OSP Journal of Pediatrics

Case Report

Murine Typhus Presenting with Generalized Tonic-Clonic Seizures in a Pediatric Patient

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Received: August 23, 2020; **Accepted:** August 28, 2020; **Published:** September 08, 2020

Abstract

Though rare in the United States, murine typhus is still relatively common in endemic regions including South Texas and California. Due its non-specific, diverse clinical presentation and prevalence in endemic regions, it's exceedingly important to recognize MT for timely treatment with doxycycline and prevention of further complications. We report a case of murine typhus in a 7 year-old male who presented with a generalized tonic-clonic seizure secondary to hyponatremia.

Key Terms: Murine Typhus; Seizures, Generalized Tonic-Clonic; Pediatrics

Introduction

Murine typhus (MT), also known as endemic typhus, is a flea-borne disease caused by *Rickettsia typhi,* a gram-negative, obligate intracellular bacteria [1, 2]. The bacterium is transmitted by the oriental rat flea, *Xenopsylla cheopis*, the cat flea, *Ctenocephalides felis*, and the mouse flea, *Leptopsylla segnis* [3]. Children and adults can become infected when flea feces contact damaged skin or mucous membranes. Common reservoirs include rats, opossums, feral cats, and household pets [4]. The bacteria incubates for 6-14 days before causing a systemic vasculitis [4].

MT commonly presents as febrile illness with associated symptoms of headache, nausea, rash, chills, myalgias, and anorexia [1]. A classic triad of fever, headache, and rash has been described, although it may only be present in 1/3 of patients [5]. Though rare, reported complications include bronchiolitis, pneumonia, meningitis, septic shock, cholecystitis, pancreatitis, myositis, and rhabdomyolysis [2]. Associated laboratory findings include elevated erythrocyte sedimentation rate, elevated serum transaminases, hyponatremia, thrombocytopenia, elevated lactate dehydrogenase, hypoalbuminemia, and elevated band count with normal total white blood cell count [6].

Case Presentation

The patient was a 7-year-old male who presented to the Emergency Department (ED) with a three-day history of vomiting, diarrhea, abdominal pain, fever, and one seizure episode. Past medical history included left hydronephrosis secondary to vesicoureteral reflux. His initial symptoms were fever, 3-5 daily episodes of non-bloody, non-bilious emesis with associated headaches, and 5 daily episodes of non-bloody, non-mucoid, foul smelling diarrhea. On the day of presentation, a caretaker observed the patient having a generalized tonic-clonic seizure lasting 5 minutes, followed by a 20-minute period of confusion. There was no history chest pain, shortness of breath, cough, congestion, earache, sore throat, hematuria, dysuria, neck stiffness, or recent travel.

The patient was previously healthy and lived at home with his parents, grandparents, and dogs who are positive for fleas. His parents reported he was active and played multiple sports, with no regular medication use and no known allergies. He visited a waterpark 4 days prior to symptom onset.

The patient was evaluated in the ED during his post-ictal state and was found to have hyponatremia (122 mEq/L) and a fever of 105 °F. Two 500mL boluses of 0.9% normal saline (NS), Zofran, and Tylenol were administered. Initial workup was significant for leukocytosis (20,500/mm3) with neutrophil predominance (82%), thrombocytopenia (147,000/mm3), hypochloremia (89 mEq/L) and bicarbonate of 17 mEq/L. Urinalysis showed mild proteinuria (30mg), trace blood without RBCs, and mild ketonuria. Gastroenteritis PCR panel, fecal WBC, and urine drug screen were negative. A CT scan of the head showed no intracranial abnormalities.

The patient was transferred to a pediatric ED for higher level of care. Physical exam was positive for dry mucous membranes, cracked lips, and dry skin. No rashes or other skin abnormalities were noted. Repeat CMP showed normal Na (135 mEq/L), K (3.7 mEq/L) and Cl (101 mEq/L), low bicarbonate (15 mEq/L), and hypoalbuminemia (3.2 g/dL). Patient was started on maintenance IV fluids with D5% 0.9% NS, and was admitted to the inpatient hospitalist for further management and observation.

Initially, differential diagnosis included acute gastroenteritis, urinary tract infection, and MT. Urine culture was positive for *Enterococcus Faecalis* and the patient was started on on ampicillin. Despite 48 hours of anti-pyretics and ampicillin for a UTI, the patient remained febrile with persistent diarrhea, emesis, abdominal pain. Due to persistent diarrhea and emesis the patient had mild hypokalemia treated with oral and IV potassium repletion.

After a comprehensive negative work-up, clinical suspicion for murine typhus was high due his fevers, initial labs showing hyponatremia, hypoalbuminemia, and thrombocytopenia, exposure to fleas, and residence in South Texas. The patient was started empirically on Doxycycline. Soon after, the Rickettsial panel resulted in positive IgM titers (1:64), with negative titers for *Rickettsia Rikettsi*.

24 hours following initiation of Doxycycline, the patient defervesced and remained hemodynamically stable. He was discharged with Doxycycline 30mg twice daily for a total of 7 days and Amoxicillin 400mg three times daily for 5 days with instructions to follow up with his PCP.

Discussion

While rare, murine typhus is endemic in select regions of the United States that have warm, coastal climates such as South Texas and California. While historically associated with transmission by the rat flea, *Xenopsylla cheopis*, MT spread by rats has drastically decreased with sanitation and vector control efforts in the United States. Blanton et al. have identified opossums as an important reservoir for the cat flea, *Ctenocephalides felis* in outbreaks in Galveston, TX [8]. Feral cats and domesticated dogs have also been reported as significant reservoirs in endemic regions of Texas [9]. Thus, it is exceedingly important to obtain a detailed history regarding animal exposure and outdoor activity in febrile children with an unknown etiology. We suspect that our patient was infected by *Rickettsia typhi,* transmitted by fleas from his pet dog based on history.

Based on a review of literature, presentation of MT differs between children and adults. The pediatric clinical presentation of MT more commonly includes abdominal pain, diarrhea, and rash [2]. In regards to differences in laboratory findings, Tsioutis et al. reported a tetrad of anemia, elevated ESR, liver transaminases, and lactate dehydrogenase associated with children [5]. Fergie et al. noted similar findings in their pediatric study though hypoalbuminemia was observed more frequently than anemia [6]. Fergie et al. also found a high frequency of elevated bands with normal leukocyte counts, hyponatremia, hypokalemia, and thrombocytopenia in their pediatric patients [6]. Thus, there are disparities among studies regarding findings in pediatric populations.

This patient presented with lab findings consistent with MT including hypoalbuminemia, hyponatremia, elevated WBC, and CRP. He did not have elevated transaminases or LDH, which are the two most common laboratory findings in pediatric patients [5] He also did not have the characteristic maculopapular rash, although this finding was present in only 47.3% of patients [5].

Symptom-wise, this patient presented with fever, vomiting, diarrhea and a generalized tonic-clonic seizure. We hypothesize that the hyponatremia secondary to MT, which was exacerbated by vomiting and diarrhea, caused the seizure in our patient. Hyponatremia, vomiting, and diarrhea can all be seen with MT, and pediatric patients present more frequently than adults with vomiting (22.5%) and diarrhea (27.5 %.).5 Headache and confusion were the most frequently reported neurological sequelae, with rare cases reporting seizures. Simon et al. reported rare case of MT in an adult patient who presented with seizure activity and aseptic meningoencephalitis in the absence of typical typhus-like symptoms [10]. Shafi and Hipolito also reported a case of MT in a 31-year-old patient who presented with two generalized tonic-clonic seizures but normal serum sodium that resolved following abortifacient and antibiotic therapy [11].

The diagnosis of typhus is often difficult due to its rarity and complexity of findings. Fergie et al. found misdiagnosis included Kawaski disease, influenza, acute gastroenteritis, and acute appendicitis, which led to a delay in diagnosis and treatment [6]. The early recognition and treatment of MT is associated with shorter hospital stays and better outcomes [6]. In our patient, diagnosis was delayed due to his atypical presentation of primarily vomiting and seizures, and concurrent UTI.

The first line treatment for MT is doxycycline, oral or intravenous, which should be started empirically with high clinical suspicion [12]. It is important to note that other common antibiotics such as penicillins, cephalosporins, and sulfonamides are not effective for treatment [12]. Per the CDC, MT is generally diagnosed by serologic tests using immunofluorescent assays to detect IgM or IgG antibodies [13]. The diagnosis is confirmed by a four-fold rise in antibody titers between an acute sample, taken during the first week of illness, and a convalescent sample, taken 2-4 weeks later [13]. IgG antibodies are considered more specific though they not become detectable until 7-10 days after the onset of the illness [13]. Thus, the timing of serology is important to consider in the advent of a negative result despite high clinical suspicion. Additionally, the IgG antibodies to typhus may persist for several years so it is important to confirm an acute change as clinicians may forgo the convalescent titer if the patient improves clinically [13].

Conclusion

The diagnosis of MT may be difficult and delayed, such as with our patient, due to non-specific lab findings and atypical presentations in pediatric populations. While rare reports describing seizures secondary to MT in adults have been reported, there is no literature describing the phenomenon of seizure activity in MT pediatric patients. Thus, it is important to consider MT in children who present with a non-specific syndrome of fever, seizures, and hyponatremia of unknown etiology, especially in endemic areas.

Acknowledgements

The authors would like to thank the Department of Pediatrics at Driscoll Children's and the Texas A&M College of Medicine.

Disclosure Statements:

The authors report no conflicts of interest.References

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