Plague in a Pediatric Patient: Case Report and Use of Polymerase Chain Reaction as a Diagnostic Aid

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We report a case of bubonic plague in a 7-year-old patient who presented with a core temperature of 107°F, seizures, vomiting, altered mental status, and septic shock. This case highlights the utility of polymerase chain reaction (PCR) as a diagnostic aid for rapid presumptive identification of Yersinia pestis as well as the importance of correlating PCR results with clinical data. We discuss the various manifestations of plague as they relate to infection control, postexposure prophylaxis, antimicrobial therapy, and treatment duration.

Key words. bubonic plague; infection control; pediatric; polymerase chain reaction; Yersinia pestis.

CASE REPORT

A 7-year-old, previously healthy girl from rural southwestern Colorado presented in August 2012 with 2 days of fatigue and subjective fevers followed by multiple episodes of emesis. There were no known ill contacts, but during the preceding 3 weeks she had played in a crawl space underneath the family’s new house and swept a dusty chicken coop that contained mouse droppings. Four days before onset of symptoms, the patient and her family picnicked at a nearby national forest campground, where she found and attempted to bury a dead squirrel with a stick.

On the day of admission she had multiple episodes of emesis followed by a generalized tonic-clonic seizure. Upon arrival to the local emergency room, she was confused, had a core temperature of 107°F, and a white blood cell (WBC) count of 12,200/mm³. Providers instituted cooling measures then transferred the patient to a tertiary hospital.

On admission to the hospital, the patient had intermittent delirium and visual hallucinations. Her exam was notable for clear breath sounds and the absence of nuchal rigidity or other signs of meningealism. She developed worsening tachycardia, tachypnea, and hypotension, consistent with septic shock, and was transferred to the Pediatric Intensive Care Unit. At that time, several insect bites were noted on both flanks. She was also noted to have a large, extremely tender left inguinal lymph node without overlying erythema. The patient held her left leg in an externally rotated position due to pain and discomfort.

Laboratory studies on admission were significant for WBC count of 13,700/mm³ with 62% neutrophils and 15% bands, hemoglobin of 13.5 g/dL, platelet count of 108,000/mm³, aspartate aminotransferase level of 69 U/L, and alanine aminotransferase level of 27 U/L. Laboratory findings were consistent with disseminated intravascular coagulation (D-dimer, 61,319 µg/L; fibrin split products, 160 mcg/mL; international normalized ratio, 2.3).

The patient did not have respiratory symptoms such as cough or shortness of breath. She was intubated for airway protection during a procedure requiring sedation. Chest radiographs demonstrated bilateral opacities compatible with fluid overload and dependent bilateral basilar opacities consistent with atelectasis. A noncontrast computed tomography (CT) scan of the head was normal. The results of cerebrospinal fluid (CSF) examination demonstrated 12
WBCs (10% poly-morphonuclear leukocytes, 67% lymphocytes, 23% monocytes), 497 red blood cells (RBCs), 57 mg/dL glucose, and 24 mg/dL protein.

Parenteral ceftriaxone was initiated empirically shortly after admission after blood and CSF studies were obtained. The patient was transitioned to parenteral vancomycin, meropenem, and acyclovir in light of her worsening clinical status. Gentamicin was added due to concern for *Yersinia pestis* infection (Figure 1).

Blood cultures collected at both the local hospital and the tertiary facility were positive for a gram-negative, bipolar-staining rod. Polymerase chain reaction (PCR) testing of the blood specimen from the tertiary facility conducted at the state public health laboratory using Laboratory Response Network real-time assays presumptively identified *Y pestis*. Subsequently, the organism was isolated from blood culture on agar plates and confirmed as *Y pestis* by bacteriophage lysis. Polymerase chain reaction tests conducted on tracheal aspirate and CSF specimens were also positive, whereas both specimens were negative by culture.

Despite initiation of gentamicin, the patient’s clinical status worsened over the next 48 hours and she required ongoing pressor support. Her WBC count peaked at 40,500/mm$^3$. By hospital day 5, she began to improve and was subsequently extubated and weaned off of pressors. Magnetic resonance imaging of the brain was negative for cerebritis or meningitis. During her hospital course, the patient also developed an elevated serum lipase (maximum 2077) but never had any clinical signs or symptoms of pancreatitis. She completed a 10-day course of gentamicin for treatment of bubonic plague and recovered completely.

An environmental investigation was conducted by the San Juan Basin Health Department (SJBHD) in collaboration with the Colorado Department of Public Health and Environment and National Forest Service staff to determine the infection source and implement prevention measures. The family had 3 indoor/outdoor cats that were reportedly healthy and had no signs of ectoparasites. There was no evidence of rodent die-off under or around the home.

Additional history revealed that at the national forest campground, the patient had taken off her sweatshirt and laid it on the ground next to the dead squirrel. When her parents called her away, she picked up the sweatshirt and wrapped it around her waist. Considering this history and the presence of insect bites on the patient’s trunk, we hypothesize she was infected by fleas that jumped from the dead, presumably plague-infected squirrel onto the sweatshirt. The SJBHD and National Forest Service staff surveyed the campground area and surrounding trails for

![Timeline of events](image)

**Figure 1. Timeline of events.**
signs of rodent die-off and posted warning signs for the public with prevention messaging. No rodent carcasses were found, and no distinct rodent burrows were identified from which fleas could be collected; however, chipmunks and squirrels that are usually common in that area were not seen on the ground during the investigation.

DISCUSSION

Plague, historically known as the “Black Death,” is caused by the bacterium Y pestis and has resulted in millions of deaths worldwide since the Middle Ages. Plague is a rapidly progressive disease that causes significant morbidity and has a high mortality rate if not treated promptly [1]. Although the number of US cases has decreased since the 1930s, plague continues to infect humans sporadically—from 1990 to 2010, there were 1–17 reported cases of plague per year (median 7) in western states [2]. The public health importance of plague is heightened since it has been used historically as a biological weapon and continues to be a bioterrorism threat.

The 3 primary forms of plague are bubonic (approximately 80% of US patients present this way), septicemic, and pneumonic. Additional, less common manifestations include cutaneous, pharyngeal, and meningeal disease. Although human-to-human transmission of plague is rare, it has occurred when patients in the late stages of pneumonic disease cough bloody sputum near close contacts [3]. Due to the potential for human-to-human transmission, the Centers for Disease Control and Prevention recommends that patients with documented pneumonic disease be placed on droplet precautions until patients have received 48 hours of appropriate antimicrobial therapy [4].

Meningitis may develop in 0.2%–7% of all patients and up to 11% of children with plague [5, 6]. Although meningitis can be a primary manifestation, it has been typically reported >1 week after initial infection in patients who received delayed or inadequate treatment. Younger patients and those with axillary buboes appear to be at greater risk for plague meningitis [7, 8]. The recommended treatment for plague meningitis is chloramphenicol for a minimum of 10 days.

Yersinia pestis can be presumptively identified via direct testing of clinical specimens using immunofluorescence or PCR assays. Real-time PCR of lymph node aspirates from patients in Madagascar with bubonic plague was shown to be 81% sensitive and 100% specific [9]; there is little information on performance of real-time PCR for other clinical specimens such as blood and CSF. Plague is typically confirmed by culture of blood or bubo aspirate. Sputum and tracheal aspirates may be cultured in patients with pneumonic plague. A Y pestis-specific fraction 1 capsular (F1) antigen test is available for rapid identification of culture isolates [10]; clinical trials are under way to determine its usefulness for direct testing of clinical specimens [2]. In the patient described, initial Gram stain of blood cultures suggested Y pestis, whereas PCR provided rapid presumptive identification of Y pestis as the cause of illness (although gentamicin was already begun based on clinical suspicion). The patient’s CSF was PCR positive, but her clinical presentation, normal CT and MRI, and negative CSF culture were not consistent with meningitis. Seizures and altered mental status on admission were likely due to extremely high body temperature and septic shock. Therefore, the treatment team decided not to initiate chloramphenicol for treatment of plague meningitis. Likewise, the patient’s tracheal aspirate was PCR positive, but her clinical presentation, imaging studies, and negative respiratory culture were not compatible with pneumonic plague. Accordingly, postexposure prophylaxis was not deemed necessary for the family or healthcare workers. Our patient was initially placed on droplet and contact precautions based on clinical suspicion that were discontinued after 48 hours of therapy.

There are several hypotheses why the tracheal and CSF PCR tests were positive without associated clinical signs of disease or positive cultures. These include contamination of the CSF specimen with bacteremic blood when specimens were drawn (RBCs were observed in the CSF), suboptimal transport of specimens leading to nonviable organisms, laboratory contamination during testing (although unlikely due to strict workflow and cleaning protocols), or infection with a small number of viable organisms that did not cause local disease and were not readily cultivable as blood (high threshold cycle values for both the CSF and tracheal aspirate indicated a low concentration of target in these specimens). In addition, meropenem is active against Y pestis in vitro and was given before the tracheal aspirate was obtained [11]; thus, pretreatment could have affected viability of any organisms that may have been present in respiratory secretions. As with any infectious agent, clinical samples obtained after treatment can be positive by PCR but negative by culture.

In this report, we highlight the utility of PCR as a diagnostic aid for rapid presumptive identification of Y pestis. This case also illustrates that PCR results may complicate clinical management and infection control decisions when they are discordant with the clinical picture. Diagnosis of pneumonic or meningeal plague has significant implications on infection control, postexposure prophylaxis for contacts, choice of antibiotic for patients, and treatment duration. Therefore, although it is essential to exercise caution with this serious disease, healthcare providers and
infection control practitioners should also correlate PCR results with the clinical picture.

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References

2. Centers for Disease Control and Prevention surveillance data, unpublished data.