

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



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## INTRODUCTION

Spotted fever group rickettsiae (SFGR) represent gram-negative intracellular bacteria transmitted to human hosts through tick bites.<sup>1,2</sup> 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/mm<sup>3</sup>, 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

### Abbreviations used:

IIF:	indirect immunofluorescence assay
PCR:	polymerase chain reaction
RMSF:	Rocky Mountain spotted fever
SFGR:	spotted fever group rickettsiae

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

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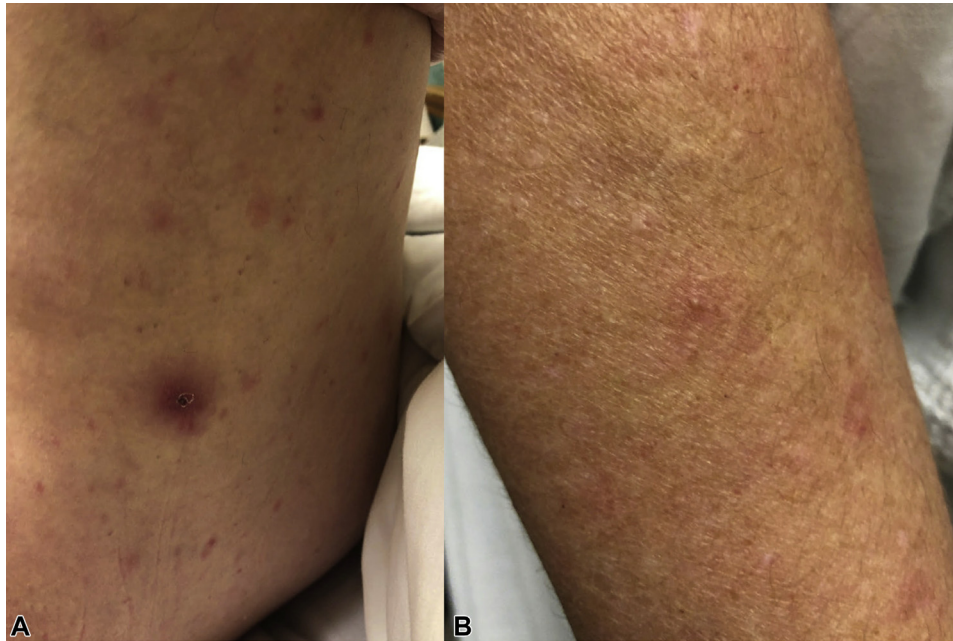
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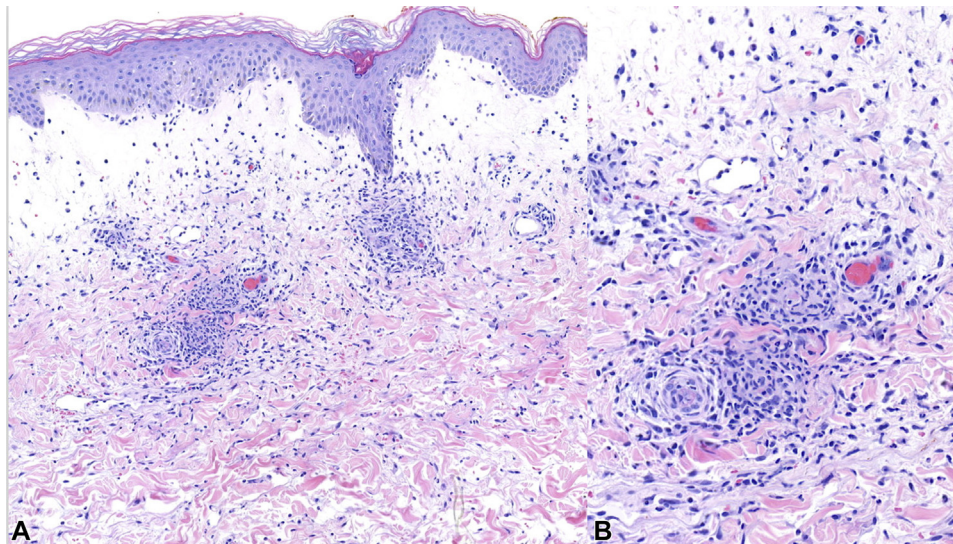
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**Fig 1.** **A**, Eschar with surrounding erythema. **B**, Scattered papulovesicles with an erythematous base.



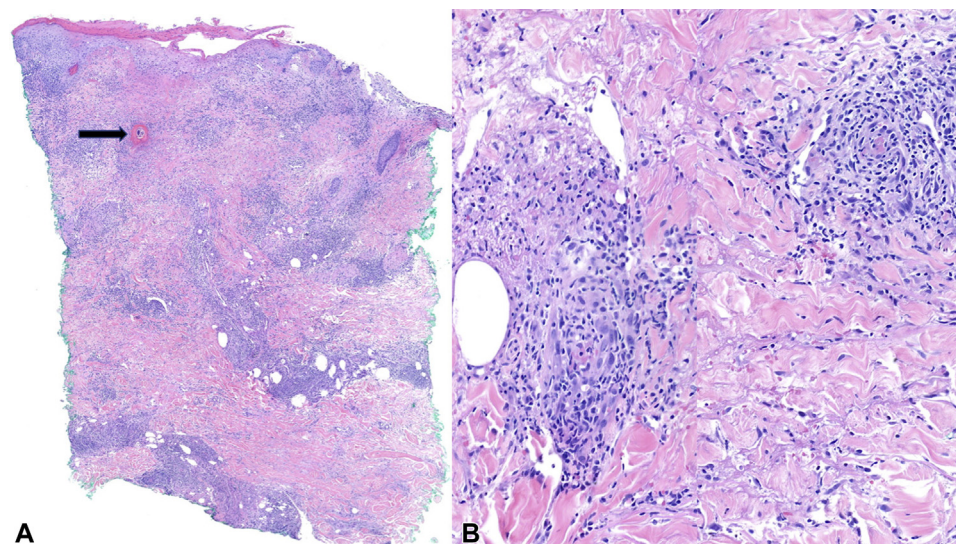
**Fig 2.** **A**, Biopsy of a papulovesicle demonstrates papillary dermal edema and a perivascular infiltrate predominantly composed of lymphocytes. **B**, Lymphocytic small vessel vasculitis is reflected by prominent endothelial swelling with luminal obliteration, thrombosis, and red blood cell extravasation. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 100$ ; **B**,  $\times 200$ .)

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).

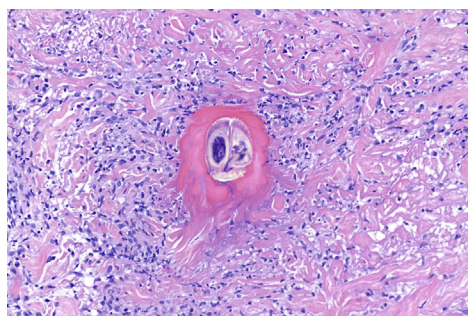
A diagnosis of *R parkeri* rickettsiosis was confirmed, and a 10-day course of doxycycline produced rapid resolution.

#### DISCUSSION

SFGR include a family of genetically linked *Rickettsia* organisms, with RMSF being the most common infection associated with this group.



**Fig 3.** **A**, Biopsy of the eschar demonstrates ulceration, dermal necrosis, and a superficial and deep perivascular mixed inflammatory infiltrate. A chitinous structure (*arrow*) represents retained tick mouthparts. **B**, A granulomatous small vessel vasculitis is highlighted, including endothelial swelling with luminal obliteration and red blood cell extravasation. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 20$ ; **B**,  $\times 200$ .)



**Fig 4.** Retained tick mouthparts. (Hematoxylin-eosin stain; original magnification:  $\times 200$ .)

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.<sup>1,2</sup> Hence, geography is helpful in identifying the likely causative *Rickettsia* species within patients.

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

The typical manifestations of *R parkeri* reflect a relatively mild disease pattern associated with

**Table I.** Differentiation of select tick-borne illnesses endemic to the United States based on clinical morphology<sup>3,7</sup>

Clinical feature	Associated diseases
Morbilliform or petechial rash	<i>Rickettsia parkeri</i> rickettsiosis, ehrlichiosis, anaplasmosis, Rocky Mountain spotted fever
Eschar	<i>R parkeri</i> rickettsiosis, rickettsialpox, <i>Rickettsia</i> species 346D rickettsiosis
Vesicles and eschar	<i>R parkeri</i> rickettsiosis, rickettsialpox

characteristic necrotic eschars identified in  $>90\%$  of infections.<sup>1,3,4</sup> 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.<sup>5</sup> Thrombocytopenia, transaminitis, and leukopenia may also be observed, but these findings are relatively nonspecific.<sup>6</sup>

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.<sup>1,3,7</sup>

While *R parkeri* rickettsiosis and RMSF both typically present with fever, myalgias, headache, and a diffuse eruption of macules and papules that

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

Diagnostic method	Specimen*	Affected by treatment with doxycycline <sup>†</sup>	Cross-reactive among species or specific <sup>‡</sup>	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.

<sup>†</sup>For diagnostic methods affected by treatment, specimens should be collected within 24 hours of doxycycline administration.

<sup>‡</sup>Cross-reactivity occurs between Spotted fever group rickettsiae as well as *Rickettsia akari*.

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 *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.<sup>1,2</sup>

Clinically, infection associated with *R parkeri* is milder than infection associated with RMSF and rickettsialpox. The majority of patients infected with *R parkeri* demonstrate a 100% rate of clinical recovery, and no deaths have been reported secondary to *R parkeri* infection.<sup>3,4</sup> *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).<sup>7</sup>

On histopathologic examination, biopsy of *R parkeri* vesicular lesions demonstrate edema and lymphocytic vasculitis, while eschars show necrosis, ulceration, and granulomatous vasculitis.<sup>8</sup> In contrast, rickettsialpox may demonstrate neutrophilic infiltrates in addition to these features.<sup>9</sup> Compared with vesicular eruptions and eschar, morbilliform or petechial exanthems are nonspecific among rickettsioses and demonstrate lymphocytic vasculitis.<sup>3,9</sup>

Several laboratory tests can aid in the diagnosis of rickettsioses (Table II).<sup>3</sup> 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 *R akari*.<sup>4</sup> 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.<sup>4,10</sup> 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 *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.

#### Conflicts of interest

None disclosed.

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