Persistent *Legionella* Infection in a Patient after Bone Marrow Transplantation

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We report on a patient who developed *Legionella* pneumonia after bone marrow transplantation. Despite appropriate antibiotic treatment, disease progressed. The patient developed a lung abscess from which *Legionella* and *Prevotella* were isolated. Cure was achieved by surgical resection. The resected material was sterile, but 16S ribosomal DNA analysis revealed *Legionella* DNA.

CASE REPORT

A 45-year-old male was admitted to the Department of Hematology, University Hospital Mainz, due to a low-grade fever (38.5°C) and an abnormal chest radiograph demonstrating infiltrates in the right lower and middle lobes accompanied by a small pleural effusion. The patient did not complain of cough. A bronchoalveolar lavage (BAL) was performed and yielded *Legionella pneumophila* serotype 1 and also 1,000 bacteria/ml belonging to the oral flora and one colony of *Aspergillus*. Urine tested positive for *Legionella* antigen. Ten months prior to admission, the patient had been diagnosed with chronic myelogenous leukemia, and 4 months later he received a matched related bone marrow transplantation. After bone marrow transplantation, he developed acute grade II graft-versus-host disease of the skin and acute grade III graft-versus-host disease of the liver, which were controlled by cyclosporin A and steroids. After the diagnosis of *Legionella* pneumonia was established, the patient received ciprofloxacin (400 mg twice a day) and rifampicin (600 mg/day) for 2.5 weeks intravenously. The source of *Legionella* infection could not be determined. Water samples taken from the patient’s home were negative for *Legionella*. *Aspergillus* could be demonstrated in only one BAL but not in repeated sputum cultures. However, the patient was started on itraconazole (400 mg/day). Control chest radiographs did not show progression during intravenous antibiotic therapy for *Legionella*. Ciprofloxacin was changed to clarithromycin because the patient had developed severe central nervous system adverse effects. He was discharged on oral rifampicin (600 mg/day) and clarithromycin (500 mg/day) for 4 weeks. A follow-up chest radiograph revealed consolidation, with a central abscess formation with a diameter of 3.5 cm. The patient was readmitted, and a BAL was performed which revealed polymorphonuclear neutrophils and less than 10,000 gram-positive bacteria/ml belonging to the physiological oral flora. Purulent material was obtained from the lung abscess by a computed tomography (CT)-guided aspirate (Fig. 1). Additionally, a biopsy of the abscess wall was performed. A *Prevotella* species was cultured from the purulent material, and the biopsy yielded *Legionella pneumophila* serogroup 1. Urine tested positive for *Legionella* antigen. On admission, *Aspergillus* was suspected to cause the abscess formation, and amphotericin (80 mg/day) was started empirically. In order to effectively treat the infection with the *Prevotella* and *Legionella* species, the patient received imipenem (0.5 g three times a day), rifampicin (600 mg/day), and roxythromycin (300 mg/day). Twelve days after initiation of therapy, the patient developed a large pleural effusion, and CT scans verfied the persistence of the cavitation (size, 4 by 5 cm), accompanied by a pleural effusion (Fig. 2). Therapy was continued for 2 weeks. Due to an allergic skin reaction, imipenem was replaced by clindamycin (600 mg four times a day) and aztreonam (1 g three times a day). At this point in time, the patient complained of increasing thoracic pain. The C-reactive protein increased from 98 to 264 mg/liter, though the patient did not develop fever. He underwent thoracic surgery, and the entire middle and parts of the upper and lower lung lobes were resected. The patient recovered quickly without any signs of infection. In addition, the C-reactive protein decreased. The histopathological examination did not demonstrate any fungal hyphae in the lung tissue, and amphotericin was discontinued. Treatment with clindamycin,

![FIG. 1. Chest CT scan demonstrating a large cavitation in the middle lobe of 4 by 5 cm.](image-url)
Legionella pneumophila ranks among the three most common microbial pathogens involved in community-acquired pneumonia. Cell-mediated immunity represents the primary host defense against Legionella. Thus, Legionnaires’ disease is more common and more severe in patients with depressed cell-mediated immunity, including transplant recipients, patients with AIDS, or those with drug-induced immunosuppression (8). Here we report the case of a persistent (12 weeks) Legionella infection that was refractory to treatment with conventional antibiotics.

Concomitant infection with different pulmonary or systemic pathogens may occur in Legionella pneumonia (2, 6). Abscess formation, however, has generally been regarded as a complication of monoinfection with Legionella, particularly in immunocompromised hosts (3, 7). To our knowledge, this represents the first documented case of abscess formation associated with Legionella pneumonia and accompanying Prevotella infection. Prevotella species represent an anaerobic bacterium that is mainly found in the oral cavity and ranks among the pathogens that are most frequently isolated from lung abscesses. We suspect that superinfection with this agent played a pivotal role in abscess formation in our patient.

Interestingly in this case, the patient had not been critically ill, though the abscess formation did not resolve under appropriate antibiotic therapy. Presumably, therapeutic levels of the antibiotics were not reached in the cavitation tissue. Surgery, which is not a generally recommended measure to treat lung abscesses, led to control of the infection in this case.

Antibiotic treatment probably rendered the specimens culture negative, but bacterial identification could successfully be undertaken by the direct 16S rDNA sequencing of amplification products from clinical material. The fact that only Legionella DNA could be amplified from lung tissue supports the notion that persistence of infection was due exclusively to Legionella pneumophila and not to the Prevotella superinfection.

In summary, these observations indicate that Legionella infection may persist despite appropriate treatment in immunocompromised patients and that clinical presentations may be quite benign. Lung abscess formation occurring during Legionella infection may be indicative of coinfection with other bacterial agents. When treatment with antibiotics fails to eradicate the pathogen, surgery may become an important therapeutic option. Demonstration of persistent Legionella infection may require noncultural methods like the use of 16S rDNA analysis. Thus, application of this molecular technique appears appropriate when pathological findings persist in the face of negative bacterial cultures.

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REFERENCES