An Unsuspected Case of Rocky Mountain Spotted Fever: A Lesson to Keep a Broad Differential

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Abstract

Rocky Mountain spotted fever (RMSF), a tick-borne illness, can cause serious illness or death even in a healthy individual. Unfortunately, this illness can be difficult to diagnose as symptoms are nonspecific and oftentimes mimic benign viral illnesses. Delayed diagnosis can be detrimental as the timing of antibiotic administration is critical to prevent associated morbidity and mortality. A careful travel and social history can sometimes provide clues to make the diagnosis. Being aware of lesser-known objective findings such as hyponatremia, neurologic derangements, transaminitis, and thrombocytopenia may help raise suspicion for the disease. This is a case of a 72-year-old woman who presented with nonspecific symptoms and hyponatremia without known tick exposure. She was eventually diagnosed with RMSF. The timing of her presentation corresponded with a surge in COVID-19 infections throughout her area of residence, which further complicated her presentation and contributed to a delayed diagnosis.

Keywords

Rocky Mountain spotted fever, rickettsial disease, tick-borne illness, hyponatremia

Introduction

Rocky Mountain spotted fever (RMSF) is a tick-borne illness caused by the gram-negative bacteria Rickettsia rickettsii. Transmission occurs primarily through the American dog tick (Dermacentor variabilis) and the Rocky Mountain wood tick (Dermacentor andersonii) typically during the summer months.¹ Tick-borne rickettsial diseases continue to cause severe illness and even death in otherwise healthy individuals despite the availability of low-cost, effective antimicrobial therapy. Early signs and symptoms of these illnesses are notoriously nonspecific, commonly mimicking benign viral illnesses, which creates a diagnostic dilemma for clinicians early in the clinical course when antibiotic therapy is most effective. Oftentimes a careful travel history or social history will provide clues to potential exposures, but this is not always the case. Lesser-known characteristics of RMSF including hyponatremia may provide additional clues to aid in the diagnosis, but they may also distract from the underlying cause. Consideration of tick-borne diseases, even in patients with low pretest probability, is essential to reduce morbidity and mortality associated with these conditions.

Case

A 72-year-old woman with a medical history of hypertension, environmental allergies, and recurrent herpes simplex virus (HSV) presented to her primary care clinic in early March for a 2-day history of fever, myalgias, fatigue, and dry cough. She was seen via video visit due to her worrisome presenting symptoms in the setting of the COVID-19 pandemic. A COVID-19 home test was negative. She was offered oseltamivir due to concern for influenza, but declined. Supportive care with symptom-based therapies was recommended.

On day 7 of symptoms, she presented in person to the same clinic for ongoing fevers up to 103.9 °F and now with associated nausea, decreased appetite, headache, and nonpruritic diffuse rash. She had no recent travel due to social isolation during the pandemic. She denied any new topical skin products, change in diet or medications, or insect bites. The patient is retired and lives in a house in urban coastal South Carolina with her husband and dog. Her dog primarily lives indoors but does roam the backyard. During her clinic visit, she was hemodynamically stable with a blood pressure of 124/62 mm Hg, heart rate of 94 beats/min, and temperature of

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99.5 °F. Her physical examination was notable for 2 painful oral lesions present on the roof of her mouth. There was a new nonpruritic, nonpainful rash that initially started as a spot on her face (Photo 1) and spread down her chest, abdomen, arms, and legs (Photo 2). Her cardiopulmonary and abdominal examinations were unremarkable.

Initial workup that same day revealed hyponatremia of 126 mmol/L and elevated liver enzymes. Herpes simplex virus viral swab of the oral lesion was negative as were additional serologic viral tests (Table 1). Rapid COVID-19 and influenza tests were negative. Because of hyponatremia, she was sent to the emergency department (ED). There, further infectious workup was negative, including urinalysis and chest radiography. The ED provider diagnosed her with an unspecified viral illness and dehydration. She was given intravenous fluids and instructed to hold her hydrochlorothiazide. As the patient was overall feeling better after intravenous fluids, the ED provider felt she could be safely discharged with strict return precautions and close primary care follow-up in the next 1 to 2 days.

On day 8, she contacted her physician due to new arthralgias involving her left wrist, right knee, and fingers. Further laboratory studies including additional infectious and rheumatologic workup were negative (Table 1). High-sensitivity C-reactive protein (CRP) was elevated at 4.130. Her sodium continued to be low (129 mmol/L). Additional tick-borne illness tests were ordered. Due to the expected delay in lab results, she was started on empiric doxycycline for a 10-day course. Over the next week, her fever curve trended down to normal and symptoms began to improve. She did continue to

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**Table 1. Laboratory Values.**

| Lab                        | Patient value | Reference range       |
|----------------------------|---------------|-----------------------|
| Day 7                      |               |                       |
| White blood cell count     | 8.55 K/cumm   | 4.8-10.8 K/cumm       |
| Platelet Count             | 239 K/cumm    | 140-440 K/cumm        |
| Sodium                     | 126 mmol/L    | 135-145 mmol/L        |
| Chloride                   | 90 mmol/L     | 98-108 mmol/L         |
| Creatinine                 | 0.8 mg/dL     | 0.6-1.1 mg/dL         |
| Urea nitrogen              | 11 mg/dL      | 8-26 mg/dL            |
| Aspartate aminotransferase (AST) | 42 U/L     | 5-34 U/L              |
| Alanine aminotransferase (ALT) | 46 U/L     | 46 U/L                |
| HSV viral swab             | Negative      |                       |
| EBV IgM                    | 0.3 AI        | ≤0.8 AI               |
| CMV IgM                    | <0.2 AI       | ≤0.8 AI               |
| VZV IgM                    | Negative      |                       |
| Day 8                      |               |                       |
| Sodium                     | 129 mmol/L    | 135-145 mmol/L        |
| AST                        | 37 U/L        | 5-34 U/L              |
| ALT                        | 53 U/L        | 46 U/L                |
| Antinuclear antibody       | Negative      |                       |
| C3 level                   | 151.6 mg/dL   | 82-193 mg/dL          |
| C4 level                   | 42.3 mg/dL    | 15-57 mg/dL           |
| Cryoglobulins              | Negative      |                       |
| Anti-neutrophilic cytoplasmic Ab | Negative |                       |
| CRP                        | 4.130         | 0.0-0.5 mg/dL         |
| Sedimentation rate         | 30 mm/h       | 0-30 mm/h             |
| HIV 1 and 2 Ab             | Nonreactive   |                       |
| Hepatitis A IgM Ab         | Nonreactive   |                       |
| Hepatitis B core IgM       | Nonreactive   |                       |
| Hepatitis B surface antigen| Nonreactive   |                       |
| Hepatitis C Ab             | Nonreactive   |                       |
| Day 14                     |               |                       |
| Sodium                     | 131 mmol/L    | 135-145 mmol/L        |
| Ehrlichia chaffeensis IgG Ab| <1:64        | <1:64 indicates negative|
| Anaplasma phagocytophilum IgG Ab | <1:64       | <1:64 indicates negative|
| Rocky Mountain spotted fever IgG Ab | 1:1024     | >1:256 indicated positive|
| Rocky Mountain spotted fever IgM Ab | ≥1:64     | ≥1:64 indicates positive|

Abbreviations: HSV, herpes simplex virus; CRP, C-reactive protein; CMV, cytomegalovirus; EBV, Epstein-Barr virus; VZV, varicella-zoster virus.
experience mental “fogginess,” however. On day 14, 6 days after labs were drawn, her tick-borne disease panel returned positive for RMSF antibodies (IgM >1:64 and IgG 1:1024).

On day 17, she began experiencing myodesopsia and blurry vision in both eyes. She was referred to ophthalmology who felt her examination was consistent with retinal vasculitis secondary to RMSF. Upon completion of her antibiotic course, her sodium levels normalized as did her transaminases. Her brain fog and ocular symptoms lingered but eventually improved over time. A few months after her initial diagnosis, she returned to her prior state of health.

Discussion

This case of RMSF illustrates a classic example of how this disease, which often mimics common viral illnesses, can easily be overlooked. The typical presenting triad for RMSF consists of fever, headache, and rash. Atypical presentations are commonly seen, however, and may complicate diagnosis. Up to 15% of patients do not develop a rash, and only 49% of people have a rash in the first 3 days of symptom onset. The rash, when present, typically starts on the ankles and wrists, spreads to the trunk, and involves the palms and soles with sparing of the face. Our patient’s rash was subtle and a bit delayed in onset. Her rash also spread in the opposite manner as the classic rash, making diagnosis less obvious.

Known tick exposure is helpful in making the diagnosis of RMSF, but many times it is not apparent. Clinicians may pick up clues from social history such as seasonality or recent travel, but this is not always the case. The initial level of suspicion for RMSF in our patient was low given that she presented during the winter and had been fairly homebound due to the ongoing pandemic. She presented during peak influenza season and also at a time in which COVID-19 was surging in her area. Her dog roamed the backyard of their urban home and was likely the only source of tick exposure. It is important to remember that tick-borne illnesses are still very much present during the winter months. The seasonality difference is typically due to a decrease in human activity levels outdoors, thus decreasing the risk of exposure to the ticks.

Rickettsial infection causes vascular injury, which can lead to a number of unfortunate complications. Neurologic sequelae such as headache, difficulty concentrating, and ophthalmologic changes as was seen in our patient are common. Early initiation of antibiotics can significantly improve the morbidity and mortality associated with RMSF. Initiation of doxycycline within 5 days of symptom onset has shown to decrease mortality rates when compared with 5 days after symptom onset (6.5% and 22.9%, respectively). Because the initial few days of infection often mimic benign viral illnesses, awareness of lesser-known features of RMSF may expedite diagnostic consideration and ultimately antibiotic therapy.

Hyponatremia, as seen in our patient, is found in about 50% of cases of RMSF. When present, it is often seen in cases with central nervous system (CNC) involvement. The mechanism behind the hyponatremia is thought to be secondary to Rickettsia-induced CNS vasculitis and inflammation, leading to inappropriate anti-diuretic hormone release. Sodium levels will often not normalize until antibiotic therapy is initiated, which was the case in our patient.

Although not present in this case, thrombocytopenia is also a common finding in patients with RMSF. This is likely a function of intravascular destruction of platelets due to vascular injury. Elevated prothrombin time/partial thromboplastin time and low fibrinogen can also be seen, but overt disseminated intravascular coagulation is rare. Other findings that can be seen are azotemia and elevated liver function tests, among others.
Conclusion

Rocky Mountain spotted fever and other tick-borne illnesses present a diagnostic challenge for physicians. A careful social history and understanding of some of the less classic findings of RMSF may expedite diagnosis. Quick recognition of the infection is important as early therapy with doxycycline is critical in reducing the morbidity and mortality associated with RMSF.

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

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