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Brief communication

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Rickettsia sibirica mongolitimonae infection in a woman travelling from Cameroon: a case report and review of the literature

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Abstract

Rickettsia sibirica mongolitimonae is now a well-known cause of human rickettsial infection, with 52 reported cases, including 47 in southern Europe and one in South Africa. We report the first case of *R. sibirica mongolitimonae* in Central Africa, likely a sentinel case for a more common disease than originally suspected.

Key words: Rickettsiosis, Exanthema, Cameroon, *Rickettsia sibirica mongolitimonae*

Introduction

Tick-borne spotted fever group (SFG) rickettsioses are a common source of febrile exanthema in travellers, particularly in Sub-Saharan Africa (SSA), where an increasing number of cases are being encountered,[1] but the epidemiology of rickettsioses in SSA is still not very well known. Two tick-borne SFG rickettsioses have been repeatedly reported in SSA: African Tick-Bite Fever (ATBF), caused by *Rickettsia africae*, and mediterranean spotted fever, caused by *Rickettsia conorii conorii*. One case of Astrakhan fever caused by *Rickettsia conorii caspia*, and one rickettsia case caused by *Rickettsia aeschlimannii* were described in this area.[2]

Rickettsia sibirica mongolitimonae was first isolated in 1991 in ticks in Inner Mongolia,[3] and has subsequently been associated with human infections in Southern Europe, Algeria, Egypt and Turkey.[4–6] It has been detected in ticks in Niger and Senegal, but there is only one case of human infection reported in SSA, in South Africa in 2002.[7] We report a case of *R. sibirica mongolitimonae* infection in a woman travelling from Cameroon.

Case report

A previously healthy 54-year-old woman, native of Cameroon, presented in May in our department with a 5-day history of fever, chills, headache, arthralgia and myalgia. She arrived on the day before from Cameroon, where she had spent 3 weeks in the countryside around Yaoundé. She did not report any other trip or any tick-bite.

On physical examination, she was febrile around 40°C and hemodynamically stable. A black crust surrounded by an inflammatory halo measuring 2 cm in diameter suggestive of an inoculation eschar was noted on her back (Figure 1), with a maculopapular exanthema predominantly affecting the proximal limbs and the trunk , without palmoplantar nor facial involvement. No tick was found on the patient. She did not have lymphadenopathy or lymphangitis.

Laboratory tests showed lymphopenia at 560/mm3, hepatic cytolysis (alanin aminotransferase and aspartate aminotransferase at 1,5 and 2,5 times the normal concentration, respectively) and gamma glutamyl transferase at twice the norm. Thick and thin smears for malaria were negative. Serological tests for

dengue virus, human immunodeficiency virus, hepatitis B and C viruses, and *Treponema pallidum* were negative, as well as PCR on serum for dengue and chikungunya viruses. We suspected a SFG rickettsiosis and a regimen of doxycycline, 200 mg once daily for 7 days, was started. Four days later, she was afebrile with complete resolution of all symptoms.

Serological tests with microimmunofluorescence and Western blot for *Rickettsia* spp performed at the National Reference Centre for *Rickettsia* (Marseille, France) were negative on the acute-phase serum sample. No convalescent-phase serum sample was available because the patient had returned to Cameroon. We extracted total genomic DNA from three eschar samples (a lesion swab, a piece of the crust and an eschar biopsy) by using a QIAamp tissue kit (QIAGEN, Hilden, Germany). DNA was then used as a template in a previously described quantitative PCR assay selective for a 109 bp fragment of a hypothetical protein[8] and all samples were positives. PCR amplification and sequencing selective for the gltA and ompA genes were also performed[8] and confirmed the diagnosis of *R. sibirica mongolitimonae*. In addition, samples from the eschar's biopsy were cultured in human embryonic lung fibroblasts and were also positives.

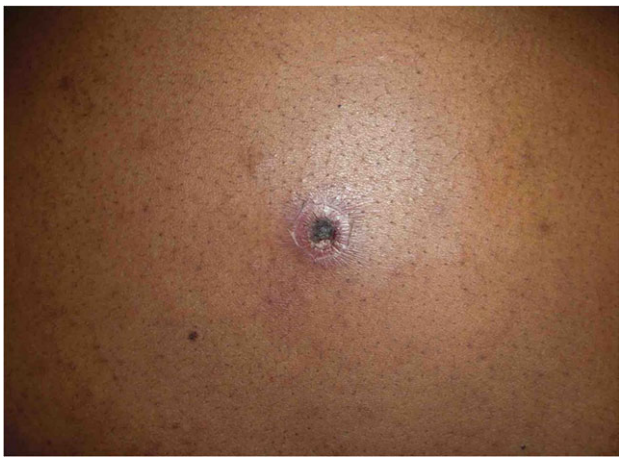

Figure 1. Inoculation eschar of the back.

Discussion

The first human case of *R. sibirica mongolitimonae* infection was described in France in 1996,[4] followed by 32 cases: 28 in southern Europe (France, Portugal, Greece and Spain), 1 in Turkey[6] and 3 in Africa (Algeria, Egypt and South Africa) (Figure 2).[5,7] For years, *R. sibirica mongolitimonae* was considered a rare pathogen but it was recently reported as a common rickettsiosis in France, with 20 additional cases.[5]

This infection typically presents with high fever, single or multiple inoculation eschars with an inflammatory halo, a flu-like syndrome with myalgias and headaches, a mild maculopapular exanthema, and enlarged draining lymph nodes, all these signs being found in more than two-third of published cases. However, these signs are also found in other SFG rickettsioses. Our patient did not show any lymphangitis, even though a particular clinical entity called 'lymphangitis-associated rickettsiosis' (LAR) was described with this subspecies.[5,9] It presents as a rope-like, deep, erythematous lymphangitis that extends from the inoculation eschar to the draining lymph node. Lymphangitis has been described in other rickettsial infections, especially in ATBF, where it seems less common (10 of more than 270 reported ATBF cases) and less pronounced, with pale erythematous streaks.[10,11] This rather specific rope-like lymphangitis is however found in only 33% of cases of *R. sibirica mongolitimonae* infections (17 of 52 cases).[5] Therefore, presumption of the *Rickettsia* species from clinical findings only remains difficult. Besides, three cases of scalp eschar and neck lymphadenopathy after tick-bite (SENLAT) syndrome caused by *R. sibirica mongolitimonae* were recently reported.[12] Thus, the established clinical spectrum of that infection can be questioned, the term 'LAR' having already been discussed by others.[13,14]

In most cases, *R. sibirica mongolitimonae* infection causes a mild, not fatal disease, but some complications have been described, such as shock,[14] disseminated intravascular coagulation,

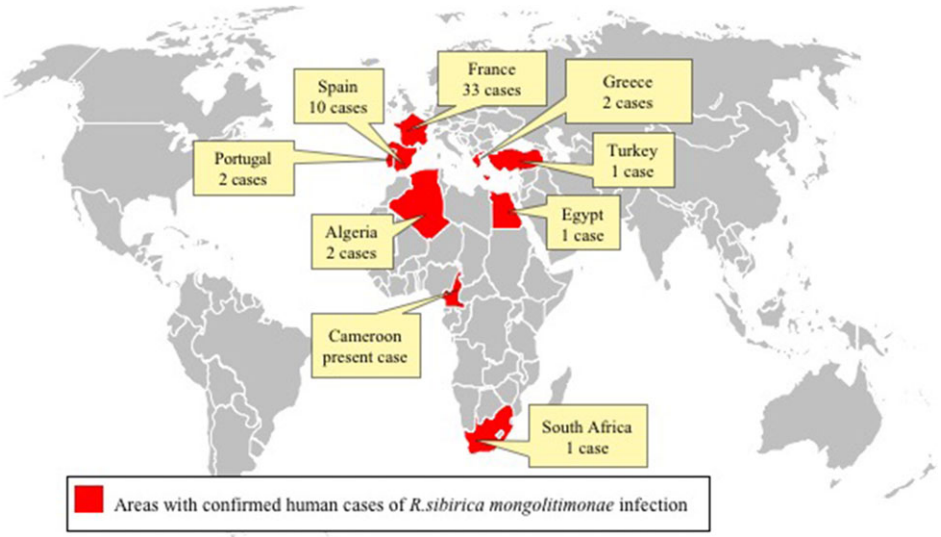

Figure 2. World distribution of *Rickettsia sibirica mongolitimonae* confirmed human cases in 2017.

neurological disorders, acute renal failure, atrial fibrillation and retinal vasculitis.

The median incubation period is 6 days (range 3–8 days),[9] confirming that our patient was bitten by the tick in the countryside around Yaoundé. In Europe, the infection mostly occurs during spring and summer, corresponding to the abundance and activity of the vector ticks in this region.[2,5]

The most useful diagnostic procedure for this infection is real-time PCR performed on samples from the inoculation eschar, a lesion swab, a crust's sample or a skin biopsy, as illustrated in our case.[8,15] These tests have sensitivity around 90% and specificity close to 100%.[8,15] The diagnosis was also confirmed in our case by culture, even though *R. sibirica mongolitimonae* is difficult to grow on cellular cultures.[15] Serological tests are less reliable for diagnosis because of the seroconversion time of 2–3 weeks, and cross-reactions between the different SFG rickettsioses.[8] Therefore, in cases of clinical suspicion of rickettsiosis, the quick diagnosis with identification of *Rickettsia*'s species using molecular biology on samples easily taken from the inoculation eschar should be systematized. However, empiric therapy should not await biological diagnostic confirmation, especially as serial serologies might be the only diagnostic tool available in smaller hospitals.

Treatment of this infection is currently based solely on clinical observations and spontaneous healing may be possible. However, by analogy with the other rickettsiosis, a regimen of doxycycline, 200 mg per day, for 3–7 days, is often prescribed.[5]

In conclusion, the epidemiology and clinical spectrum of *R. sibirica mongolitimonae* infection require further investigation. Geographic distribution is likely to be more widespread than originally thought and clinicians should consider this pathogen in the differential diagnosis of patients with an eschar or a rash in, or returning from, Cameroon. This case also confirms that the lymphatic pattern is not characteristic of *R. sibirica mongolitimonae* infection and that some unconventional presentations of rickettsial diseases are now emerging.

Author contributions

A.N. wrote the initial drafts of this article. G.M., M.J. and A.J. were responsible for the clinical management. E.A. was responsible for microbiological laboratory testing. All authors contributed to revising the manuscript on critical points concerning their specific field, providing substantial intellectual input.

Conflict of interest: None declared.

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