



## CASE REPORT

# Rhabdomyolysis and Multisystem Organ Failure Due to Fulminant Ehrlichiosis Infection

Alex C. Overmiller, MD; Cindy C. Bitter, MD, MPH

*Saint Louis University School of Medicine, Division of Emergency Medicine, St. Louis, MO*

A previously healthy 51-y-old male presented to his local emergency department with subjective fevers, myalgias, dyspnea, and generalized weakness that had been progressive for several weeks. He was initially diagnosed with bilateral pneumonia, septic shock, and rhabdomyolysis requiring transfer to a tertiary care facility. He was treated for sepsis with broad-spectrum antibiotics, steroids, and a fluid bolus before transfer. Once he arrived at the tertiary care facility, he developed respiratory failure requiring intubation and ventilatory support. Ceftriaxone and metronidazole were started in the intensive care unit to cover common causes of community-acquired versus aspiration pneumonia, and doxycycline was included to cover tick-borne disease based on a history of tick exposure from working in his rural yard. Blood polymerase chain reaction testing later confirmed ehrlichiosis. The patient had a prolonged hospital course requiring ventilatory support and vasopressors, followed by a 4-wk stay in a rehabilitation unit after discharge. Wilderness medical providers should counsel their patients on prevention of tick bites and keep tickborne illness in the differential for acute illness, based on local epidemiology.

*Keywords:* tickborne disease, vector range, zoonosis

## Introduction

Cases of tickborne disease (TBD) have doubled in the United States in recent years.<sup>1</sup> There were 47,743 cases of TBD reported to the US Centers for Disease Control and Prevention in 2018, including 6123 cases of ehrlichiosis and the related disease anaplasmosis.<sup>2</sup> However, there are few reports of septic shock, rhabdomyolysis, and multisystem organ failure secondary to ehrlichial infections. This is the case of a previously healthy 51-y-old male with untreated ehrlichiosis infection leading to septic shock and rhabdomyolysis.

## Case

The patient was a 51-y-old male from southern Illinois who presented to his local emergency room in May with a chief symptom of weakness and shortness of breath.

Corresponding author: Alex C. Overmiller, MD, Saint Louis University, Emergency Medicine, 3691 Rutger Avenue, Saint Louis, MO 63110; e-mail: [alex.overmiller@health.slu.edu](mailto:alex.overmiller@health.slu.edu).

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The patient presented with pain and weakness of the bilateral lower extremities that had progressed over the previous month such that he could no longer stand unassisted. He had developed shortness of breath, anorexia, and chills over the previous 3 to 4 d. On questioning, he reported spending a lot of time outdoors working in his rural wooded yard and recalled multiple tick bites over the previous 2 mo. The patient denied having any medical or surgical history, but he had not seen a physician since childhood. The patient's social history was significant for daily drinking, which he quantified as 6 to 7 shots per day and 5 to 6 cans of beer per day.

The patient was noted to be a cachectic middle-aged male in moderate respiratory distress. Vital signs were notable for a pulse of 128 beats·min<sup>-1</sup>, a respiratory rate of 33 breaths·min<sup>-1</sup>, a blood pressure of 93/67 mm Hg, and pulse oximetry of 93% on room air. Physical examination was positive for tachycardia and increased respiratory effort with bilateral wheezing. The patient's skin was warm and dry without rash. The patient was awake and alert on arrival to the intensive care unit and was following commands.

Routine laboratory testing was sent (Table 1). Initial chest x-ray showed bilateral infiltrates. Computed

**Table 1.** Laboratory values on initial patient presentation

| Test                                      | Value  | Reference range |
|---|--------|-----------------|
| Sodium (mEq·L <sup>-1</sup> )             | 124    | 136–145         |
| Potassium (mEq·L <sup>-1</sup> )          | 2.0    | 3.5–4.5         |
| AST (U·L <sup>-1</sup> )                  | 554    | 5–34            |
| ALT (U·L <sup>-1</sup> )                  | 80     | 0–55            |
| Creatinine kinase (IU·L <sup>-1</sup> )   | 24,000 | 30–200          |
| C reactive protein (mg·dL <sup>-1</sup> ) | 8.57   | 0.00–0.50       |
| Procalcitonin (ng·mL <sup>-1</sup> )      | 3.71   | ≤0.10           |
| Lactic acid (mmol·L <sup>-1</sup> )       | 13.9   | 0.5–2.0         |
| D-dimer (mg·L <sup>-1</sup> )             | 9.67   | <0.5            |
| Platelets (·μL <sup>-1</sup> )            | 49,000 | 150,000–400,000 |

AST, aspartate aminotransferase; ALT, alanine aminotransferase

tomography of the chest showed diffuse alveolar process in all lung fields. Hepatomegaly with fatty changes versus acute inflammation was seen on computed tomography of the abdomen and pelvis. Blood was submitted for polymerase chain reaction (PCR) testing for common respiratory viral pathogens and for tickborne pathogens including *Ehrlichia* and *Anaplasma* species.

The patient was started on ceftriaxone, metronidazole, and doxycycline based on our differential diagnosis, which included bacterial pneumonia, viral pneumonia, fungal pneumonia, aspiration pneumonitis, TBD, and subsequent organ failure from severe sepsis. He developed hypoxic respiratory failure on hospital day 2, requiring endotracheal intubation and mechanical ventilation for a total of 6 d. Once his disease progressed to respiratory failure, he underwent bronchoscopy, with multiple cultures of his bronchial washings. His blood was additionally recultured for bacterial and fungal pathogens; he was tested for *Legionella pneumophila* and *Streptococcus pneumoniae* with urinary antigen testing. He also required vasopressor support for profound hypotension. His clinical course was complicated by alcohol withdrawal. Antibiotics were weaned to doxycycline alone after PCR testing was positive for Ehrlichiosis and sputum cultures, blood cultures, viral panels, and urine tests were negative for other pathogens. He completed a 10-d course of doxycycline. The patient spent 9 d in the intensive care unit, 3 wk in the hospital, and 4 wk in a rehabilitation unit.

## Discussion

Ehrlichiosis is the general name used in the United States to describe a group of diseases caused by the bacteria *Ehrlichia chaffeensis*, *E ewingii*, or *E muris eauclairensis*.<sup>3</sup> Tick vectors carry these bacteria; most common are the lone star tick *Amblyomma americanum* and the blacklegged tick *Ixodes scapularis*. The natural host of

ehrlichiosis is the white-tailed deer, which shows minimal symptoms in the carrier state. Tick feedings transmit the disease. When the larval phase feeds on an infected mammal, it acquires the infection; when the tick feeds during the nymph stage, it transmits the infection to a second host.<sup>4</sup>

Although the first human case of ehrlichiosis was reported in 1987, the disease has long been known to veterinarians owing to cases in livestock and companion animals.<sup>5</sup> Ehrlichiosis became a reportable disease in 1999; since then, the number of cases has steadily risen, and the case fatality rate has decreased to about 3%.<sup>6,7</sup> Ehrlichiosis is most often seen in the southeastern and midwestern United States, and cases have a seasonal distribution, likely based on human-tick encounters being higher in the spring and summer months. Early ehrlichiosis infections present with flu-like symptoms, including fevers, chills, headache, myalgia, malaise, and gastrointestinal symptoms. A rash is reported in 60% of children and less than 30% of adults.<sup>8</sup> Respiratory symptoms are present in 28% of patients.<sup>9</sup> If the infection goes untreated, there are cases of progression to cerebral infections, cerebral hemorrhage, acute respiratory distress syndrome, septic shock, renal failure, and hepatic failure.<sup>10–12</sup> Although myalgias are common in ehrlichiosis, clinically significant rhabdomyolysis is rare.<sup>13,14</sup> A history of tick bite within 14 d can only be elicited in 68% of individuals diagnosed with ehrlichiosis.<sup>15</sup> With tick bite providing such a low sensitivity of disease presence, practitioners in endemic areas must consider TBD regardless of tick bite history.

Pneumonia caused by ehrlichiosis has been described; however, the typical regimen for community-acquired pneumonia does not cover this pathogen. If TBD are not caught and treated in their early stages of infection, the practitioner must consider them in the presentation of more severe diseases by eliciting a history of tick bites or time spent outdoors with potential tick exposure. Practitioners must also integrate their location and local prevalence of TBD because a history of a bite alone is not sensitive for disease presence.

Risk factors for severe disease include immunosuppression, extremes of age, and delay in diagnosis.<sup>9</sup> Our patient likely experienced a more severe course owing to immunosuppression from undiagnosed diabetes and alcoholism, as well as a delay in presentation.

If the diagnosis is suspected, TBD should be covered empirically while awaiting confirmatory testing. Clues in routine bloodwork include leukopenia, thrombocytopenia, hyponatremia, and elevated liver enzymes. Anemia, coagulopathies, and lactic acidosis may also be seen.<sup>8,9</sup> Morulae (a neutrophil with an intracytoplasmic inclusion body) may be seen on blood smears



**Figure 1.** Reprinted by permission from Springer Nature Customer Service Centre GmbH: Springer Nature, *Modern Pathology*, Characteristic peripheral blood findings in human ehrlichiosis, Hamilton KS, Standaert SM, Kinney MC, Copyright 2004. <https://www.nature.com/articles/3800075#:~:text=In%20this%20study%2C%2038%25%20of,%20detection%20was%20only%2017%25.33>

(Figure 1).<sup>16</sup> A rapid PCR test for ehrlichiosis and anaplasmosis is currently under development.<sup>17</sup> In the United States, tetracyclines, including doxycycline, are the preferred agents for the treatment of most tick-borne illnesses, regardless of the patient's age.<sup>18</sup> Ehrlichiosis, spotted fever rickettsiosis, and tularemia are endemic TBD in the lower midwestern United States; doxycycline provides coverage for these organisms. It should be noted that tetracyclines do not cover babesiosis.

Cases of ehrlichiosis are increasing, and cases are being reported in more counties than in previous years.<sup>12</sup> Although this may represent increased knowledge of the disease and better reporting of cases, most authors believe the disease remains underreported and the incidence is indeed rising.<sup>6-8,12,18-20</sup> It has been theorized that ehrlichiosis and other TBD are becoming more common as the tick vectors appear to be expanding their ranges because of climate change.<sup>21-23</sup> The range of *A. americanum* has expanded into the midwestern and the northern United States from its origins in the southeastern United States, and the number of counties with *Ixodes* ticks has more than doubled in the past 20 years.<sup>24,25</sup> Although previously considered diseases of rural areas and wilderness recreation, several recent studies have found disease-carrying ticks in urban and suburban parks.<sup>26-28</sup> The tick vector range has been predicted to expand further with climate change modeling.<sup>29</sup>

Wilderness medical practitioners should be prepared to recognize TBD in their patients and start empiric treatment while awaiting confirmatory testing. Patients at

risk for TBD may not recall an exposure or recognize early symptoms.<sup>30,31</sup> Knowledge of local disease patterns is crucial. The US Centers for Disease Control and Prevention has excellent resources for TBD, including images of tick vectors, maps of disease prevalence, and information on clinical presentations, diagnosis, and management.<sup>32</sup> Counseling patients on personal protective measures, including appropriate clothing, repellents, need for tick checks of both humans and companion animals, and proper removal of ticks may also reduce the burden of disease.

## Conclusions

Although the current mortality rate associated with ehrlichiosis is only 3%, this case demonstrates that TBD can become fulminant and life threatening if left untreated. Vector-borne disease should be included in the differential of patients presenting with febrile illness during the spring, summer, and fall months, with diagnostic testing initiated in patients with possible exposures even without a recalled history of a tick bite. More acutely ill patients may require empiric treatment while awaiting confirmation.

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