

## **Acute Fever, Rash, Headache and Vomiting in a 13-Year-Old Male.**

Marcela Svojsik MD, University of Florida

Mary Katherine Scott Siebenaler MD, University of Florida

### **Case Report**

A previously healthy 13-year-old male presented to the emergency department for evaluation of four days of fever (maximum temperature 101.4 F), abdominal pain, non-bloody and non-bilious emesis, diarrhea, and one day of rash. The abdominal pain was mild in severity, diffuse, and not worsened by movement. Stools were loose, watery, and non-bloody. One day prior to admission (the fourth day of illness), he developed a non-pruritic, erythematous, raised rash on his abdomen that spread to his chest and proximal extremities, but spared his palms and soles. He denied neck pain, shortness of breath, dysuria, or blood in his urine.

Review of systems revealed a recent history of preseptal cellulitis two weeks prior to his current illness that resolved with oral trimethoprim-sulfamethoxazole and erythromycin eye ointment. The patient lived with his mother and step-father in a wooded area in rural Central Florida. Animal exposures included several family pets including a dog, a ferret, and 4 outdoor adult cats, all of which were healthy and vaccinated. He denied any animal scratches or bites from these animals. The family reported seeing a tick on his body 6 months prior to admission and did not recall more recent exposures. The remaining past medical, social, family and exposure history was non-contributory.

On physical examination, the patient had bilateral, non-exudative conjunctival injection and his abdomen was diffusely tender to palpation without guarding, rebound tenderness or hepatosplenomegaly. He had a patchy, blanching, erythematous, pinpoint papular rash over his trunk, abdomen, and bilateral proximal upper and lower extremities without excoriation. The remainder of the examination was normal.

Laboratory studies were significant for leukopenia with WBC 2500 cu/mm with absolute lymphocyte count of 1225 cu/mm (normal 1400-3800 cu/mm) and the presence of frequent atypical lymphocytes. Platelets were decreased to 83 thou/cu mm and transaminases were mildly elevated (AST 62 U/L, ALT 82 U/L). Hemoglobin and hematocrit were normal. Coagulation studies showed a slightly elevated prothrombin time of 15.3 seconds, INR of 1.2, and PTT of 36 seconds. A chest radiograph and abdominal ultrasound were normal. Viral hepatitis serologies were negative.

### **Hospital Course**

The morning after admission, the patient continued to have fever, abdominal pain, vomiting, conjunctivitis, and anorexia. The rash appeared more erythematous. His absolute leukocyte count and platelet count continued to decrease. Initial viral testing for enterovirus, parvovirus, adenovirus, cytomegalovirus and Epstein-Barr virus was negative. The vague symptoms upon presentation, laboratory findings of transaminitis with worsening leukopenia and thrombocytopenia, and his history of previous tick exposure increased the concern that his illness was due to ehrlichiosis. Due to the risk of morbidity and mortality from ehrlichiosis and

the low risk of therapy with antibiotics, doxycycline was empirically started. Within 24 hours of starting antibiotics, the fever and rash resolved, and laboratory data improved (see Table 1). Ehrlichia PCR testing was positive for Ehrlichia chaffeensis.

Table 1. Laboratory Data Before and After Treatment of Ehrlichiosis

	Admission	Hospital day 2	Hospital Day 4 (~24 hours after therapy started)
White blood cell count (thou/cu mm)	2.5	2.9	7.6
Absolute leukocyte count (cu/mm)	1225	551	4104
Platelets (thou/ cu mm)	83	65	133

### Discussion

Ehrlichiosis is the most commonly reported tick-borne illness in the southern United States<sup>2</sup>. Human Ehrlichiosis refers to infections typically caused by Ehrlichia chaffeensis, a small intracellular bacterium that infects monocytes.<sup>3,11</sup> Ehrlichiosis is transmitted by the lone star tick, Amblyomma americanum, which is mainly found in white tailed deer, dogs, rabbits, foxes and raccoons<sup>4</sup>. Infections are most common in the early summer months from May to July, but can occur year-round<sup>4</sup>. Clinical symptoms typically develop five to ten days after a bite from an infected tick; however, many tick bites go unrecognized and are unreported by patients later found to have ehrlichiosis.

Ehrlichiosis can result in severe disease, with an estimated 40% of infected patients requiring hospitalization and a reported mortality rate of 3%<sup>3</sup>. It typically presents with nonspecific symptoms of fever, malaise, myalgias and arthralgias. Fever is often the predominant symptom affecting 97% of patients. 30% of patients with ehrlichiosis develop a rash that is maculopapular initially and becomes petechial roughly five days after the initial onset of symptoms. Complications from ehrlichiosis are rare and can occur at any point during the disease course, even after the initial infection has resolved<sup>5</sup>. Complications are more common among immunocompromised hosts, and include sepsis, meningitis, renal failure, myocarditis, among others.

Laboratory findings for ehrlichiosis are nonspecific and include leukopenia, thrombocytopenia and evidence of liver disease with elevated transaminases and abnormal coagulation studies, all of which were seen in our patient. On Wright stain, one may see intracytoplasmic inclusions or morulae (stippled blue inclusions of bacteria in monocytes), but the sensitivity of peripheral smear for diagnosis is low.<sup>3</sup> Serology testing showing seroconversion, or a four-fold increase in antibody titers during the convalescent phase occurring 2-4 weeks after initial onset of symptoms, is diagnostic<sup>5</sup>. However, antibodies including IgM are typically negative during the first 7-10 days of illness, when most patients present with clinical symptoms. Additionally, once IgG antibodies develop, they can persist for months to years after infection, even without clinical

signs or relapse<sup>5</sup>. Because of this, PCR is becoming the diagnostic test of choice for ehrlichiosis, particularly early in the disease course when antibody levels are low.<sup>3,5</sup>

Treatment for ehrlichiosis is doxycycline, regardless of the patient's age<sup>6</sup>. The recommended dose is 4 mg/kg/day divided BID (max 100 mg/ dose) for 5-10 days, and at least 3 days after defervescence<sup>1</sup>. Doxycycline should be started as soon as the diagnosis is suspected, even when no confirmatory testing is available. Clinical improvement within 24- 48 hours is expected<sup>3</sup>. If no clinical improvement is seen within 48 hours, an alternative diagnosis should be considered. There has been concern about using tetracyclines in children <8 years of age due to the potential for teeth staining; however, as Dahlgren et al reported in 2015, there are no reports in the current literature of doxycycline causing teeth staining in children, especially when used in the recommended doses for rickettsial diseases<sup>6,7</sup>. Treatment with trimethoprim-sulfamethoxazole, as occurred in our patient is contraindicated in patients with suspected ehrlichiosis as it may be associated with a more severe disease course<sup>1,8,9</sup>.

### Conclusion

We presented a case of a 13-year-old boy with fever, vague gastrointestinal complaints, headache, and rash from rural Central Florida found to have ehrlichiosis. This case highlights the importance of keeping a broad differential diagnosis for tick-borne illnesses as they often manifest with non-specific symptoms that could easily be confused with more common childhood illnesses like gastroenteritis, streptococcal pharyngitis and viral syndromes<sup>10</sup>. Furthermore, as seen in this case, patients are often unaware of tick bites or recent tick exposures making the diagnosis more challenging.<sup>11</sup> Physicians practicing in rural areas where the lone star tick is prevalent, namely Southern and Southeastern United States, should keep a high index of suspicion for ehrlichiosis in order to provide prompt treatment and decrease morbidity and mortality.

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