Letter to the editor

First human case of *Rickettsia felis* reported in Guatemala

DOI: 10.5377/alerta.v5i2.14502

Beatriz López[1*], Jahn Jaramillo[2], Paige A. Armstrong[3], Maria Renee Lopez[4], Arlyn N. Gleaton[5], Ida H. Chung[6], Cecilia Y. Kato[7], Lissette Reyes[8], Manuel Sagastume[9], John P. McCracken[10], Andrés Espinosa-Bode[11]

1-2 y 11. Division of Global Health Protection, Central American Regional Office, U.S. Centers for Disease Control and Prevention, Guatemala City, Guatemala.
2. Public Health Institute, PHI/CDC Global Health Fellowship Program, Oakland, California, USA.
3, 5-7. Rickettsial Zoonoses Branch, Division of Vector-Borne Diseases, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA.
4, 10. Center for Health Studies, Universidad del Valle de Guatemala, Guatemala City, Guatemala.
8-9. Department of Epidemiology, Ministry of Public Health and Social Welfare, Guatemala City, Guatemala.

*Correspondence
fdx8@cdc.gov

1. 0000-0003-1353-9948
2. 0000-0002-7395-6551
3. 0000-0002-5529-8786
4. 0000-0001-7498-5840
5. 0000-0003-2171-9228
6. 0000-0003-0048-7843
7. 0000-0001-6963-6849
8. 0000-0003-3139-2599
9. 0000-0002-2969-1533
10. 0000-0002-0714 2971
11. 0000-0003-1578-6125

Dear Editor:

Rickettsia felis infection (*R. felis*) is considered a threat to human health. *R. felis*, a gram-negative bacterium considered an emerging arthropod-borne pathogen that has been identified in numerous human cases worldwide, represents an important cause of febrile illness, usually associated with *Ctenocephalides felis* found in cats and dogs[1]. Early clinical manifestations include fever, headache, myalgia, rash, cough and vomiting, which can mimic other febrile diseases such as dengue and malaria, thus complicating clinical diagnosis[1,2]. Severe, potentially lethal symptoms could be developed without treatment.

The sentinel surveillance of acute febrile diseases, through the Collaborative Integrated Surveillance that was developed in Guatemala from 2013 to 2018[3], allowed the discovery of the first case of *R. felis* in Guatemala. 612 patients who met the criteria of the case definition for acute febrile syndrome were chosen[3]: medical consultation or hospitalization for fever without apparent cause with less than seven days of evolution, or quantified fever greater than or equal to 38 °C during the consultation or during the first 24 hours of hospitalization. Blood samples were taken for the analysis of malaria, leptospirosis, dengue and rickettsiosis, which were processed in the laboratories of Universidad del Valle in Guatemala. The positive sample for *Rickettsia spp*. was analyzed by conventional polymerase chain reaction (PCR) for the detection of the rickettsial antigen gene 17 kDa, found in spotted fever group (SFGR) and typhus group *Rickettsia* DNA. Semi-nested amplification of 70–602 nucleotide fragment of rickettsial outer membrane protein (OmpA) gene was performed for identification of SFGR. Finally, the finding was confirmed by the Rickettsial Zoonoses Branch at U.S. Centers for Disease Control and Prevention, where *Rickettsia spp*. was confirmed by real time PCR using PanR8 assay and nested PCR targeting the SFGR 17 kDa gene. *R. felis* was identified by the sequencing of the SFGR 17 kDa amplification product.

The sample belonged to a three-year-old boy treated on December 2017 at a health center in Santa Rosa, Guatemala. At the time of sample taking, the patient reported two days of fever, cough, dyspnea, vomiting, abdominal pain and fatigue. It was reported as an exposure risk factor that his pet was a cat.

R. felis infection can cause an acute febrile syndrome with other symptoms[1]. In some cases, it is a mild illness without fever; also, isolated cases of children who had rashes or scabs have been registered[1]. Afebrile presentation also may contribute to non-detection[4].

The identification of this infection in febrile illness surveillance studies in Africa

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Suggested citation:
López B, Jaramillo J, Armstrong PA, López MR, Gleaton AN, Chung IH, *et al*. First human case of *Rickettsia felis* reported in Guatemala. Alerta. 2022;5(2):159-160. DOI: 10.5377/alerta.v5i2.14502

Received:
June 24, 2022.

Accepted:
June 30, 2022.

Published:
July 20, 2022.

Author contribution:
BL[1]: conception, design of the manuscript, bibliographic search, writing, revision and edition. JJ[2]: manuscript design, bibliographic search, writing, revision and editing. PAA[3]: writing, revision and editing. MRL[4]: data collection, writing, review and editing. ANG[5], IHC[6], CYK[7]: data analysis, writing, revision and editing. LR[8], MS[9]: writing, proofreading and editing. JPM[10]: study conception, data collection, writing, revision and edition. AEB[11]: manuscript design, writing, revision and edition.

Conflicts of interest:
The authors declare there are no conflicts of interest.

and Asia suggests that it produces clinically relevant illness in individuals with immunosuppression[2].

The low availability of diagnostic tests is a limitation. Besides, since there is a cross-reactivity of serology among Rocky Mountain spotted fevers (RMSF), this makes it difficult to interpret the results, which limits the usefulness of the diagnosis[1]. Studies have shown serological evidence of a disseminated exposure to RMSF, coinciding with the isolation of *R. felis*[5]. Also, molecular testing gives a species-specific result, but sensitivity could decrease over time and treatment[1]. A high proportion of immunofluorescence assay cases never receive a definitive diagnosis.

Non-human mammals are the asymptomatic reservoirs. The paucity of reported human cases in Central America, despite ample documented evidence of *R. felis* in arthropod vectors, also suggests that the disease is being under-detected[5].

Given the known prevalence in the region of *R. felis* in fleas, human infections by *R. felis* are likely undiagnosed and may be among the causes of undifferentiated acute febrile illness (AFI). Molecular assays can distinguish between several species of *Rickettsia*, which allow a better characterization of these infections[4,5]. This finding points to consider *R. felis* as an etiology in the differential diagnosis of febrile patients with respiratory, digestive or non-specific symptoms that can guide appropriate treatment and medical care. Besides, potential risk factors such as proximity to animals that may be carriers of infected fleas should be evaluated[5].

Although only one case of *R. felis* was detected in this study, the actual burden in Central America could be underreported. It is considered important to propose that molecular laboratory techniques are accessible in the region to provide a better characterization of the burden of rickettsial diseases[4].

Despite the lack of a convalescent serum sample to confirm that the immune response matched the acute disease, the proximity to acute symptoms, the lack of another etiology after exhaustive testing, and the positive result in a trial with a high limit of detection, supported *R. felis* as the etiology of this child's febrile illness. Besides, there is a known prevalence of *R. felis* in domestic animals in the same geographic area and there are multiple febrile illness studies that are relevant sources of this acute illness in children in Africa and Asia.

Expanding surveillance would allow a better description of the distribution of rickettsial diseases in the population, with consequent improvements in the clinical management and treatment of these emerging infections. Therefore, greater awareness of the presentation and diagnosis of this pathogen in Central America is suggested, which may contribute to a more complete understanding of the true burden of these diseases in the region.

Funding

This publication was supported by Cooperative Agreement No. UO1 U01GH001003 of the U.S. Centers for Disease Control and Prevention (CDC).

Acknowledgments

Department of Epidemiology, Health Center in Santa Rosa, Ministry of Public Health and Social Welfare in Guatemala for their contributions.

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