**Legionella bozemanii** Pneumonia in Three Patients with AIDS

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*Legionella bozemanii* is known to cause pneumonia often in immunocompromised hosts. To our knowledge, we describe the first three cases of *L. bozemanii* pneumonia in patients with AIDS. At the time of presentation, these patients had varied histories, physical findings, and radiological findings. All three patients had a uniformly excellent response to treatment despite receiving different antibiotic regimens. The cases illustrate the need for thorough diagnostic workups and prompt institution of antibiotic therapy when clinical suspicion for *L. bozemanii* infection is high.

*Legionella bozemanii*, one of 34 *Legionella* species of Legionellaceae, was first isolated in 1968 from the lung of a freshwater scuba diver who died of pneumonia in 1959 [1, 2]. Of the 20 culture-proven cases of pneumonia due to *L. bozemanii* reported to date, there has been a predilection toward affecting immunocompromised patients [3]. This report describes three cases of *L. bozemanii* pneumonia in patients with AIDS.

**Case Reports**

**Case 1**

A 32-year-old man presented to the emergency department complaining of cough, malaise, and fever. His medical history was significant for hemophilia A since the age of 2, hepatitis B, hepatitis C, and *Legionella pneumophila* pneumonia 2 years prior to his latest illness. The patient had had no AIDS-defining opportunistic infections to date, was receiving stable nucleoside antiretroviral therapy, had a recent CD4 cell count of 40/mm³, and had a plasma viral load of 215,000 copies of HIV RNA/mL. The patient had a smoking history. His medications included aerosolized pentamidine (every month), oral zidovudine (100 mg t.i.d.), and oral lamivudine (150 mg b.i.d.).

Physical examination revealed a nontoxic man with a blood pressure of 130/70 mm Hg, a respiratory rate of 20, a temperature of 101.5°F, and an O₂ saturation of 97% while he was breathing room air. His respiratory examination was unremarkable. A chest roentgenogram revealed a new 1.5-cm nodule in the right upper lobe. The leucocyte count was 3,000/μL, the hematocrit was 39.5%, the absolute neutrophil count was 1,800/μL, and the platelet count was 77,000/μL.

At admission, intravenous pentamidine was administered empirically to treat presumptive atypical *Pneumocystis carinii* pneumonia. The following day, an induced sputum specimen was obtained, and a thoracic CT scan revealed a solitary nodule in the posterior segment of the right upper lobe that was abutting pleura; no cavitation or calcifications were seen. Gram staining of the induced sputum specimen revealed multiple organisms consistent with oropharyngeal flora, and stains were negative for *P. carinii*. Intravenous pentamidine therapy was discontinued.

On day 3 of hospitalization, CT-guided fine-needle aspiration was performed after it was noted that the nodule had rapidly increased in size to 5.0 × 3.0 cm and that there was new adjacent airspace disease. Gram staining of the fine-needle aspirate revealed multiple polymorphonuclear cells and no organisms; stains for *P. carinii*, acid-fast bacilli (AFB), and fungi were negative. Therapy with piperacillin/tazobactam and clindamycin was started to provide treatment of potential aspiration as a cause of the pulmonary nodule. On day 4 of hospitalization, increased temperatures (maximum, 104°F) were noted, and the patient developed dyspnea with a decrease in O₂ saturation to 92% while breathing room air. Since cultures of the fine-needle aspirate and the induced sputum specimen remained negative and no definitive diagnosis had been established, the patient underwent bronchoscopy, which was nondiagnostic.

On day 6 of hospitalization, the patient began to require supplemental oxygenation, and administration of intravenous erythromycin (1 g q6h) was initiated to treat atypical pneumonia because of his worsening clinical status, lack of response to the current antibiotic regimen, and continued negative culture results. On day 7, he underwent an open lung procedure with removal of a 6-cm abscess cavity that contained necrotic and purulent material. Postoperatively, intravenous erythromycin therapy was continued. Cultures of bronchoalveolar lavage (BAL) fluid yielded *L. bozemanii* serogroup 1 on day 10. Culture of tissue obtained during segmentectomy also subsequently yielded *L. bozemanii*.

The patient’s respiratory status rapidly improved after the segmentectomy and with continued erythromycin treatment. Erythromycin monotherapy was continued after the *L. bozemanii* infection was confirmed, and rifampin was not added to therapy because of the patient’s chronically elevated liver enzyme levels. He received a 12-day course of intravenous erythromycin (1 g q6h). The antibiotic regimen was subsequently changed to intravenous ciprofloxacin (400 mg b.i.d.) because...
of a drug rash presumed to be caused by erythromycin. He received a total of 4 weeks of intravenous therapy for *L. bozemanii* infection. He recovered completely from his pneumonia with no other sequelae. Despite having two infections with *Legionella*, he had no history of risk factors, such as water exposure, that would predispose him to legionella infections.

**Case 2**

A 35-year-old man with advanced AIDS presented to the clinic with a 2-day history of cough followed by fever and pleuritic chest pain. His medical history was significant for hepatitis C, syphilis, and recurrent episodes of bacterial sinusitis. HIV infection was documented in 1991 with a baseline CD4 cell count of 310/mm³. The patient had a recent CD4 cell count of 10/mm³ and a plasma viral load of >1,000,000 copies of HIV RNA/mL. His medications included oral dapsone (100 mg q.d.), oral stavudine (40 mg q.d.), and oral amoxicillin/clavulanate (500 mg t.i.d.), which he had received for 11 days as treatment for presumed sinusitis.

Physical examination revealed a nontoxic man with a temperature of 103.2°F, a pulse rate of 110, a respiratory rate of 28, and an O₂ saturation of 93%. A chest roentgenogram demonstrated a density of the right hilum that was possibly consistent with a consolidation process, and CT of the chest was recommended for further evaluation. Routine cultures of two sets of blood specimens obtained during admission were negative. The leukocyte count was 5,300/μL, and the hematocrit was 29.6%.

At the time of admission, therapy with intravenous cefuroxime (750 mg q8h) was started for presumed bacterial pneumonia. On day 1 of hospitalization, a thoracic CT scan revealed a mass in the right apex and an opacity along the right side of the carina with a suggestion of collapse of the right lower lobe. Since culture of an induced sputum specimen obtained during admission did not yield a pathogen, diagnostic bronchoscopy was performed on day 2. The area of collapse could not be approached because of technical difficulty, but a BAL fluid specimen was obtained from the apical segment of the right upper lobe. Gram staining of the BAL fluid specimen revealed rare polymorphonuclear cells but no organisms, and stains for *P. carinii* and AFB were negative.

Over the first 5 days of hospitalization, the patient continued to spike fevers, and his oxygenation did not improve. On day 5 of hospitalization, cefuroxime treatment was stopped, and therapy with oral clarithromycin (500 mg b.i.d.) was started because of lack of clinical improvement and increased concern for infection with potentially atypical organisms. Defervescence occurred after 2 days of clarithromycin therapy. Culture of the BAL fluid specimen subsequently yielded *L. bozemanii* serogroup 1. The patient received 2 weeks of clarithromycin therapy and recovered completely from his pneumonia with no other sequelae.

**Discussion**

The fact that *L. bozemanii* has been isolated from AIDS patients with pneumonia is not surprising, since over one-half of patients described in previous reports of *L. bozemanii* pneumonia were immunocompromised hosts [3]. To our knowledge, no cases in HIV-positive patients have been previously reported. However, most of the cases reported to date in retrospective series occurred in the pre-AIDS era. Other series have documented that AIDS is a known risk factor for *L. pneumophila* pneumonia [4, 5].

The varied radiological features of our cases are consistent with *L. bozemanii* pneumonia [6]. These features can include lobar or multilobar infiltrates, nodules, cavitory nodules, and pleural effusions. The evolution of the roentgenographic changes in case 1 is also characteristic of *L. bozemanii* infection, which may begin as an expanding nodule that subsequently cavitates.

A distinctive feature of our three cases was the uniformly excellent response to treatment. The mortality rate associated with *L. bozemanii* pneumonia was 40% in prior series [3]. All three patients included in this report had very advanced HIV disease (CD4 cell count, <40/mm³) and did well with aggressive diagnostic maneuvers and appropriate antibiotic therapy. The patient in case 1 had the most complicated pneumonia with abscess formation, and segmentectomy may have contributed substantially to clinical improvement by debulking areas of...
necrotic tissue. A similar aggressive surgical approach has seemed to benefit a number of AIDS patients with *Rhodococcus equi* pneumonia [7].

Various antibiotic regimens proved to be effective for these three patients. The patient in case 1 received intravenous erythromycin followed by intravenous ciprofloxacin, the patient in case 2 received oral clarithromycin, and the patient in case 3 received oral ciprofloxacin. Different antibiotic regimens were used with varied results in the 20 previously reported cases. These antibiotic regimens included erythromycin, both erythromycin and rifampin, and ciprofloxacin. There has been some suggestion that erythromycin monotherapy for *L. bozemanii* pulmonary infection is associated with poor outcomes [3]. Azithromycin showed promise in an intracellular model of *Legionella micdadei* infection but has not been used in the clinical setting of *L. bozemanii* infection [8]. However, it has previously been demonstrated that the in vitro susceptibility of *Legionella* species to an antibiotic may not correlate well with the in vivo efficacy of that drug [9, 10].

None of the three patients were receiving prophylaxis with rifabutin or macrolide agents for *Mycobacterium avium* complex infection despite the fact that their CD4 cell counts were <50/mm$^3$. The current clinical practice of administering azithromycin or clarithromycin as prophylaxis for *M. avium* complex infection in HIV-infected patients with CD4 cell counts of <50/mm$^3$ may decrease the incidence of infections due to *Legionella* species.

These three cases illustrate the fact that *L. bozemanii* can be a treatable cause of pneumonia in patients with advanced HIV disease. The pulmonary manifestations associated with HIV infection are diverse [11]. The spectrum of clinical presentations due to unusual pulmonary pathogens such as *Legionella* and *Rhodococcus* species is likely to expand given the enhanced life expectancy of patients with AIDS who receive potent combination antiretroviral regimens containing protease inhibitors. Legionella pneumonia and pyogenic bacterial pneumonia occur with greater frequency in HIV-infected individuals than in immunocompetent individuals [12–14]. With more cases of advanced HIV disease, there will be an increased incidence of pneumonia caused by both *Pseudomonas* and other gram-negative organisms.

Since the differential diagnosis of pulmonary manifestations of advanced HIV infection is vast, an intensive diagnostic investigation is warranted for AIDS patients with pulmonary infiltrates [11]. Evaluation of an induced sputum specimen is generally indicated as an initial step to rule out *P. carinii* pneumonia as well as to identify bacterial pathogens; in addition, testing for serum cryptococcal antigen or urinary or blood *Histoplasma* antigen, AFB staining of smears, and cultures should be performed under appropriate circumstances. If the diagnostic workup for pneumonia remains negative after cultures for usual pathogens are performed or if the initial suspicion for legionella infection is high, then an assay for urinary *Legionella* antigen should be done and culture of pulmonary specimens (BAL fluid and sputum) should be performed to preferentially isolate *Legionella* species. For infections due to non-*pneumophila* species of *Legionella*, culture is required to confirm the diagnosis, since the urinary level of antigen is specific only for *L. pneumophila*. If a diagnosis is not established after evaluation of an induced sputum specimen or BAL, early consideration should be given to lung biopsy. During this workup, prompt institution of empirical therapy for coverage of *Legionella* should be considered. With appropriate aggressive management, HIV-infected patients with *L. bozemanii* infection may fully recover without long-term sequelae.

References

9. Parker MM, Macher AM, Shelhamer JH, Peloux Y, Raoult D. *Rhodococcus equi* pneumonia occur with greater frequency in HIV-infected individuals than in immunocompetent individuals [12–14]. With more cases of advanced HIV disease, there will be an increased incidence of pneumonia caused by both *Pseudomonas* and other gram-negative organisms.