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Afebrile Spotted Fever Group *Rickettsia* Infection After a Bite from a *Dermacentor variabilis* Tick Infected with *Rickettsia montanensis*

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Abstract

Several spotted fever group rickettsiae (SFGR) previously believed to be nonpathogenic are speculated to contribute to infections commonly misdiagnosed as Rocky Mountain spotted fever (RMSF) in the United States, but confirmation is difficult in cases with mild or absent systemic symptoms. We report an afebrile rash illness occurring in a patient 4 days after being bitten by a *Rickettsia montanensis*-positive *Dermacentor variabilis* tick. The patient's serological profile was consistent with confirmed SFGR infection.

Keywords

Rickettsia montanensis; *Rickettsia rickettsii*; Spotted fever group rickettsiae; Tick bite

Case Report

In June 2011, one day after hiking in a Georgia park, a previously healthy 6-year-old girl found a tick attached to the lower lash line of her left eye. The tick, which had fed overnight, was removed and saved; no subsequent swelling or erythema was observed at the site of attachment. A careful examination revealed no other attached ticks.

On day 4 following the tick bite, the child developed a nonpruritic, bilateral macular rash on the front of her thighs and ankles, extending to include a maculopapular rash on the soles of her feet (Fig. 1). The child's temperature was normal (36.7°C, 98.1°F). On day 5 following the tick bite, the patient complained of mild nausea and a headache; the rash was noted to have expanded to include the upper arms and the palm of her right hand. The child was seen by her pediatrician on day 5, when whole blood and serum samples were taken and she was prescribed doxycycline 2.2 mg/kg twice a day for presumptive Rocky Mountain spotted fever (RMSF) infection. The patient's temperature remained normal throughout the course

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of illness in the absence of antipyretics. The patient completed a 5-day course of doxycycline, and the rash and constitutional symptoms resolved within 48 h of starting treatment. A second serum sample was obtained 30 days after the first sample (35 days after the tick bite and 31 days after rash onset).

The removed tick and patient samples were submitted to the U.S. Centers for Disease Control and Prevention (CDC) for testing. The tick that was removed from the child was morphologically identified as an adult female *Dermacentor variabilis*. Rickettsial DNA was detected by polymerase chain reaction (PCR; Eremeeva et al. 2003). Through nucleic acid sequence analysis, the amplified fragment was identified as 99% identical to *Rickettsia montanensis* strains (FM883670.1 and U55823.1) in GenBank.

Nested PCR assay for spotted fever group rickettsiae (SFGR) on the patient's acute whole blood collected was negative (Eremeeva et al. 2003); PCR of whole blood is a poorly sensitive assay to detect SFGR in the acute phase of illness, and such samples are frequently negative, even for confirmed RMSF infections (CDC, unpublished data). Serology for SFGR was performed using indirect immunofluorescence assays (IFA) against *Rickettsia rickettsii* and *R. montanensis* (Nicholson et al. 1997). IgM antibodies to both organisms were detected in the acute and convalescent serum samples at 1:32 dilution. The patient demonstrated a significant rise in serum IgG antibody titers to SFGR between acute- and convalescent-phase sera, meeting laboratory criteria for confirmation of infection. The patient's highest observed titer was to *R. montanensis*, with an initial acute IgG titer of 1:8, rising to a convalescent IgG titer of 1:64. Reactivity to *R. rickettsii* was also observed, with an acute IgG titer of < 1:8, and a convalescent IgG titer of 1:32.

Discussion

Rickettsia montanensis has traditionally been considered a nonpathogenic member of the SFGR, and no human infections with this organism have been previously reported. In this report, we describe a patient with mild constitutional symptoms and rash, who was bitten by a *R. montanensis*-infected tick 4 days prior to illness onset, and who demonstrated seroconversion to SFGR within a month following illness onset. While a possible role for other ticks missed on careful examination cannot be ruled out, the evidence in this case suggests that *R. montanensis* should be examined more closely as a potential human pathogen (Stromdahl et al. 2011). The presence of *R. montanensis* DNA in the attached tick, and the fact that the patient exhibited a twofold higher antibody titer to *R. montanensis* than to *R. rickettsii* in the same assay run, suggests this patient may have been infected with *R. montanensis*. While overall titers detected were low, a significant rise in antibodies was observed between acute and convalescent specimens, which is consistent with current infection. Despite the supportive clinical and laboratory data, this patient did not meet the national surveillance case definition for confirmed or probable SFGR, which requires the presence of a fever (Centers for Disease Control and Prevention 2010).

RMSF, caused by *R. rickettsii*, is the most commonly reported tick-borne rickettsial disease in the United States; from 2005–2007 over 2000 RMSF cases were reported annually (Openshaw et al. 2010). While RMSF has traditionally been considered a moderate-to-

severe infection, fewer than 0.5% of nationally reported cases had fatal outcomes during that time (Openshaw et al.2010). *R. rickettsii* is one of several SFGR organisms that possess cross-reactive antigenic epitopes. Most cases of RMSF reported to the CDC through national surveillance systems are diagnosed on the basis of serology alone, which cannot differentiate between antigenically-related species of rickettsiae. The recent upsurge in mild RMSF cases captured by national surveillance has raised questions about a possible role for other SFGR as human pathogens (Raoult and Paddock 2005; Parola et al. 2009). Other SFGR known to cause human illness in the United States include *Rickettsia parkeri* and *Rickettsia* 364D (Paddock et al. 2008; Shapiro et al. 2010). In addition, *Rickettsia amblyommii* has also been speculated to cause human illness (Apperson et al. 2008).

Although *R. montanensis* has not been previously reported as a cause of human illness, the lack of past physical evidence is not surprising if patients experience only mild or subclinical illness. The procurement of appropriate patient specimens for PCR or culture, such as a skin biopsy of the rash site, will be important to definitely determine if *R. montanensis* is a human pathogen in future cases. The issue of differentiating or even understanding a particular causative agent may not appear important in a clinical setting, where suspected tick-borne disease patients are treated empirically with doxycycline. However, understanding the geographic prevalence of different SFGR may be useful in guiding regional diagnostic testing decisions. Furthermore, if *R. montanensis* is shown to be a human pathogen, relying on a requirement for fever for national reporting will cause some cases to be missed, and underestimate the true burden of tick-borne illness in the United States.

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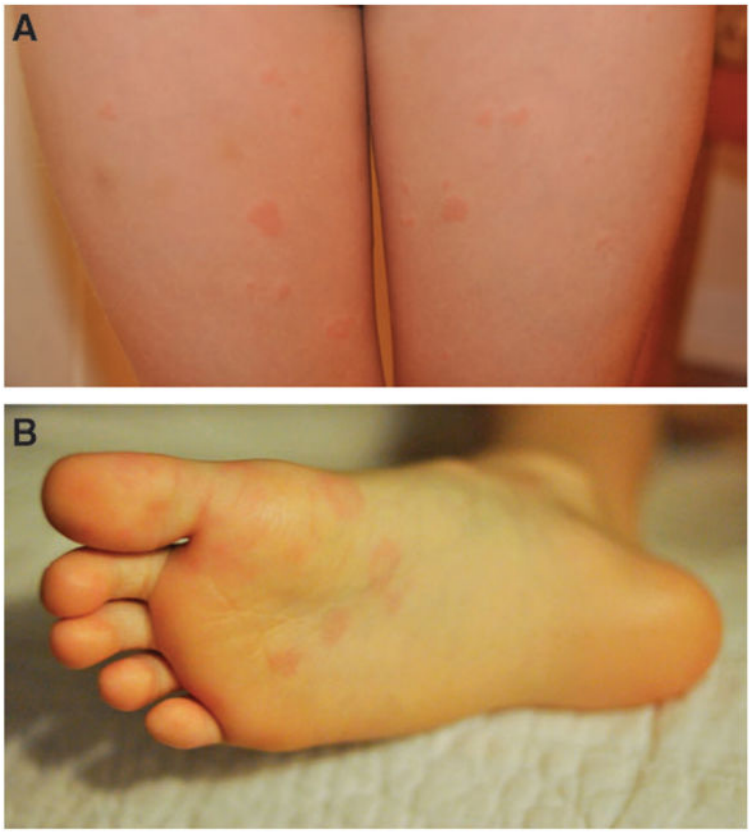

FIG. 1.

Macular rash on the front of the thighs (**A**), and maculopapular rash on the sole of the foot (**B**). Photographs taken on day 4 following tick bite.