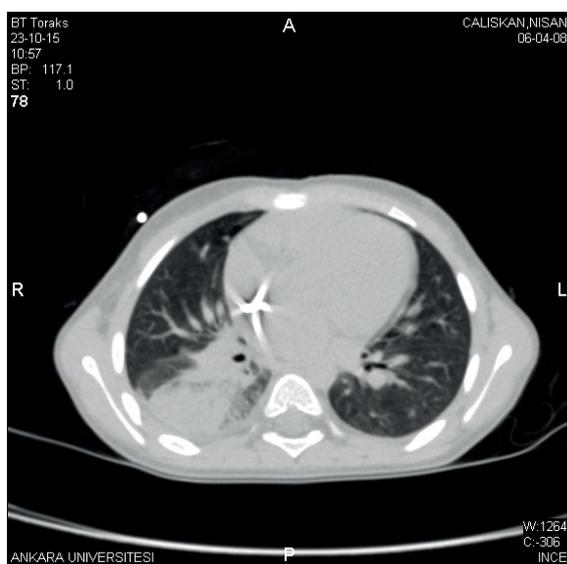
A 7-year-old girl followed-up with the diagnosis of thalassemia major (thalassemia mutation analysis IVS 1.110 G>A homozygote mutant) was hospitalized due to a second allogeneic hematopoietic stem cell transplantation (HSCT). The patient had undergone HSCT at the age of 4.5 years from her sibling with full compatible tissue type, but after three months, secondary graft rejection occurred, and recurrence of thalassemia major was considered. After three

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Received 6th April 2017, revised 12th January 2020,  
19th April 2020, accepted 26th April 2020.

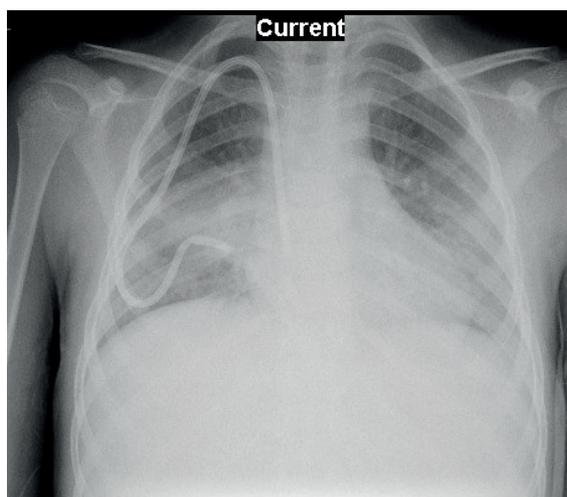
years, the patient underwent a 2<sup>nd</sup> HSCT again from her sibling with full compatible tissue type. Because of the patient's fever (38.5 C°) during anti-thymocyte globulin (ATG) therapy administered in the period of HSCT preparation, intravenous (IV) cefoperazone-sulbactam therapy was initiated. Blood, catheter, and urine cultures collected from the patient. Fever's focus was negative, and her fever did not persist. Since expected engraftment was not achieved, the patient underwent bone marrow aspiration biopsy and chimerism examination. According to the results, the case was evaluated as primary rejection. Upon having a fever that exceeded 39 C° on the 26<sup>th</sup> day after transplantation, blood, catheter, throat and urine cultures were collected, IV cefoperazone-sulbactam therapy was terminated and, IV meropenem and IV teicoplanin were initiated. Because the duration of neutropenia was prolonged, prophylactic fluconazole therapy was replaced with 1mg/kg IV liposomal amphotericin B therapy on alternate days. At follow-up, the patient had complaints of non-productive coughing, abdominal pain, and headache. On the 3<sup>rd</sup> day of fever, the respiratory sounds were decreased in the right middle and lower zones. A chest X-ray examination was carried out, and pneumonic infiltration on the lower lobe of the

right lung was detected (Fig. 1). In this period, white blood cell (WBC) count, hemoglobin (Hb) level, and platelets (Plt) count were found as 100/mm<sup>3</sup>, 9.4 g/dL, and 17000/mm<sup>3</sup>, respectively and C-reactive protein (CRP) was 200mg/L. Serum galactomannan was found as 0.3 s/co and cytomegalovirus (CMV) DNA was negative. Blood, catheter, urine, and throat cultures were also negative. Thoracic computerized tomography (CT) of the patient revealed a consolidated area in the right lung lower lobe superior segment and minimal pleural effusion (Fig. 2). Although the patient was under beta-lactam antibiotics treatment, fever persisted. Because of persistent fever, bronchoscopy was performed. Bronchoalveolar lavage (BAL) fluid was negative for bacterial and fungal cultures. BAL galactomannan level was found as 0.38 s/co, and rare leukocytes and lymphocytes were observed among alveolar macrophages. Infectious mononucleosis PCR, CMV PCR, *Pneumocystis jirovecii* PCR, *Mycobacterium tuberculosis* PCR, respiratory virus PCR panel were negative, while *L. pneumophila* PCR was positive. *L. pneumophila* antigen was negative in the urine. IV levofloxacin and PO azithromycin were added to her treatment for *Legionella* pneumonia. Autologous cells of the patient were infused because of long-term neutropenia and severe pneumonic infiltration. The patient's fever resolved on the 15<sup>th</sup> day of fever, and clinical signs of pneumonia disappeared gradually. She received azithromycin for 14 days and levofloxacin for 21 days.



**Fig. 1.** Pneumonic infiltration of the lower lobe of right and left lung, chest X-ray 2.

Upon *L. pneumophila* PCR being detected in the BAL fluid in this period, the case was reported to the local public health officials. Tap water of all floors, air conditioning systems, hot and cold water tank outlet temperatures, and chlorine levels were examined in our pediatric hospital. Cultures were collected for *Legionella spp.* Water temperature was between 39-68.4 C°, and the chlorine level varied between 0.26-0.47ppm. From the cultures collected, 12000cfu/L colonies of *L. pneumophila* serogroup 2-14 was isolated from the culture of the tap water of the patient's room. Additionally, 550000cfu/L-9000000 cfu/L



**Fig. 2.** Thoracic computerized tomography (CT) of the patient revealed consolidated area 3 and minimal pleural effusion in the right lung lower lobe superior segment.

colonies were isolated from the culture of the tap water of treatment room of neonatal intensive care unit (NICU) and the intermediate NICU.

Following the examination of *L. pneumophila*, superheating, hyper-chlorination, and hydrogen peroxide ( $H_2O_2$ ) were implemented for decontamination purposes. All faucets and showerhead filters were flushed with descaling agents. These processes were repeated two times with one-week intervals. Temperature, chlorine level, and culture samples were collected again from the same places after two weeks.

## Discussion

We report nosocomial pneumonia of *L. pneumophila* in a 7-year-old female patient in the HSCT unit. Informed consent was obtained from the family. Because *L. pneumophila* was only detected with PCR in the patient's BAL fluid, we could not reveal its genotype. The increasing risk of *L. pneumophila* pneumonia in immunocompromised patients has previously been reported.<sup>1-4,8,9</sup> In our patient, azithromycin, and levofloxacin were added to treatment without waiting for the results of water system culture samples since the patient was immunocompromised and did not give

a clinical response to beta-lactam antibiotics. After detecting the PCR positivity, potential *Legionella* case was reported, and 22 samples were collected from the water systems. The water temperature of the tap water in the patient's room was found as 39 C° and chlorine level as 0.26 ppm. 12000cfu/L colonies of *L. pneumophila* serogroup 2-14 was isolated from the culture of the tap water of the patient's room. In a study by Orsi et al.<sup>10</sup> concerning *Legionella* control in the water system of antiquated hospital buildings, similar to our water characteristics, low level of residual free chlorine and water temperatures being between 20 C° and 45 C° were reported as risk factors. Nosocomial *Legionella* infections are often transmitted via contaminated aerosol or aspiration of contaminated water. Relevant aerosol sources for hospital-acquired legionellosis include humidifiers, nebulizer masks, showers, taps, cooling towers.<sup>4-6,11-13</sup> In our case, we suggested that the infection was acquired by microaspiration of contaminated faucet water. *L. pneumophila* can create a biofilm layer, persisting for years in the water distribution system and requires biocides to be cleaned.<sup>12,14</sup> Infection control for *L. pneumophila* is challenging and includes periodic inspections, cleaning, and maintenance of the water distribution systems, and decalcification of showers/taps. Routine microbiological surveillance and chemical monitoring of the water supply is necessary.<sup>10,12,15</sup> For example, some practices for eradicating *Legionella* from the hospital water distribution system are superheating, hyper-chlorination, ultraviolet light, and the addition of copper and silver electrodes to the water.<sup>3,7</sup> In our study, after the reproduction of *L. pneumophila*, the temperature of hot water was increased to 70 C° for decontamination. Hyper-chlorination and  $H_2O_2$  were applied in the water system and tanks. All faucets and showerhead filters were cleaned with decalcification. These processes were repeated two times with 1-week intervals. Temperature, chlorine level, and culture samples were collected again from the same places after two weeks and examined. Water temperature differed between 61.9-70 C° and

chlorine level between 0.36-0.67 ppm. Oren et al.<sup>3</sup> also reported the control of the *Legionella* outbreak in their hospital, which was derived from the water system in the HSCT unit by superheating and hyper-chlorination. Likewise, the follow-up cultures collected in our hospital were negative, and the collection of water cultures was planned to take place once every two months for two years.

In brief, a nosocomial *Legionella* pneumonia outbreak originating from a water distribution system was prevented by early diagnosis, rapid treatment, and management of outbreak control with the collaboration of local public health officials. In order to prevent such outbreaks, inspections, cleaning, and maintenance of the water distribution systems, and decalcification of showers/taps should be performed periodically. There must be routine microbiological surveillance and chemical monitoring of the water supply in hospitals.

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