A Case of Fever and Rash After a Tick Bite

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A 55-year-old man with a history of diabetes mellitus type 2 presented to the Emergency Department (ED) in May with 5 days of headache, fever to 104 °F, diffuse myalgias, and generalized weakness. He denied neck stiffness or photophobia. He also denied confusion, nausea, or vomiting.

The patient lived in rural Indiana. He frequently performed yardwork, and he had noticed a tick on his arm 10 days before. He removed the tick with tweezers and reported that it was not engorged. Three weeks prior to presentation, he went camping in the forest and slept in a cabin. He had a pet dog. He also had frequent contact with his 3-year-old granddaughter who had a recent febrile upper respiratory illness. For his diabetes he took metformin.

On physical examination, temperature was 38.7 °C, blood pressure 92/60 mmHg, heart rate 123 beats per minute, and respiratory rate 18 breaths per minute. In general, he appeared diaphoretic and uncomfortable. His cardiac exam revealed an irregularly irregular rhythm, pulmonary exam was clear, and abdominal exam was benign. He was alert and oriented, and his neurologic exam was grossly within normal limits. He had negative Kernig’s and Brudzinski’s signs.

In the ED, he received a dose of intravenous (IV) ceftriaxone, after which he developed an acute, diffuse, erythematous petechial rash on his trunk and extremities, including the palms of his hands (Fig. 40.1). Complete blood count showed a white blood cell (WBC) count of 8900/μL with 78% neutrophils and 14% bands, hemoglobin of 14.6 g/dL, and platelets of 25,000/μL (normal range,150,000–450,000/μL). His complete metabolic panel (electrolytes, liver tests, creatinine, and blood urea nitrogen) was unremarkable. A lumbar puncture was deferred due to thrombocytopenia and concerns for bleeding. Computed tomography (CT) of the head and magnetic resonance imaging (MRI) scan of the brain were unremarkable. An electrocardiogram (EKG) revealed that he was in atrial fibrillation. The patient became increasingly hypotensive, and he was intubated and mechanically ventilated, started on vasoactive agents, and transferred to the medical intensive care unit.

Microbiology studies drawn on admission are shown in Table 40.1. While he had positive serum IgG for cytomegalovirus (CMV) and Epstein Barr virus (EBV), indicating prior infection with these viruses, the rest of his microbiology results did not reveal a diagnosis. He was empirically treated with vancomycin, aztreonam, levofloxacin, acyclovir, and doxycycline to cover broadly for possible meningitis, encephalitis, and rickettsial disease. β-Lactam antibiotics were avoided as it was thought that ceftriaxone might have caused his rash. Five days into his admission, his platelet...
Table 40.1  Patient’s admission microbiology test results

| Microbiology test (blood/serum unless noted) | Result |
|---------------------------------------------|--------|
| Blood culture                               | Negative |
| Urine culture                               | Negative |
| Human immunodeficiency virus (HIV) antibody | Negative |
| Respiratory viral panel<sup>a</sup>          | Negative |
| *Rickettsia rickettsii* IgM, IgG             | Negative |
| *Rickettsia typhi* IgM, IgG                  | Negative |
| *Anaplasma phagocytophilum* IgM, IgG         | Negative |
| *Ehrlichia chaffeensis* IgM, IgG             | Negative |
| Lyme disease (*Borrelia burgdorferi*) EIA    | 3.21 Lyme index units (normal range < 0.75) |
| Lyme Western blot IgM, IgG                  | Negative |
| CMV IgM                                     | Negative |
| CMV IgG                                     | Positive |
| Epstein Barr virus (EBV) IgM                | Negative |
| EBV IgG                                     | Positive |

<sup>a</sup>Polymerase chain reaction test for the following pathogens: adenovirus, coronavirus 229E, coronavirus HKU1, coronavirus OC43, coronavirus NL63, human metapneumovirus, human rhinovirus/enterovirus, influenza A, influenza A/H1, influenza A/H1–2009, influenza A/H3, influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3, parainfluenza 4, respiratory syncytial virus (RSV), *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*.
count had improved to 120,000/μL, and a lumbar puncture was deemed safe and performed. It showed a total cell count of 18 cells/μL, with 10 WBC/μL, 8 red blood cells/μL, 14% neutrophils, 68% lymphocytes, and 16% monocytes. Protein was 54 mg/dL (normal range, <45 mg/dL), and glucose 106 mg/dL. In the cerebrospinal fluid (CSF), enterovirus polymerase chain reaction (PCR), herpes simplex virus (HSV) 1 and 2 PCR, varicella zoster virus (VZV) PCR, and West Nile virus (WNV) antibodies were negative.

The differential diagnosis for fever in a patient with a petechial rash includes meningococcemia, Rocky Mountain spotted fever (RMSF) and other rickettsial diseases, drug reaction, parvovirus B19 infection (fifth disease), and infectious mononucleosis (Table 40.2). The patient’s history of tick bite raises the concern for RMSF, human granulocytic anaplasmosis, or RMSF. This patient’s severe illness and rash involving the palms is more characteristic of RMSF than rickettsiosis.

One week after his initial presentation, the rickettsial serology was repeated and this time revealed a positive RMSF IgM titer (>1:256) with a negative IgG. Based on this result, he was diagnosed with RMSF. His antibiotics were narrowed to only doxycycline. He gradually recovered and was discharged to an acute rehabilitation facility.

### 40.1 Rocky Mountain Spotted Fever (RMSF)

RMSF is a tick-borne zoonosis caused by transmission of *Rickettsia rickettsii* to a human via the bite of an infected tick. The primary vector in the United States (US) is the American dog tick (*Dermacentor variabilis*), but the pathogen is also transmitted by the Rocky Mountain wood tick (*Dermacentor andersoni*) and the brown dog tick (*Rhipicephalus sanguineus*). RMSF occurs throughout the United States, but, despite its name, cases predominantly occur in the Midwest and Southeast [1].

The mean incubation period between exposure and onset of symptoms is 7 days, with a range of 2–14 days [2]. RMSF cases follow a seasonal pattern, with 90% of infections occurring between April and September. Clinical signs and symptoms include fever, myalgias, severe headache, as well as nausea, vomiting, and abdominal pain. A characteristic petechial rash that starts around the wrists and ankles and may involve the palms and soles appears 2–5 days after the onset of fever. Less common clinical presentations include myocarditis, pneumonia, acute kidney injury, and neurologic manifestations. RMSF often causes severe illness, with a case fatality rate of 5–10%.

The diagnosis of RMSF is based on clinical signs and symptoms in a patient with possible tick exposure. Treatment should not be delayed while awaiting laboratory confirmation of the diagnosis. Laboratory abnormalities include mild hepatic transaminitis, thrombocytopenia, hyponatremia,
and mild lymphocytic pleocytosis in the CSF [3]. Immunohistochemistry performed on skin biopsy at rash onset may be useful to confirm a diagnosis. RMSF serology typically becomes positive 7–10 days after symptom onset. A fourfold increase in serum antibody titers or a convalescent titer >1:64 is diagnostic. There is possible cross-reaction between RMSF titers and other spotted fever group rickettsioses, especially *Rickettsia parkeri*, which is transmitted by the Gulf Coast tick *Amblyomma maculatum*, may have an eschar at the site of tick bite and usually causes a mild illness. The treatment of choice for RMSF is oral doxycycline 100 mg twice per day for 5–7 days, continuing at least 2–3 days after the patient defervesces. Chloramphenicol is an alternative treatment only used in cases of severe doxycycline allergy or during pregnancy if the illness is mild, but chloramphenicol is associated with increased mortality, is also associated with adverse effects, and is ineffective against other severe tick-borne infections in the differential diagnosis, i.e., human granulocytic anaplasmosis and human monocytic ehrlichiosis.

**Key Points/Pearls**

- Rocky Mountain spotted fever (RMSF) is a severe tick-borne zoonosis caused by *Rickettsia rickettsii* and transmitted by various ticks including the American dog tick, the Rocky Mountain wood tick, and the brown dog tick.
- Typical symptoms include fever and severe headache followed 2–5 days later by a maculopapular or petechial rash that starts around the wrists or ankles and may involve the palms and soles; skin biopsy may confirm the diagnosis when immunohistochemistry identifies *Rickettsia rickettsii* within the endothelium.
- The diagnosis of RMSF should be made clinically; serologic studies become positive 7–10 days after onset of symptoms.
- The treatment of choice for RMSF is doxycycline, even in children and during pregnancy.
- Severe rickettsioses to consider in the United States are RMSF, human granulocytic anaplasmosis, and human monocytic ehrlichiosis; in other regions of the world, Mediterranean spotted fever, epidemic typhus, and scrub typhus also can cause severe illness.
- In severely ill patients with fever and rash, one should consider the possibility of rickettsioses and the possible indication of adding doxycycline.

**References**

1. Parola P, Paddock CD, Socolovschi C, et al. Update on tick-borne rickettsioses around the world: a geographic approach. Clin Microbiol Rev. 2013;26(4):657–702
2. Dantas-Torres F. Rocky Mountain spotted fever. Lancet Infect Dis. 2007;7(11):724–32
3. Chapman AS, Bakken JS, Folk SM, et al. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis—United States: a practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep. 2006;55(RR-4):1–27