

CLINICAL VIGNETTE

Murine Typhus in a Patient with Hoarding Disorder

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Case

A 76-year-old female with no significant medical history was admitted from the emergency department with 3 days of altered mental status, generalized weakness, and fever. The patient was brought in by her son, who provided the initial history. He reported the patient had been in her usual state of health until 4 days prior, when she vomited, which she felt was secondary to a foodborne illness. Over the ensuing days, she had decreased oral intake and gradually became more confused, thus prompting her evaluation. Further discussion with the family revealed that the patient was a hoarder and lived in an apartment separate from her husband and son. She frequently ate spoiled food, and her living quarters were unsanitary with dirty dishes and spoiled food scattered throughout the residence. She adopted numerous stray cats and had been bitten a week prior to presentation.

On admission, the patient was febrile to 38.8°C with otherwise normal vital signs. On physical exam, she appeared frail, disheveled, and somnolent with dry mucous membranes. She had no palpable lymphadenopathy and no nuchal rigidity or meningismus. Cardiopulmonary and abdominal exams were unremarkable. On neurologic exam, she was alert but oriented only to person and place and was able to follow simple commands. She had difficulty completing the cranial nerve exam and neurologic testing due to poor concentration. She was also unable to stand and bear weight without assistance. Skin exam was remarkable for extensive erythematous patches over the knees, breasts, and back bilaterally. She had dirty hands and feet, numerous superficial scratches over her forearms, and a large blister on her right lateral breast. Admission testing was notable for hyponatremia of 122 with urine Na < 20, AST 62, and ALT 32. Initial labs, including CBC with differential, were otherwise unremarkable. Chest X-ray, CT of the head, abdomen and pelvis were negative. Patient was admitted and started on empiric antibiotics with vancomycin and piperacillin-tazobactam.

Despite broad-spectrum antibiotics, the patient continued to experience delirium and cyclical nightly fevers as high as 40 degrees Celsius. Further testing was notable for a CK elevation of 568, procalcitonin of 1.41, and a C-reactive protein of 3.2. CT sinus and MRI brain with and without contrast to assess for potential occult infection and were both unrevealing for a potential source. Lumbar puncture was significant for mildly elevated CSF glucose of 88 mg/dL; with normal protein and cell count. CSF gram-stain, bacterial and fungal cultures, and

meningitis-encephalitis PCR panel were all negative. Further infectious studies were obtained, including serum Coccidioides and Bartonella serologies, Cryptococcal antigen, CMV PCR, and a viral hepatitis panel.

Infectious disease was consulted on hospital day 3 given ongoing fevers and recommended serum *Coxiella burnetii* and Rickettsial titers. Additional discussion with the patient's family revealed that the multiple stray cats, frequently brought dead rodents into the home, which the patient removed with her bare hands. Given this information and ongoing fevers, antimicrobial therapy was adjusted. Vancomycin and piperacillin-tazobactam were discontinued, and doxycycline started. Within 24 hours, the patient defervesced and had complete resolution of her encephalopathy. She was discharged on hospital day 5 to complete a 7-day course of doxycycline. Following discharge, the Rickettsia Typhus serum titer resulted positive at >1:256, thus confirming a diagnosis of murine typhus.

Discussion

Murine typhus is caused by *Rickettsia typhi* (*R. typhi*) a gram-negative, obligate intracellular bacterium. Transmission most commonly occurs via the rat flea, however additional vectors include arthropods such as cat fleas and ticks, in addition to small vertebrates.¹ The life cycle is comprised of mammalian hosts and arthropod vectors. The bacterium multiplies in the epithelial cells of the flea's midgut and is shed in the feces.² Transmission to humans occurs most frequently via self-inoculation from the feces of fleas in bite wounds or by scratching.¹

Incubation ranges between 8-16 days, with infection typically causing a mild illness that abruptly causes nonspecific symptoms including fever, headache, rash, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain), and myalgias. The classic triad of fever, headache, and rash is reported in 35-49 percent of patients.^{3,4} The rash is most commonly maculopapular in nature, originating on the trunk with peripheral spread (sparing palms and soles).² While most cases are mild, severe disease may develop in untreated patients and may include several systems. Neurologic signs include confusion, facial paralysis, abducens nerve palsy, and meningo-encephalitis or meningitis. Other signs include relative bradycardia, electrolyte derangements, and pulmonary manifestations.⁵ Splenomegaly and ocular manifestations are less

common, though have been documented in untreated murine typhus.⁵

Lab findings are also nonspecific. Thrombocytopenia is common, reported in 40% in one series, with typical white blood cell count.⁶ Other common findings include hyponatremia, hypoalbuminuria, elevated creatine kinase levels, and elevated transaminases.³ Meningitis and meningoencephalitis have been reported in patients with murine typhus, though more often nonspecific CSF abnormalities are found.⁷

Most patients with murine typhus recover spontaneously, however, antibiotics significantly shorten the duration of illness and reduce the likelihood of complications.^{3,8,9} Empiric treatment is thus recommended in all patients suspected to have murine typhus, with doxycycline as the preferred agent of treatment. The optimal duration of treatment is unclear, though patients are generally treated with doxycycline for at least 48 hours after defervescence or for seven days total, whichever is longer. In a systematic review of treatment in 1135 patients, the median time to defervescence was 1.5-4 days in patients who received a tetracycline-containing regimen, versus 12-21 days in untreated patients.³ Alternative regimens include azithromycin, chloramphenicol, and ciprofloxacin.

This case demonstrates many of the classic epidemiologic, clinical, and laboratory findings of severe murine typhus. In addition, it exemplifies the importance of a thorough history as key to accurate diagnosis, and appropriate treatment.

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