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CLINICAL VIGNETTE

Murine Typhus: A Cause of Unexplained Fevers in Los Angeles

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Introduction

Murine typhus is a vector-borne bacterial infection caused by *Rickettsia typhi*. It presents with non-specific symptoms including fever, headache, myalgias, and rash. Because murine typhus is uncommon, with non-specific symptoms it is easily mistaken for a viral illness and can be challenging to diagnose. Los Angeles is one of the main US locations with this disease, so physicians should be familiar with it.

Case Summary

A healthy 35-year-old female presented with two weeks of fevers and chills. At the start of her illness, she had fevers, chills, and back pain. She then developed a severe headache that became worse at night, along with a mild sore throat. Over the next week, she had daily fevers up to 102°F, resolving with acetaminophen. She also had some associated nausea, mild cough, neck stiffness, and a single episode of diarrhea.

The patient presented to the emergency room after one week of fevers and bloodwork was notable for a low lymphocyte count, mildly elevated AST of 63, and elevated CRP of 7.0. Blood cultures, urine cultures, COVID testing, respiratory virus testing, Lyme testing, and parasitic testing were all negative. Group A strep test was positive and she was prescribed amoxicillin. She continued to have fevers despite taking the amoxicillin and presented to primary care on day twelve of illness.

Her history in clinic revealed no recent travel, no new sexual exposures, and a single sick contact with her sister who had strep throat the month before. The patient had a dog at home but no other animal exposures. Her physical examination was unremarkable except for a faint pink maculopapular abdominal rash.

Testing in clinic revealed a new significant increase in liver enzymes with AST of 335, ALT of 465, and alkaline phosphatase of 224. She also had a rise in increased CRP to 11.5. Additional testing was ordered, including iron stores that showed an elevated ferritin of 294 with 5% iron saturation. Other testing was normal: hepatitis A IgM, hepatitis B antigen, hepatitis C antibody, HIV PCR, CMV IgG/IgM, RPR, toxoplasmosis IgM, HSV-1 and 2 PCR, MTB-quantiferon gold, CK, ANA, RF, dsDNA, anti-liver kidney microsome IgG, anti-smooth muscle antibody, and blood cultures, EBV IgG was positive, with negative EBV IgM. Monospot testing was not available.

Infectious disease was electronically consulted and recommended empiric treatment for rickettsial diseases, specifically murine typhus, with doxycycline 100mg BID. Within 48 hours after starting antibiotics, her fevers resolved, and she felt much better, with gradually improved headaches.

Additional lab work was recommended by infectious diseases. It included positive *R. typhi* IgG and IgM at >1:256, and Rocky Mountain Spotted Fever (RSMF) IgG and IgM positive with an RSMF IgM of 1:64. Other testing recommended by infectious diseases, included negative enterovirus PCR and leptospira IgM.

Although this patient had no known exposures to cats or rats with fleas, she had classic symptoms in an endemic area. The rapid resolution of symptoms with doxycycline, and the positive *R. typhi* titers, confirmed the diagnosis of murine typhus.

Discussion

Murine typhus is an infectious disease caused by *Rickettsia typhi*, a gram-negative intracellular bacterium. The disease is mainly transmitted by rat fleas, though it can also be transmitted by cat or mouse fleas. The fleas are infected with *R. typhi* and transmit the disease to humans through infected flea feces in bite wounds.¹ Murine typhus can be prevented with flea control measures for pets, particularly domesticated cats.¹

Most murine typhus cases occur in areas with large rat populations, with the majority of U.S. cases reported in Texas, California, and Hawaii. In Los Angeles, domestic cats, opossums, and cat fleas maintain the life cycle of *R. typhi*.^{1,2} There have been many outbreaks in Los Angeles County, which accounts for 42-90% of the cases in California.¹ L.A. County cases increased from 31 in 2010 to 171 in 2022, including three deaths.^{2,3} These reported numbers are lower than the true incidence, as most patients are unaware of flea bites, and the presenting symptoms can easily be mistaken for a viral illness, as cases often resolve spontaneously. It is estimated that fewer than one-third of flea-borne typhus cases are ever diagnosed.³ Because fleas propagate more successfully in hot, dry environments, most California cases are reported in the summer and fall.¹ This case presented in January and serves as a reminder that in Los Angeles murine typhus can appear year-round.

Murine typhus typically causes a mild illness with fever, headache, and early arthralgias. Patients may also develop nausea, vomiting, and diarrhea. A faint maculopapular rash may occur around one week into the illness, although rash reports range from 20-80% of cases.¹ The rash is typically on the trunk and spreads peripherally, sparing the palms and soles. The classic triad of fever, headache, and rash only occurs in one-third of patients.⁴

Laboratory findings in murine typhus also tend to be non-specific. Nearly half of patients have thrombocytopenia, and mild leukocytosis or leukopenia may occur. Hyponatremia, hypoalbuminemia, and transaminitis are often present.⁴

Although this disease is typically mild and limited, severe manifestations can occur – including renal, hepatic, pulmonary, cardiac, and neurologic dysfunction.⁵ In Los Angeles County, about one-third of infected patients have ICU care for associated aseptic meningitis, seizures, acute respiratory distress syndrome, or septic shock.² Mortality rates are around 4% in untreated disease compared to <1% when treated. Thus it is important to recognize and treat the illness.^{1,2} Even mild untreated cases have 15 days mean duration of fever with possible severe headaches.³

The diagnosis of murine typhus is clinical, based on symptoms. Because titers take a long to result and can be low early in the illness, empiric antibiotics should be started if murine typhus is suspected. This shortens the duration of the illness and reduces mortality.^{2,5} As with other rickettsial illnesses, the treatment of choice is doxycycline 100mg BID, which should continue for 7 days and at least 48 hours after defervescence.⁶

While improvement in symptoms and defervescence alone is likely diagnostic, it is important to serologically confirm the diagnosis with antibody testing. A four-fold rise in IgG over two weeks or a positive IgM confirms the diagnosis.⁷ In our patient, RMSF IgG/IgM were also positive. Other rickettsial antibodies also can cross-react with the *R. typhi* antibodies.⁶ Given that there is not much RMSF in Los Angeles, but murine typhus is endemic here, it was reasonable to conclude this patient was falsely positive secondary to cross-reactivity.

Conclusion

Murine typhus should be suspected in patients presenting with otherwise unexplained fever, headache, maculopapular rash sparing the palms and soles, transaminitis, and thrombocytopenia. Given the non-specific presentation, the disease is challenging to identify and easy to misdiagnose. Murine typhus should be considered in the differential of a patient with these symptoms, particularly in an endemic area like Los Angeles. Increased awareness of the disease prevalence in L.A. County and early initiation of doxycycline treatment in suspected cases is needed for prevention and treatment.

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