

# Heterophile Antibodies and the Diagnosis of Rocky Mountain Spotted Fever

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Rocky Mountain spotted fever is notorious as a potentially lethal, but treatable illness. Even experienced physicians, however, may find recognition difficult, as other conditions may present similarly.<sup>1</sup> Meningococemia, enterovirus infections, and measles are cited as the primary and potentially most confusing alternative diagnostic possibilities.<sup>2</sup> Infectious mononucleosis is also mentioned in the differential diagnosis by some authors,<sup>3</sup> but is viewed as less of a problem because its usual clinical picture generally can be distinguished from that of Rocky Mountain spotted fever.<sup>4</sup> There are instances, however, in which infectious mononucleosis is less easily distinguished, as illustrated by the following case report.

## CASE REPORT

The patient is a 41-year-old woman whose prior health had been good. Seven days before her office visit she developed a sudden onset of fever and chills with a band-like headache. She had no other symptoms referable to ear, nose, or throat other than some mild hoarseness. She denied pulmonary, gastrointestinal, or genitourinary symptoms, but did experience myalgias and arthralgias without joint swelling. On the fifth day of her illness she developed a rash, beginning on her wrists and ankles, then spreading to her trunk. The rash was not vesicular, hemorrhagic, weeping, or pruritic. She denied exposure to ticks. Her social history was noteworthy in that she was moving out of state in two days. In addition, she did not have health insurance coverage and wished to minimize expenses.

Examination revealed a well-developed, well-nourished woman in no acute distress, but who did appear uncomfortable. Oral temperature was 101 °F. There was a dif-

fusely scattered maculopapular rash on her arms, legs, and torso, excluding palms and soles, without mucosal involvement. The rash blanched upon pressure. Funduscopic examination was normal, and the neck was supple. The chest was clear to percussion and auscultation, and the heart revealed normal sinus rhythm with no murmurs or rubs. No abdominal tenderness or organomegaly was found. There was no evidence of arthritis or muscular weakness, and neurologic examination was otherwise normal. A colleague who was asked to examine the patient discovered an axillary lymph node and some shotty posterior cervical adenopathy. The remainder of the physical examination was within normal limits.

Results of laboratory studies, which were limited in view of her cost concerns, included a normal urinalysis, and a white blood cell count of  $7.6 \times 10^3/\mu\text{L}$  with 75 percent polymorphonuclear leukocytes and 25 percent lymphocytes; no atypical lymphocytes were seen. A heterophile antibody screening test (Monosticon Dri-Dot, Organon, Inc) was positive, and a throat culture obtained at this time was subsequently negative. Finally, blood for an immunofluorescent, mixed, immunoglobulin M and immunoglobulin G (IgM, IgG) spotted fever antibody test was drawn.

The initial impression was infectious mononucleosis. Further discussion with colleagues, however, caused this assessment to be modified in view of the risks of not treating possible Rocky Mountain spotted fever. Hospitalization was recommended, which the patient refused, although she did agree to start tetracycline, 500 mg, four times a day.

The patient persisted with her plans to move. She was contacted by telephone 48 hours later and indicated she was feeling markedly better after ten doses of tetracycline. Her spotted fever antibody titer of 1:512 was received six days later.

## DISCUSSION

Helmick<sup>5</sup> stated laboratory diagnostic criteria for confirmation of Rocky Mountain spotted fever in a 1984 review,

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### DIAGNOSIS OF ROCKY MOUNTAIN SPOTTED FEVER

including among these a single, high titer of immunofluorescent antibody (greater than 1:64) in a patient with appropriate clinical features. Hence, with an immunofluorescent antibody titer of 1:512 in the patient just described, a diagnosis of Rocky Mountain spotted fever is justified.

The presence of adenopathy was the finding that raised the possibility of infectious mononucleosis and resultant ordering of a heterophile antibody screening test. While the absence of pharyngitis, lymphocytosis, and atypical lymphocytes would be unusual in a younger individual with infectious mononucleosis, this would not be inconsistent with the disease in a patient aged 41 years. Infectious mononucleosis after the age of 30 years is well documented though not common,<sup>6</sup> and variable presentation, often without classic features, is the rule.<sup>7</sup> Viewed in retrospect, the diagnosis of infectious mononucleosis on clinical grounds was a possibility but a relatively unlikely one. A positive heterophile antibody screening test, however, greatly amplified consideration of infectious mononucleosis. This potentially confusing occurrence has not been emphasized in prior reviews of Rocky Mountain spotted fever.

To explain the finding of a positive heterophile antibody screening test in Rocky Mountain spotted fever, two possibilities are suggested. The first is that the patient had infectious mononucleosis in recent months, and the positive heterophile antibody screening test, which can detect mononucleosis up to a year after infection,<sup>8</sup> was a reaction to that earlier event. An Epstein-Barr virus-specific antibody titer could have documented such prior exposure,<sup>9</sup> but could not be done in this situation.

Alternatively, heterophile antibodies are not specific for infectious mononucleosis, and there may be cross-reactivity between infectious mononucleosis antibodies and IgM antibodies in Rocky Mountain spotted fever. Further study to assess the incidence of positive mononucleosis serology results in patients with Rocky Mountain spotted fever would help to clarify the mechanism and clinical importance of this phenomenon.

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