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Murine Typhus: A Life-Threatening Presentation of a Case in Galveston, Texas

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Christopher Perez**
B 2 **Diaa Hamouda**
FG 1 **Bernard Karnath**

1 Department of Internal Medicine, University of Texas Medical Branch (UTMB), Galveston, TX, U.S.A.
2 Department of Neurology, University of Texas Medical Branch (UTMB), Galveston, TX, U.S.A.

Corresponding Author: Christopher Perez, e-mail: chrperez@utmb.edu
Conflict of interest: None declared

Patient: Male, 22
Final Diagnosis: Murine typhus
Symptoms: Fatigue • fever • headache • malaise • nosebleed • rash
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare disease
Background: Murine typhus is a rare bacterial infection caused by *Rickettsia typhi*, which is transmitted from rodents to humans through the infected *Xenopsylla cheopis* flea. The disease presentation is often non-specific, leading to unnecessary tests, and a delay in diagnosis and treatment.
Case Report: A report is presented of a 22-year-old, previously healthy man, who presented with several symptoms and signs that increased in severity, requiring admission to the medical intensive care unit (MICU). After an extensive bacterial and viral laboratory workup, IgM and IgG titers confirmed the diagnosis of murine typhus due to infection by *Rickettsia typhi*. The patient was treated with doxycycline, which resulted in significant clinical improvement.
Conclusions: Murine typhus can present with a characteristic triad of fever, headache, and rash but also with other symptoms and signs and can vary in severity. Given its increasing prevalence in coastal cities, awareness of this infection and early diagnosis and treatment with doxycycline can reduce patient morbidity.

MeSH Keywords: Bacterial Infections • Doxycycline • *Rickettsia typhi* • *Xenopsylla*

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Background

Murine typhus is an infection caused by the *Rickettsia typhi*. It is typically transmitted from rodents to humans through the bite from an infected *Xenopsylla cheopis* flea. Murine typhus can present with a characteristic triad of fever, headache, and rash but also with other symptoms and signs that can vary in severity, including myalgia, arthralgia, nausea, vomiting, and occasionally with neurological symptoms including confusion. The classic triad of fever, headache, and rash, which is the hallmark of the murine typhus occurs in only one-third of the patients [1].

Murine typhus occurs more commonly in the coastlines states of California, Hawaii, and Southeast Texas. Although murine typhus is rare, it is important to recognize because the symptoms and signs can vary and can be initially diagnosed as due to viral infection, resulting in a delay in treatment. Early diagnosis of murine typhus and early treatment with doxycycline leads to a reduction in morbidity and rapid recovery [1]. This report presents a rare case of murine typhus in a 22-year-old man in Galveston, Texas, USA.

Case Report

The patient was a 22-year-old Hispanic man with no significant past medical history who presented to the emergency department with a two-week history of intermittent fevers, headache, fatigue, malaise, nausea, vomiting, occasional episodes of diarrhea, and nosebleeds. He also reported having a non-productive cough, sore throat and stated his headache was associated with light sensitivity. Three to five days before admission to the hospital, he developed a rash that began over his thighs and spread to involve the skin of his entire body. There was no history of shortness of breath, chest pain, bloody stools, or neck stiffness.

He was previously healthy and had recently begun working as a taxidermist, three days before presentation. There was no history of regular medication use or allergies. At home, he had a cat and two dogs, which he believed might have had fleas. He claimed that he had also seen rats in his home, although this was not confirmed.

In the emergency department, the patient was afebrile, his blood pressure was 97/47, his pulse rate was 136 beats per minute, and his respiratory rate was 22 breaths per minute. On physical examination, he was found to have a petechial rash on his trunk, and upper and lower extremities (Figures 1, 2). There was no nuchal rigidity.

Laboratory tests showed that he was hyponatremic with sodium of 126 mmol/L (Normal range: 135–145 mmol/L), blood

Figure 1. A 22-year-old man with life-threatening infection due to murine typhus (*Rickettsia typhi*). The patient's presenting signs included a generalized skin rash. The image shows petechiae in the skin of the left leg.

Figure 2. A 22-year-old man with life-threatening infection due to murine typhus (*Rickettsia typhi*). The patient's presenting signs included a generalized skin rash. The image shows petechiae in the skin of the right thigh.

urea nitrogen (BUN) and creatinine were elevated at 111 mg/dL (Normal range: 7–23 mg/dL) and 3.14 mg/dL (Normal range: 0.60–1.25 mg/dL), respectively. His liver enzymes were also elevated, and included aspartate transaminase (AST) of 421 U/L (Normal range: 13–40 U/L), alanine aminotransferase (ALT) of 135 U/L (Normal range: 9–51 U/L), and alkaline phosphatase (ALP) of 158 U/L (Normal range: 34–122 U/L). He also had an elevated D-dimer of 17.55 micrograms per milliliter (Normal value: <0.41 µg/mL), a low fibrinogen level of 94 mg/dL (Normal range: 214–470 mg/dL), and an elevated lactic acid of 2.34 mmol/L (Normal range: 0.50–2.20 mmol/L). His platelets were low at 35,000 per mm³ (Normal range: 150,000–400,000 per mm³), and his white blood cell count (WBC) was elevated at 13,830 per mm³ (Normal range: 4,300–10,800 per mm³). The patient was diagnosed with severe sepsis with disseminated intravascular coagulation (DIC). He was admitted to the medical intensive care unit (MICU) where vancomycin and ceftriaxone treatment were begun due to concerns for possible meningococemia. A lumbar puncture was unable to be performed at the time due to his thrombocytopenia.

The patient was stabilized and seen by an infectious diseases specialist on the day after admission, who suggested a

differential diagnosis that included a possible viral infection, ehrlichiosis, or murine typhus. Further laboratory tests included serological tests, including: Epstein-Barr virus (EBV) viral capsid antibody (EBV VCA), IgM, and IgG antibodies; parvovirus serology, including IgM and IgG antibodies; and a molecular assay for Ehrlichial DNA, which were all negative. *Rickettsia typhi* titers for IgM and IgG were also requested a day after admission, and these were positive. Vancomycin was changed to doxycycline to treat *Rickettsia typhi* infection. The hematology service was consulted for management of his coagulopathy, who suggested administration of cryoprecipitate to maintain his fibrinogen levels above 150 mg/dL. No red blood cell fragments (schistocytes) were seen on the peripheral blood smear, and so DIC at this stage was excluded. The patient's fever resolved following treatment with doxycycline. He was hemodynamically stable enough for transfer out of the MICU by the third day of hospitalization.

Five days following hospital admission, a repeat infection work-up showed residual high *Rickettsia typhi* serum antibody titers including IgM 1: 2048 (Normal value: <1: 64), and IgG of 1: 512 (Normal value: <1: 64), confirming infection with *Rickettsia typhi* with continued negative serology for other infections. The patient remained solely on oral doxycycline 100 mg twice per day for five days. He was discharged after an improvement in his symptoms.

Discussion

Murine typhus is caused by infection with *Rickettsia typhi* and can present with a variety of symptoms and signs. The hallmark triad of fever, headache, and rash occurs in only one-third of patients, and in most cases, the rash is macular or maculopapular, located on the trunk, and spreads outward with sparing of the palms and soles [1]. Other common symptoms include malaise, chills, myalgia, anorexia, arthralgia, nausea, and vomiting [1]. Laboratory abnormalities characteristic of murine typhus can include elevated liver enzymes, elevated lactate dehydrogenase (LDH), hypoalbuminemia, an increased erythrocyte sedimentation rate (ESR), thrombocytopenia, increased alkaline phosphatase (ALP), and hyponatremia [1].

Since 2012, there has been a re-emergence of murine typhus in Galveston, Texas in the USA. This re-emergence of murine typhus is believed to be due to increasing transmission from cat and opossum fleas. A recent study of 12 opossums found that eight had the presence of anti-*Rickettsia typhi* antibodies, and all 12 opossums had fleas, supporting the possibility that opossum fleas play a role in the city's recent resurgence of murine typhus [2].

The diagnosis of murine typhus is usually based on clinical assessment in the context of the appropriate epidemiologic setting. A complete history is essential to determine whether the

patient has been around animals, exposed to any fleas, traveled recently to a coastal state, or lives in an area where the disease is prevalent [1,3]. Careful clinical examination of the skin in patients with murine typhus will usually detect a rash that is macular or maculopapular, located on the trunk and that spares the palms and soles [1]. The differential diagnosis of a fever, headache and rash is broad, and includes infection from viruses, bacteria, spirochetes, and rickettsia, as well as non-infectious causes, including drug reactions [1,3]. Detection of serum IgG antibodies to *Rickettsia typhi* by an indirect fluorescent antibody (IFA) test is commonly used (Normal value: <1: 64) with a fourfold antibody titer rise in convalescent serum samples being diagnostic [4,5].

Treatment with tetracyclines have been shown to reduce the duration of the disease significantly, and other antibiotics used include chloramphenicol particularly in pregnant women. Murine typhus can be a self-limiting illness, and the typical duration of fever without treatment can range from 12–21 days [1]. Treatment with doxycycline has been shown to reduce the duration of fever to 1.5–4 days, while chloramphenicol treatment reduced the duration of fever to 2.5–4 days [1]. Therefore, early diagnosis and treatment of murine typhus with doxycycline reduces morbidity and leads to faster patient recovery.

Conclusions

Murine typhus, due to infection from *Rickettsia typhi*, is a condition that occurs in coastal cities of the USA, including in Hawaii, California, and Southeast Texas. Murine typhus can present with a range of symptoms with varying disease severity, ranging from a self-limiting illness to a severe life-threatening infection in approximately 10% of cases. Because of its non-specific symptoms, the diagnosis of murine typhus is often delayed. The previously described clinical triad on presentation of fever, headache, and rash only occurs in one-third of patients. In areas where murine typhus occurs, or in patients who have recently traveled from US coastal cities, healthcare providers should be aware of this condition and include it in their differential diagnosis in patients presenting with non-specific findings, including in patients who present when critically ill. Early treatment with doxycycline can decrease the duration of illness and can be life-saving.

Department and Institution where work was done

Department of Internal Medicine, Division of General Medicine, University of Texas Medical Branch (UTMB), Galveston, TX, U.S.A.

Conflict of interest

None.

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