

Is Rocky Mountain spotted fever the only disease of the spotted fever group rickettsioses found in Mexico?

¿La fiebre manchada de las Montañas Rocosas es la única enfermedad del grupo de las rickettsiosis de fiebres manchadas que se encuentra en México?

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Dear Editor,

We have read with great interest the articles published in your journal about the experience in the states of Coahuila and Sonora concerning pediatric cases of Rocky Mountain spotted fever (RMSF)^{1,2}, which allows us to comment on aspects of the epidemiological and clinical relevance of this disease.

RMSF has been widely documented in the country. However, unlike the clinical characteristics reported in these publications (which are usually similar), national case fatality rates (CFRs) vary between 20.2% and 92%^{1,3}, remaining high even when doxycycline is administered in the first 5 days of evolution³. Such differences are even more significant when compared to those published by the United States, where the CFR is < 1%⁴.

Some of the factors proposed as an explanation for the variation in the CFR include the variability in virulence among *Rickettsia rickettsii* strains, as described in the initial reports of RMSF among the state of Idaho (where CFR was 5%) and Montana (where CFR was

70-80%)⁵, with regional evidence from the state of Baja California, where an unidentified strain of *R. rickettsii* was reported⁶. Furthermore, the increase in the aggressiveness of *Rhipicephalus sanguineus* s.l., the vector of RMSF in Sonora and Coahuila, has been documented in relation to the rise in ambient temperature⁷. Similarly, some case reports of patients with enzymatic alterations, such as glucose-6-phosphate dehydrogenase deficiency, are associated with a worse prognosis. Therefore, a higher prevalence of this phenomenon in the Mexican population could influence high CFR⁸.

Although the diagnosis of RMSF is currently based on well-defined diagnostic criteria, such as the polymerase chain reaction (PCR) for genus and species, as well as a 4-fold rise in titres by indirect immunofluorescence assay (IFA), access to these tests in the country is limited. Therefore, some publications include case series with compatible clinical conditions but no laboratory tests or with a single elevation of antibodies by IFA (compatible cases). Due to the elevation of antibodies by cross-reaction with other species of the

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spotted fever group rickettsioses (SFGR), the diagnosis could be confusing, which would explain the variation in the CFR between case series that include only confirmed patients and those that include compatible and confirmed cases.

Together with other species capable of causing disease in humans, *R. rickettsii* is part of the SFGR. Although it is currently the only species recognized as a human pathogen in Mexico, other species of this group that can produce a disease with a similar clinical picture have recently been identified in the northwest of the country. Unlike RMSF, these species have not been responsible for any fatal cases registered so far. There are reports of infections with *Rickettsia parkeri* in *Amblyomma maculatum* and *R. sanguineus* s.l. in Sonora and Baja California^{9,10}, *Rickettsia massiliae* in *R. sanguineus* s.l. in Chihuahua and Baja California¹⁰, and a third suspected taxon, *Rickettsia 364D*, which has not yet been identified, but evidence shows that its vector, *Dermacentor occidentalis*, is found in Baja California, Sinaloa, and Coahuila¹¹. In addition, two other species of the SFGR have been reported in the state of Coahuila. Although their pathogenicity is still unknown, they can generate cross-reactivity with *R. rickettsii*: *Rickettsia amblyommatys* in *Amblyomma mixtum* and *Rickettsia rhipicephali* in *R. sanguineus* s.l.^{12,13}.

Moreover, due to the similar initial clinical picture between RMSF and SFGR, the clinical distinction is difficult. However, the presence of signs, such as the necrotic eschar at the site of the tick bite and regional lymphadenopathy, can help its identification as SFGR and not RMSF¹⁴.

Based on the current guidelines of the National Institute of Diagnosis and Reference, and through the implementation of the qPCR for the detection of the citrate synthase gene present in all rickettsial species¹⁵, diagnosis is limited to *Rickettsia* spp. Therefore, these results should be interpreted as genus and not as a particular species, unless otherwise specified. An unpaired positive IFA titer may be due to infection with *R. rickettsii*, cross-reaction with other SFGR, or immunological memory to a previous infection. Therefore, these cases should not be considered as confirmed cases of RMSF.

The proper interpretation of diagnostic tests will allow not only to identify other SFGR species that are currently circulating in the country and being erroneously diagnosed as RMSF, but it will also help to define the

vectors involved and their distribution (with 100 species of recorded ticks in the country currently). Furthermore, the adequate interpretation of diagnostic tests will describe the epidemiology of SFGR in the country, as well as the clinical and laboratory data to differentiate them from RMSF, and most importantly, to define their prognosis, given the high lethality of RMSF in the country against the absence of fatal cases in patients with other SFGR.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. López-Castillo DC, Vaquera-Aparicio D, González-Soto MA, Martínez-Ramírez R, Rodríguez-Muñoz L, Solórzano-Santos F. Fiebre manchada de montañas rocosas: experiencia de 5 años de vigilancia activa en un hospital pediátrico de segundo nivel en el noreste de México. Bol Med Hosp Infant Mex. 2008;75:303-8.
2. Martínez-Medina MA. Rocky Mountain spotted fever in a pediatric hospital in Northeastern Mexico. Bol Med Hosp Infant Mex. 2019;76:97-8.
3. Delgado-de la Mora J, Licona-Enríquez JD, Leyva-Gastelum M, Delgado-de la Mora D, Rascón-Alcantar A, Álvarez-Hernández G. [A fatal case series of Rocky Mountain spotted fever in Sonora, Mexico]. Biomedica. 2018;38:69-76.
4. Drexler NA, Dahlgren FS, Heitman KH, Massung RF, Paddock CD, Behravesh CB. National surveillance of spotted fever group rickettsioses in the United States, 2008-2012. Am J Trop Med Hyg. 2016;94:26-34.
5. Weiss E. History of rickettsiology. In: Walker DH, editor. Biology of Rickettsial Disease. Boca Raton, Florida: CRC Press; 1988. p. 15-32.
6. Ereemeva ME, Zambrano ML, Anaya L, Beati L, Karpathy SE, Santos-Silva MM, et al. *Rickettsia rickettsii* in *Rhipicephalus* ticks, Mexico. J Med Entomol. 2011;48:418-21.
7. Parola P, Socolovschi C, Jeanjean L, Bitam I, Fournier PE, Sotto A, et al. Warmer weather linked to tick attack and the emergence of severe rickettsioses. PLoS Negl Trop Dis. 2008;11:e338.
8. Walker DH, Hawkins HK, Hudson P. Fulminant Rocky Mountain spotted fever. Its pathogenic characteristics associated with glucose-6-phosphate dehydrogenase deficiency. Arch Pathol Lab Med. 1983;107:121-5.
9. Delgado-de la Mora J, Sánchez-Montes S, Licona-Enríquez JD, Delgado-de la Mora D, Paddock CD, Beati L, et al. *Rickettsia parkeri* and *Candidatus Rickettsia andeanae* in ticks of the *Amblyomma maculatum* group, Mexico. Emerg Infect Dis. 2019;25:836-8.
10. Pieracci EG, De La Rosa J, Rubio DL, Perales M, Contreras MV, Drexler NA, et al. Seroprevalence of spotted fever group rickettsiae in canines along the United States-Mexico border. Zoonoses Public Health. 2019;66:918-26.
11. Guzmán-Cornejo C, Robbins RG, Guglielmone AA, Montiel-Parra G, Rivas G, Pérez TM. The *Dermacentor* (*Acari*, *Ixodida*, *Ixodidae*) of Mexico: hosts, geographical distribution and new records. Zookeys. 2016;569:1-22.
12. Santibáñez S, Portillo A, Palomar AM, Oteo JA. Isolation of *Rickettsia amblyommatys* in HUVEC line. New Microbes New Infect. 2017;21:117-21.
13. Ortega-Morales AI, Nava-Reyna E, Ávila-Rodríguez V, González-Álvarez VH, Castillo-Martínez A, Siller-Rodríguez QK, et al. Detection of *Rickettsia* spp. in *Rhipicephalus sanguineus* (Sensu Lato) collected from free-roaming dogs in Coahuila state, Northern Mexico. Parasit Vectors. 2019;12:130.
14. Paddock CD, Finley RW, Wright CS, Robinson HN, Schrodt BJ, Lane CC, et al. *Rickettsia parkeri* rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. Clin Infect Dis. 2008;47:1186-96.
15. Instituto de Diagnóstico y Referencia Epidemiológicos Dr. Manuel Martínez Báez. Lineamientos para la Vigilancia por Laboratorio de las Rickettsiosis. InDRE. Mexico: Secretaría de Salud; 2017.