Fatal Acute Necrotizing Pneumonia in a Patient with HIV/AIDS

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CASE REPORT

A 31 year-old African-American woman with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) diagnosed 10 years prior (CD4 count = 6; viral load = 263,360/µL) was admitted to the hospital with new onset of altered mental status, fever, and a productive cough. Laboratories were significant for an elevated aspartate aminotransferase (AST) at 116U/L (<45), hypoalbuminemia at 1.5gm/dL (3.4-5.0) and hyponatremia at 132mmol/L (135-146). Notable was long-standing historical documentation of noncompliance with antiretroviral or prophylaxis therapeutic regimens. In the emergency room, she was given intravenous fluids and supplemental oxygen. She was pan-cultured and treated with broad spectrum antibiotics. She was admitted to the intensive care unit where she subsequently required intubation and blood pressure support. Later that day, hypotension became refractory and she developed pulseless electrical activity and then died. Antemortem blood and sputum cultures were negative. An unlimited autopsy examination was granted under coroner authorization.

At the time of autopsy, the decedent was noted to be cachectic with an estimated body weight of less than ninety pounds. A total of 200ml of semi-opaque and viscous fluid was found in the pleural cavities. The lung parenchyma was studded with well-delineated hemorrhagic and necrotic appearing lesions in all five lobes. The right ventricular cardiac chamber was dilated on initial apical cross section. All postmortem bacterial, acid-fast bacillus, and fungal cultures were negative. Representative microscopic images from the lung are demonstrated on the next page in Figure 1.

What is the diagnosis and which microbial organism is responsible?
Answer is on p. 44
Figure 1A: Representative histologic section from lung parenchyma demonstrating an intraalveolar exudate of neutrophils and fibrin associated with septal wall necrosis (40x, H&E)

Figure 1B: Silver stain from paraffin embedded lung highlighting numerous coccobacilli organisms. (40x, Steiner)
DISCUSSION

Legionnaires’ disease was discovered following a widely publicized epidemic of pneumonia that occurred in over 200 individuals at an American Legion convention in Philadelphia in 1976. Despite continuing to carry a reputation of being an exotic infection, the incidence of Legionella ranges from 2-15% of all cases of community-acquired pneumonia (CAP) and is now recognized as the fourth leading cause of CAP in the US. There are greater than 40 species and 60 serogroups of the Legionella bacteria, of which 18 can cause disease. The majority of the disease causing subtypes produce an acute necrotizing pneumonia and, as a group, these infections are properly referred to as the Legionella pneumonias or legionellosis. Common modes of transmission are inhalation of aerosol, ingestion, and micro-aspiration of contaminated water sources such as cooling towers, whirlpools, hot tubes and ice machines. The incubation period ranges from 2-10 days and the onset of symptoms is often abrupt. Among the 221 original epidemic cases in Philadelphia, 34 were fatal. The current overall incidence of legionellosis is difficult to ascertain and whether the disease is sporadic or nosocomial.

Following the incubation period, patients with legionellosis enter a prodromal phase lasting hours to days and characterized by fever, headache, myalgia, asthenia, anorexia and dry cough. Subsequently, severe pneumonia develops that is associated with an inflammatory sputum and exudative pleural effusions or empyema; a clinical picture that is similar to pneumococcal pneumonia. Extrapulmonary manifestations such as mental status change and diarrhea can also be seen; and are more likely to be seen in those with an underlying immunodeficiency. Liver function tests often indicate some hepatic dysfunction and hyponatremia has been documented. Several studies have investigated the ability for a clinical criteria system to detect cases of legionellosis based on clinical and laboratory parameters. However, the reliability of such systems has not been consistently reproducible. The patient detailed in the current case presented with the classic clinical features as well as laboratory parameters that have been attributed to Legionella pneumonia. In fatal cases of Legionnaires’ disease, death typically occurs during the acute phase of the infection with postmortem lung pathology confirming the confluent and necrotizing nature of the pneumonia; again much like the classic images included here.

The ability to diagnoses Legionella is limited not only by the nonspecific clinical presentation but also by the shortcomings of diagnostic testing, thus promulgating the importance of maintaining a high clinical index of suspicion. Growth in culture requires special media as well as technical expertise; and routine histologic stains hematoxylin and eosin or H&E fail to highlight the organism in tissue. Both silver impregnation stains and electron microscopy, however, successfully reveal the bacteria in tissue. Serologic assays are available but the reported sensitivities vary substantially from 40-94 percent. Detection of the Legionella antigen in urine is now a widely accepted and rapid diagnostic method with a specificity of >99 percent. Though the sensitivity ranges from 70-90 percent depending on which serogroup of L. pneumophila is present; it is highest for L. pneumophila serogroup 1, which is the causal subtype in >90% of Legionella pneumonia. Antigenuria can be detected as early as one day after onset of symptoms and persists for days to weeks. Recently, DNA detection techniques for legionellosis have shown promise but availability of molecular based techniques at the current time are neither widespread nor approved for clinical testing.

The inherent complexities in the diagnosis of legionellosis, as well as the nonspecific clinical presentation, undoubtedly suggest that Legionella infection is under recognized. As is customary for legionellosis, the current case demonstrates a severe and rapidly progressive pneumonia despite prompt and broad spectrum antibiotic therapy in the presence of negative cultures and no microorganisms on H&E stains in the postmortem lung tissue. Due to informed evidence-based clinical reasoning that was well-supported by published guidelines on CAP in adults, urine from the decedent was collected and submitted for the presence of the Legionella antigen prior to death. However, due to the rapidity of the patient’s demise, the results confirmed the antigenuria after death. As was anticipated, silver staining of paraffin embedded lung sections with Steiner stain confirmed innumerable organisms with a morphology consistent with that of Legionella (Figure 1B).

The microscopic pathology of the pneumonia due to legionellosis is one of acute necrotizing pneumonia with coagulation necrosis, microabscess formation, and alveolar septal wall destruction that results in foci of recent alveolar hemorrhage. Alveolar and bronchiolar exudate is fibrinous-purulent with neutrophils admixed with deposits of stringy fibrin and proteinaceous material. Silver stain methods confirm the coccobacilli.

In addition to contaminated water sources as a risk factor for Legionella, relative immunosuppression such as that which occurs with corticosteroid use also serves as an...
independent risk factor for infection. Somewhat surprising, however, is that Legionella has only been infrequently described among HIV-infected patients, with an incidence of less than 1-8 percent of pneumonias in retrospective case series. The lower than expected incidence may be partially due to patient receiving prophylaxis against Pneumocystis jiroveci with trimethoprim/sulfamethoxazole, which has activity against Legionella. Despite its rarity in the HIV community, several case series have established that legionellosis in association with HIV/AIDS is more severe, more often associated with extrapulmonary symptomatology, and carries an overall higher mortality rate at approximately 20-30 percent.

In conclusion, the current case of fatal legionellosis contributes to the unique attention given to CAP in HIV/AIDS patients, particularly those who are non-compliant with anti-retroviral or prophylaxis protocols. Though bacterial pneumonia remains more common in this population of patients, Legionella pneumonia carries with it a severe course and a poor outcome. Additionally, a high index of clinical suspicion is required, as was present in the case here, in order to confirm infection by one of the approved diagnostic modalities since routine culture and routine histopathology fail to identify the organism.

REFERENCES


Dr. Moss is a first year pathology resident and Dr. McGoey is an Associate Professor of Pathology and Residency Program Director in the Department of Pathology at Louisiana State University School of Medicine in New Orleans.

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