CASE REPORT

Vesicular spotted fever due to *Rickettsia parkeri* simulates the clinicopathologic features of rickettsialpox

Ali Malik, BS, Penelope Kallis Skopis, MD, Clinton Enos, MD, Addie Walker, MD, and Kiran Motaparthi, MD

*Gainesville, Florida*

**Key words:** *Rickettsia akari*; rickettsialpox; *Rickettsia parkeri*; Rocky Mountain spotted fever; SFGR; spotted fever group rickettsiae; vesicular spotted fever.

**INTRODUCTION**

Spotted fever group rickettsiae (SFGR) represent gram-negative intracellular bacteria transmitted to human hosts through tick bites. Although Rocky Mountain spotted fever (RMSF) represents the prototypical rickettsiosis associated with SFGR, this group also includes *Rickettsia parkeri*. Among the SFGR, *R parkeri* may produce a distinct vesicular eruption preceded by an eschar. Thus, *R parkeri* rickettsiosis may clinically and histopathologically simulate rickettsialpox due to *Rickettsia akari*. Herein, we present a case of vesicular spotted fever due to *R parkeri*.

**CASE REPORT**

A 50-year-old previously healthy woman presented with rapid-onset fever, arthralgia, and rash. Three days earlier, she had developed an eschar on the thigh followed by a rash that started on the trunk and spread centrifugally to involve her face, upper and lower extremities, buttocks, and trunk. She experienced mild pruritus. She denied recent travel outside of Florida.

Physical examination revealed a generalized eruption consisting of papulovesicles on erythematous bases, along with an eschar with surrounding erythema noted on the posterior aspect of the thigh (Fig 1). With regard to laboratory investigations, the platelet count was 128,000/mm³, demonstrating significant thrombocytopenia. The results of liver function tests and complete blood cell count were unremarkable. Given the presence of an eschar (tache noir) followed by a generalized papulovesicular eruption associated with fever, along with the elicited social history, the clinical impression was rickettsialpox due to *R akari*. A punch biopsy performed on a papulovesicle on the thigh revealed papillary dermal edema, lymphocytic vasculitis, and hemorrhage (Fig 2). The patient was started on doxycycline 100 mg daily empirically, and serologies for rickettsiae (which are cross-reactive among the species *Rickettsia rickettsii*, *R akari*, *R parkeri*, *Rickettsia conorii*, *Rickettsia australis*, and *Rickettsia sibirica*) and *Ehrlichia chaffeensis* were obtained. A punch biopsy of the eschar obtained for histopathologic review demonstrated ulceration, necrosis, and a granulomatous vasculitis (Fig 3). Deeper levels were examined, revealing tick mouthparts (Fig 4) and thereby excluding the possibility of infection due to *R akari*, which is solely transmitted by the bite of the house mouse mite.

Each biopsy and whole blood was used to identify the causative *Rickettsia* species. An immunohistochemical stain for SFGR was positive. Real-time quantitative polymerase chain reaction (PCR) detected the presence of *R parkeri*—specific DNA in the biopsy from the papulovesicle. PCR was negative in whole blood and in the biopsy of the eschar, given that doxycycline administration preceded the

From the Department of Dermatology, University of Florida College of Medicine, Gainesville.

Funding sources: None.

IRB approval status: Not applicable.

Correspondence to: Kiran Motaparthi, MD, Department of Dermatology, University of Florida College of Medicine, 4037 NW 86 Terrace, 4th Floor, Room 4123 Springhill, Gainesville, FL 32606. E-mail: kmotaparthi@dermatology.med.ufl.edu.

JAAD Case Reports 2021;17:87-91.
2352-5126 © 2021 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
https://doi.org/10.1016/j.jdcr.2021.09.024

87
collection of these specimens. Indirect immunofluorescence (IIF) of whole blood collected 3 days after symptom onset (acute phase) and 6 weeks later (convalescent phase) demonstrated IgG antibodies with cross-reactivity to *R. rickettsii* (titers, 1:128 and 1:2048, respectively), *R. akari* (1:128 and 1:1024, respectively), and *R. parkeri* (1:128 and 1:1024, respectively).

A diagnosis of *R. parkeri* rickettsiosis was confirmed, and a 10-day course of doxycycline produced rapid resolution.

**DISCUSSION**

SFGR include a family of genetically linked *Rickettsia* organisms, with RMSF being the most common infection associated with this group.
Other SFGR infections endemic to the United States include Pacific Coast tick fever caused by *Rickettsia* species 346D, rickettsialpox caused by *R* akari in the urban Northeast, and rickettsiosis caused by *R* parkeri and transmitted by the Gulf Coast tick in the Southeastern United States, particularly in Florida.\(^1,2\) Hence, geography is helpful in identifying the likely causative *Rickettsia* species within patients.

Identification of *R* parkeri rickettsiosis was first documented in 2004.\(^2\) More than 40 patients infected with *R* parkeri have been reported.\(^2\) Appropriate diagnosis of *R* parkeri infection in recent years has contributed to an improved understanding of its domestic epidemiologic and clinical impact.\(^1,2\) The Gulf Coast tick, *Amblyomma maculatum*, is chiefly responsible for transmission.\(^1,2\)

The typical manifestations of *R* parkeri reflect a relatively mild disease pattern associated with characteristic necrotic eschars identified in >90% of infections.\(^1,3,4\) In addition to *R* parkeri infection, other rickettsioses can produce eschar combined with vesicles, including rickettsialpox, Mediterranean spotted fever, Queensland tick typhus, and African tick bite fever.\(^5\) Thrombocytopenia, transaminitis, and leukopenia may also be observed, but these findings are relatively nonspecific.\(^6\)

Doxycycline is the cornerstone of treatment of *R* parkeri infection and all other rickettsioses in patients of all ages. In pediatric patients, the dose is 2.2 mg/kg twice daily (up to maximum of 200 mg/d) for 7 days; in adults, the dose is 100 mg twice daily for 7 days.\(^1,5,7\)

While *R* parkeri rickettsiosis and RMSF both typically present with fever, myalgias, headache, and a diffuse eruption of macules and papules that
may extend to involve the palms and soles, vesicles and eschar are absent in RMSF. Manifestations of infection typically last approximately 1 week following contact with an infectious tick. Interestingly, many patients ultimately diagnosed with \textit{R. parkeri} may receive a misdiagnosis of RMSF at some point during the clinical assessment due to cross-reactivity with other SFGR observed in available diagnostic tests, including IIF.\textsuperscript{1,2}

Clinically, infection associated with \textit{R. parkeri} is milder than infection associated with RMSF and rickettsialpox. The majority of patients infected with \textit{R. parkeri} demonstrate a 100\% rate of clinical recovery, and no deaths have been reported secondary to \textit{R. parkeri} infection.\textsuperscript{3,4} \textit{R. parkeri} rickettsiosis clinically resembles rickettsialpox, with the characteristic eschar at the site of the bite, followed by fever, headache, and a potentially vesicular eruption. In contrast, Pacific Coast tick fever may present with eschar but without vesicular eruption (Table I).\textsuperscript{7}

On histopathologic examination, biopsy of \textit{R. parkeri} vesicular lesions demonstrate edema and lymphocytic vasculitis, while eschars show necrosis, ulceration, and granulomatous vasculitis.\textsuperscript{5,6} In contrast, rickettsialpox may demonstrate neutrophilic infiltrates in addition to these features.\textsuperscript{9} Compared with vesicular eruptions and eschar, morbilliform or petechial exanthems are nonspecific among rickettsioses and demonstrate lymphocytic vasculitis.\textsuperscript{3,9}

Several laboratory tests can aid in the diagnosis of rickettsioses (Table II).\textsuperscript{3} Of these, PCR using patient tissue or blood specimens is species-specific. In contrast, IIF, direct immunofluorescence, and immunohistochemistry are nonspecific due to cross-reactivity between SFGR and \textit{R. akari}.\textsuperscript{4} Historically, IIF has been viewed as the “gold standard” for diagnosis of rickettsioses but requires baseline testing and patient follow-up for titers obtained during the convalescent phase of disease. Importantly, IIF is not affected by treatment and becomes positive approximately 1 week after disease onset, while PCR, immunohistochemistry, and direct immunofluorescence are affected by treatment within 24 hours.\textsuperscript{4,10} If IIF is the only method used for diagnosis, and if convalescent titers are not obtained after baseline (at disease onset), then this method will not confirm disease. In the case of noncompliance, clinicians should perform a single IIF roughly one week after disease onset to ensure a confirmatory diagnostic result. Cultures are impractical and of low yield. Consequently, rickettsioses, including \textit{R. parkeri} rickettsiosis, are likely underdiagnosed owing to early institution of empiric doxycycline therapy, lack of clinician knowledge regarding nuances of diagnostic testing, and access to diagnostic methods.

### Table II. Diagnostic methods used for diagnosis of rickettsioses, including spotted fever group diseases and rickettsialpox

| Diagnostic method | Specimen* | Affected by treatment with doxycycline\textsuperscript{1} | Cross-reactive among species or specific\textsuperscript{1} | Both baseline and follow-up testing required |
|-------------------|-----------|-------------------------------------------------------------|------------------------------------------------------------|---------------------------------------------|
| IIF               | Whole blood or serum | No | Cross-reactive | Yes |
| DIF               | Fresh tissue | Yes | Cross-reactive | No |
| PCR               | Fixed tissue | Yes | Specific | No |
| IHC               | Fixed tissue | Yes | Cross-reactive | No |

DIF, Direct immunofluorescence; IHC, immunohistochemistry; IIF, indirect immunofluorescence; PCR, polymerase chain reaction.

*Fresh tissue can also be submitted for PCR and IHC.

1For diagnostic methods affected by treatment, specimens should be collected within 24 hours of doxycycline administration.

Cross-reactivity occurs between Spotted fever group rickettsiae as well as \textit{Rickettsia akari}.  

### Conflicts of interest

None disclosed.

### REFERENCES

1. Paddock CD, Sumner JW, Comer JA, et al. \textit{Rickettsia parkeri}: a newly recognized cause of spotted fever rickettsiosis in the United States. \textit{Clin Infect Dis}. 2004;38(6):805-811. https://doi.org/10.1086/381894

2. Paddock CD, Finley RW, Wright CS, et al. \textit{Rickettsia parkeri} rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. \textit{Clin Infect Dis}. 2008;47(9):1188-1196. https://doi.org/10.1086/592254

3. Silva-Ramos CR, Hidalgo M, Faccini-Martinez AA. Clinical, epidemiological, and laboratory features of \textit{Rickettsia parkeri} rickettsiosis: a systematic review. \textit{Ticks Tick Borne Dis}. 2021;12(4):101734. https://doi.org/10.1016/j.ttbdis.2021.101734

4. Myers T, Lalani T, Dent M, et al. Detecting \textit{Rickettsia parkeri} infection from eschar swab specimens. \textit{Emerg Infect Dis}. 2013;19(5):778-780. https://doi.org/10.3201/eid1905.120622

5. Walker DH. Rickettsiae. In: Baron S, ed. \textit{Medical Microbiology}. 4th ed. University of Texas Medical Branch at Galveston; 1996: chap 38.

6. Diaz JH. Ticks, including tick paralysis. \textit{Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases}. 2015:3266-3279.e1. https://doi.org/10.1016/8978-1-4557-4801-3.00298-8
7. Centers for Disease Control and Prevention. Other Spotted Fever Group Rickettsioses: Information for Health Care Providers. U.S. Department of Health and Human Services; 2021. Accessed August 14, 2021. https://www.cdc.gov/otherspottedfever/healthcare-providers/index.html

8. Kaskas NM, Ledet JJ, Wong A, Muzny CA, Elopre L, Hughey L. Rickettsia parkeri: eschar diagnosis. J Am Acad Dermatol. 2014;71(3):e87-e89. https://doi.org/10.1016/j.jaad.2014.03.024

9. Vyas NS, Shieh WJ, Phelps RG. Investigating the histopathological findings and immunolocalization of rickettsialpox infection in skin biopsies: a case series and review of the literature. J Cutan Pathol. 2020;47(5):451-458. https://doi.org/10.1111/cup.13649

10. Kaplan JE, Schonberger LB. The sensitivity of various serologic tests in the diagnosis of Rocky Mountain spotted fever. Am J Trop Med Hyg. 1986;35(4):840-844. https://doi.org/10.4269/ajtmh.1986.35.840