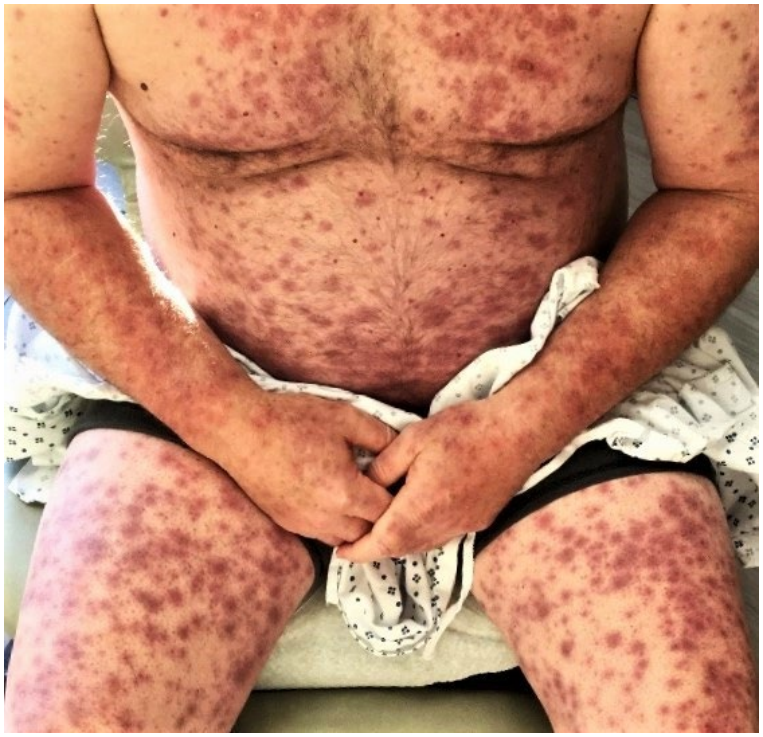
KANSAS JOURNAL of MEDICINE

Rocky Mountain Spotted Fever Misdiagnosed as an Acute Drug Reaction: Diagnostic Clues and Evaluation Recommendations

Atieh Jibbe, M.D.[1], Brett C. Neill, M.D.[1], Stan N. Tolkachjov, M.D.[2]
[1]University of Kansas Medical Center, Kansas City, KS
Department of Internal Medicine, Division of Dermatology
[2]Epiphany Dermatology, Dallas, TX

Received Feb. 24, 2021; Accepted for publication April 1, 2021; Published online July 9, 2021
https://doi.org/10.17161/kjm.vol1415223



CASE DESCRIPTION

History and Exam. A 52-year-old healthy male presented to the dermatology clinic with fever, rash, and myalgias. Two days prior, he had been discharged from the hospital for a presumed drug rash secondary to an opiate. The petechial rash initially involved his hands, wrists, and ankles, and was spreading centripetally, involving the proximal upper and lower extremities and trunk (Figure). Of note, the patient recently started summer gardening at his home in the southeast U.S. which caused worsening back pain for which he took oxycodone/acetaminophen. He denied a tick bite history.

Presumptive Diagnosis. Further workup was unremarkable except for mildly elevated AST/ALT. Based on a high clinical suspicion with the characteristic petechial rash and systemic symptoms, Rocky Mountain Spotted Fever (RMSF) was the presumptive diagnosis and empiric treatment was begun with doxycycline.

Confirmatory Diagnosis. After initiating doxycycline, the patient had a skin biopsy with direct immunofluorescence consistent with vasculitis and subtle features of RMSF histopathology: basal layer vacuolar degeneration with mild interface and lymphocytic exocytosis. Serum RMSF titers via indirect immunofluorescence, drawn one week after likely infection, were positive confirming the diagnosis.

DISCUSSION

RMSF is the most common fatal tickborne disease in the U.S.[1] Incidence of Spotted Fever Rickettsiosis has increased from 2000 to 2017 with 495 to 6,248 cases, respectively. RMSF is transmitted by the Dermacentor variabilis tick most prevalent in the eastern U.S.[2,3] The incubation period ranges from 3 - 12 days. RMSF presents with a classic triad of fever, headache, and rash, however, this triad is not identified often. It is estimated that only 3% of patients present with this triad within the first three days of illness. Early disease presents with non-specific symptoms including fever, headache, malaise, myalgia, nausea, vomiting, and photophobia.[3] RMSF rash usually presents two to five days after the onset of symptoms with blanching erythematous macules that progress to form petechiae and spread centrifugally.[3,4] This rash can be absent in 10 - 15% of patients, typically older adults and African-Americans.[3] Labs in RMSF can vary with possible leukocytosis, thrombocytopenia, elevated liver enzymes, and hyponatremia.[5]

Our case was challenging due to the lack of tick bite history. In a 1995 study of 79 RMSF patients, only 40% of patients recalled a tick bite.[4] In our case, the history of summertime gardening in an endemic area, purpuric rash starting on wrists and spreading centripetally, elevated AST/ALT, myalgias, and the rarity of oxycodone/acetaminophen causing a rash provided the index of suspicion for RMSF.

The mainstay of diagnosis for RMSF is serology with indirect immunofluorescence assay. Antibodies to RMSF usually develop 7 - 10 days after illness onset, but serologies should be obtained 14 - 21 days after symptom onset due to the likelihood of false negatives in the acute phase. A single reactive titer may suggest RMSF, but a four-fold increase in IgG titers from acute to convalescent phase can confirm the diagnosis.[4] A skin biopsy can assist in the diagnosis but is not confirmatory. In a study of 26 cases of RMSF, the major histopathologic features were lympho-histiocytic capillaritis and venulitis with extravasation of erythrocytes, edema, predominantly perivascular with some interstitial infiltrate, and leukocytoclastic vasculitis.[6]

Empiric treatment comprises of doxycycline 100 mg (2.2 mg/kg for children) twice-daily for > 3 days after defeverence with 5 - 7-day minimum duration.[3] Treatment should be initiated if RMSF is suspected even if symptoms are mild or laboratory evidence is lacking. The importance of early treatment is highlighted by a study of 94 patients that revealed patients treated within five days of symptoms onset had lower mortality rates than those treated after the fifth day (6.5% vs. 22.9%).[7] Chloramphenicol (50 mg/kg/day in four divided doses) is the only known alternative agent for the treatment of RMSF. It appears to be less effective than doxycycline and typically is used in the rare setting when an individual has a history of a severe adverse reaction to doxycycline.

RMSF is suspected in patients with fever, headache, and constitutional symptoms, during the summer in endemic areas, and known tick-bite history. This diagnosis remains a clinical challenge for providers due to its non-specific symptoms, absence or delayed rash, lack of tick-bite history, and sporadic distribution of the disease in endemic areas.

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Keywords: Rocky Mountain spotted fever, adverse drug reaction, diagnosis, misdiagnosis