Case Report: A Confirmed Case of Rickettsia parkeri Infection in a Traveler from Uruguay

Aránzazu Portillo, Concepción García-García, M. Mercedes Sanz, Sonia Santibáñez, José M. Venzal, and José A. Oteo*

Departamento de Enfermedades Infecciosas, Hospital San Pedro-Centro de Investigación Biomédica de La Rioja (CIBIR),

Logroño, La Rioja, Spain; Departamento de Parasitología Veterinaria, Universidad de La República, Salto, Uruguay

Abstract. The first confirmed case of *Rickettsia parkeri* infection in Uruguay is reported. To date, in South America, molecularly confirmed cases of human infection have been found in Argentina and probably, Brazil. Our patient returned to Spain after a 7-day trip to Colonia Suiza (Southwestern Uruguay). He presented fever (39°C), chills, and two eschars (tache noire-like) surrounded by an indurated, erythematous halo on the inner side of the left ankle besides a maculopapular rash on the legs. After treatment with doxycycline for 7 days, he fully recovered. *R. parkeri* infection was diagnosed by molecular-based detection of the microorganism in a swab specimen of the eschar. Diagnosis was supported by seroconversion between acute- and convalescent-phase sera specimens.

Until recently, Rocky Mountain spotted fever (RMSF) or *Rickettsia rickettsii* infection was the unique tick-borne rickettsiosis known in the New World. However, during last decades, new *Rickettsia* species have been identified as human tick-borne pathogens, which is the case of *R. parkeri*. Human cases caused by this microorganism and confirmed using molecular assays have been mainly described in North America,^{1–5} and retrospective analyses have shown that some cases of RMSF could be now attributed to *R. parkeri*.⁶ In South America, two molecularly confirmed cases of human infection with *R. parkeri* have been reported in Argentina, and recent molecular results strongly suggest that this infection is also distributed in Brazil.^{7–9} Herein, we report a confirmed case of *R. parkeri* human disease in a patient who returned to Spain after acquiring the infection in Uruguay.

A 54-year-old man returned to Spain on December 16, 2012 after a 7-day trip to Uruguay. He did not notice any arthropod bites. A risk factor for being bitten by ticks is walking in grassy areas, and our patient had been walking barefoot along a grassy area in Colonia Suiza (southwestern Uruguay). Two days after arrival in Spain, he noticed two crusted lesions on the inner side of the left ankle. The next day, he presented with malaise, fever, and chills. He was treated with amoxicillinclavulanic acid and mupirocin cream for 4 days by a primary care physician, but his symptoms persisted. On December 25, he was admitted to the Hospital San Pedro in La Rioja (Spain) with the presumptive diagnosis of cellulitis after probable arthropod bite. Examination showed fever (39°C) and two eschars (tache noire-like) surrounded by an indurated, erythematous halo on the inner side of the left ankle (Figure 1). A petechial rash was also observed on legs. Rickettsiosis was suspected, and DNA was extracted from ethylenediaminetetraacetic acid disodium salt-treated blood and cutaneous swab specimens from the eschar using the DNeasy Blood & Tissue Kit (QIAGEN, Hilden, Germany) and tested for the presence of Rickettsia spp. using polymerase chain reaction (PCR) assays for gltA and ompA genes (Table 1).^{10,11} In addition, acute and convalescent sera specimens (collected 2 weeks after the onset of the illness) were tested by immunofluorescence assays (IFAs) using R. conorii (VIRCELL S.L., Granada, Spain) and R. rickettsii (FOCUS Diagnostics, Cypress, CA)

*Address correspondence to José A. Oteo, Departamento de Enfermedades Infecciosas, Hospital San Pedro-CIBIR, C/ Piqueras 98, 26006 Logroño (La Rioja), Spain. E-mail: jaoteo@riojasalud.es as antigens. Fragments of *gltA* and *ompA* rickettsial genes were amplified from the swab sample. Partial *gltA* (285/285 bp) and *ompA* (535/536 bp) sequences showed 100% and 99.8% identity to the corresponding sequences of *R. parkeri*. Diagnostic antibodies against spotted fever group rickettsiae were not detected in the acute serum specimen, but the convalescent specimen was positive for immunoglobulin G (IgG) at a titer of 4,096 with both antigens. Doxycycline (100 mg/12 hours) was administered for 7 days, and the patient fully recovered (fever disappeared in the first 24 hours after initiation of doxycycline therapy).

Previously considered non-pathogenic in humans, *R. parkeri* was first described in *Amblyomma maculatum* ticks.¹² In 2004, Paddock and others¹ described the first human cases associated with this bacterium in the United States. At the same time, this *Rickettsia* species was also suspected to be the responsible agent for the tick-borne spotted fevers in Uruguay, because it was amplified from one *A. triste* tick attached to a patient who developed a rickettsial syndrome.¹³ Regarding clinical features, it seems that *R. parkeri* causes a spotted fever syndrome that is less severe than RMSF. Also, it can be differentiated from RMSF by the presence of an eschar at the site of the tick attachment.³ In South America, rickettsial illness caused by *R. parkeri* has been described in Uruguay, Argentina, and probably, Brazil.¹⁴ Cases from Argentina have been confirmed



FIGURE 1. Crusted lesions on the inner side of the left ankle.

Primers used for amplification of partial rickettsial genes				
Primer name	Primer sequence $(5' \rightarrow 3')$	Amplified fragment (bp)	Annealing temperature (°C)	Ref
ompA				
Rr190.70p	ATGGCGAATATTTCTCCAAAA	631	46	10
Rr190.701n	GTTCCGTTAATGGCAGCATCT			
Rr190.70p	ATGGCGAATATTTCTCCAAAA	532	48	10
Rr190.602n	AGTGCAGCATTCGCTCCCCCT			
gltA				
RpCS.877p	GGGGGCCTGCTCACGGCGG	381	48	10
RpCS.1,258n	ATTGCAAAAAGTACAGTGAACA			
RpCS.896p	GGCTAATGAAGCAGTGATAA	337	56	11
RpCS.1,233n	GCGACGGTATACCCATAGC			

TABLE 1 Primers used for amplification of partial rickettsial genes

with molecular tools,⁷ whereas rickettsial taxonomy related to Brazilian cases remains unclear.^{8,9} All confirmed and probable cases referred to tick bites. Most presented an eschar at the tick bite site besides a maculopapular rash that was accompanied by fever, myalgias, or headache. As we observed in our patient, the clinical course was benign in all published cases, with clinical resolution after doxycycline prescription.⁷ Recently, two cases of spotted fever group rickettsiosis caused by a noncultured *Rickettsia* closely related to *R. parkeri* as well as *R. africae* and *R. sibirica* have been reported in Brazil.^{8,9} To date, whether these taxonomic names may be considered a single species is discussed.¹⁵

R. parkeri is a common microorganism found in ticks from South American countries.^{13,16–19} In Uruguay, *R. parkeri* is present in a relatively high percentage of *A. triste* ticks.²⁰ *A. triste* is present in at least 12 other Latin American countries, and it is probable that this infection is widely distributed in most of the continent.^{21,22} Higher *R. parkeri* infection rates among tick populations, compared with *R. rickettsii*, suggest that *R. parkeri* rickettsiosis is likely to be misdiagnosed.²³ In conclusion, we must consider the possibility of rickettsiosis in people returning from South America.

Received July 29, 2013. Accepted for publication September 17, 2013.

Published online October 28, 2013.

Acknowledgments: The American Committee on Clinical Tropical Medicine and Travelers' Health (ACCTMTH) assisted with publication expenses.

Authors' addresses: Aránzazu Portillo, Concepción García-García, M. Mercedes Sanz, Sonia Santibáñez, and José A. Oteo, Departamento de Enfermedades Infecciosas, Hospital San Pedro-CIBIR, Logroño, La Rioja, Spain, E-mails: aportillo@riojasalud.es, cgarciag@riojasalud.es, mmsanz@riojasalud.es, ssantibanez@riojasalud.es, and jaoteo@ riojasalud.es. José M. Venzal, Departamento de Parasitología Veterinaria, Universidad de La República, Salto, Uruguay, E-mail: dpvuru@hotmail.com.

REFERENCES

- Paddock CD, Sumner JW, Comer JA, Zaki SR, Goldsmith CS, Goddard J, McLellan SL, Tamminga CL, Ohl CA, 2004. *Rickettsia parkeri*: a newly recognized cause of spotted fever rickettsiosis in the United States. *Clin Infect Dis 38:* 805–811.
- Whitman TJ, Richards AL, Paddock CD, Tamminga CL, Sniezek PJ, Jiang J, 2007. *Rickettsia parkeri* infection after tick bite, Virginia. *Emerg Infect Dis* 13: 334–336.
- Paddock CD, Finley RW, Wright CS, Robinson HN, Schrodt BJ, Lane CC, Ekenna O, Blass MA, Tamminga CL, Ohl CA, McLellan SL, Goddard J, Holman RC, Openshaw JJ, Sumner

JW, Zaki SR, Eremeeva ME, 2008. *Rickettsia parkeri* rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. *Clin Infect Dis* 47: 1188–1196.

- Cragun WC, Bartlett BL, Ellis MW, Hoover AZ, Tyring SK, Mendoza N, Vento TJ, Nicholson WL, Eremeeva ME, Olano JP, Rapini RP, Paddock CD, 2010. The expanding spectrum of eschar-associated rickettsioses in the United States. *Arch Dermatol* 146: 641–648.
- Myers T, Lalani T, Dent M, Jiang J, Daly PL, Maguire JD, Richards AL, 2013. Detecting *Rickettsia parkeri* infection from eschar swab specimens. *Emerg Infect Dis* 19: 778–780.
- Raoult D, Paddock CD, 2005. *Rickettsia parkeri* infection and other spotted fevers in the United States. *N Engl J Med* 353: 626–627.
- Romer Y, Seijo AC, Crudo F, Nicholson WL, Varela-Stokes A, Lash RR, Paddock CD, 2011. *Rickettsia parkeri* rickettsiosis, Argentina. *Emerg Infect Dis* 17: 1169–1173.
- Spolidorio MG, Labruna MB, Mantovani E, Brandao PE, Richtzenhain LJ, Yoshinari NH, 2010. Novel spotted fever group rickettsiosis, Brazil. *Emerg Infect Dis* 16: 521–523.
- Silva N, Eremeeva ME, Rozental T, Ribeiro GS, Paddock CD, Ramos EAG, Favacho ARM, Reis MG, Dasch GA, de Lemos ERS, Ko AI, 2011. Eschar-associated spotted fever rickettsiosis, Bahia, Brazil. *Emerg Infect Dis 17:* 275–278.
- Regnery RL, Spruill CL, Plikaytis BD, 1991. Genotypic identification of rickettsiae and estimation of intraspecies sequence divergence for portions of two rickettsial genes. *J Bacteriol* 173: 1576–1589.
- 11. Choi YJ, Jang WJ, Ryu JS, Lee SH, Park KH, Paik HS, Koh YS, Choi MS, Kim IS, 2005. Spotted fever group and typhus group rickettsioses in humans, South Korea. *Emerg Infect Dis* 11: 237–244.
- 12. Parker RR, Kohls GM, Cox GW, Davis GE, 1939. Observations on an infectious agent from *Amblyomma maculatum*. *Public Health Rep 54*: 1482–1484.
- Venzal JM, Portillo A, Estrada-Peña A, Castro O, Cabrera PA, Oteo JA, 2004. Rickettsia parkeri in Amblyomma triste from Uruguay. Emerg Infect Dis 10: 1493–1495.
- Labruna MB, Mattar S, Nava S, Bermudez S, Venzal JM, Dolz G, Abarca K, Romero L, de Sousa R, Oteo J, Zavala-Castro J, 2011. Rickettsioses in Latin America, Caribbean, Spain and Portugal. *Rev MVZ Córdoba 16*: 2435–2457.
- Walker DH, Ismail N, 2008. Emerging and re-emerging rickettsioses: endothelial cell infection and early disease events. *Nat Rev Microbiol 6:* 375–386.
- Silveira I, Pacheco RC, Szabó MP, Ramos HG, Labruna MB, 2007. Rickettsia parkeri in Brazil. Emerg Infect Dis 13: 1111–1113.
- Nava S, Elshewany Y, Eremeeva ME, Sumner JW, Mastropaolo M, Paddock CD, 2008. *Rickettsia parkeri* in Argentina. *Emerg Infect Dis 14*: 1894–1897.
- Tomassone L, Conte V, Parrilla G, De Meneghi D, 2010. Rickettsia infection in dogs and Rickettsia parkeri in Amblyomma tigrinum ticks, Cochabamba Department, Bolivia. Vector Borne Zoonotic Dis 10: 953–958.
- Flores-Mendoza C, Florin D, Felices V, Pozo EJ, Graf PC, Burrus RG, Richards AL, 2013. Detection of *Rickettsia parkeri* from within Piura, Peru, and the first reported presence of

Candidatus Rickettsia andeanae in the tick Rhipicephalus sanguineus. Vector Borne Zoonotic Dis 13: 505-508.

- 20. Venzal JM, Estrada-Peña A, Portillo A, Mangold AJ, Castro O, De Souza CG, Félix ML, Pérez-Martínez L, Santibánez S, Oteo JA, 2012. Rickettsia parkeri: a rickettsial pathogen transmitted by ticks in endemic areas for spotted fever rickettsiosis in southern Uruguay. Rev Inst Med Trop Sao Paulo 54: 131-134.
- 21. Guglielmone AA, Estrada-Peña A, Keirans JE, Robbins RG, 2003. Ticks (Acari: Ixodida) of the neotropical zoogeographic region. International Consortium on Ticks and Tick-Borne Diseases, Atalanta, Houten, The Netherlands, 173 pp.
- 22. Pacheco RC, Venzal JM, Richtzenhain LJ, Labruna MB, 2006.
- Rickettsia parkeri in Uruguay. Emerg Infect Dis 12: 1804–1805.
 23. Labruna MB, 2009. Ecology of Rickettsia in South America. Ann N Y Acad Sci 1166: 156–166.