

Septic shock in a patient infected with *Rickettsia sibirica mongolitimonae*, Spain

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Abstract

In 1996, the first human case of infection by *Rickettsia sibirica* subsp. *mongolitimonae* was described in France. Subsequently, other human cases were reported in the same country. The acronym LAR (lymphangitis-associated rickettsiosis) has been proposed to designate this disease because lymphangitis is one of the main clinical manifestations. Later, a few more cases were described in Portugal, South Africa, Egypt, Greece and Spain. We report a case of *R. sibirica mongolitimonae* infection as a cause of septic shock in a Spanish patient living in La Rioja (northern Spain). In addition, the broad clinical spectrum of this tick-borne disease is discussed.

Keywords: *Rickettsia sibirica mongolitimonae*, septic shock, Spain, Mediterranean spotted fever (MSF), lymphangitis-associated rickettsiosis (LAR).

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Recently, *Rickettsia sibirica mongolitimonae* has been implicated as the aetiological agent of human rickettsioses in the Mediterranean area [1]. The acronym LAR (lymphangitis-associated rickettsiosis) has been proposed to designate this disease because lymphangitis is one of the main clinical manifestations. We describe here a case of septic shock caused by this rickettsia species in Spain, and discuss the broad clinical spectrum of this tick-borne disease.

A 69-year-old man was admitted to the Hospital San Pedro in La Rioja (Spain) on September 2011, with a 4-day history of fever, myalgia, headache and prostration. The patient, who had hypertension, atrial fibrillation and mitral regurgitation, was being treated with irbesartan (150 mg/day), digoxin and acenocumarol. Seven days before, he had returned from a 2-week vacation in a rural area in the South-East of La Rioja. He was in contact with domestic animals but did not notice any tick bite.

On physical examination, his vital signs included: temperature, 39.9°C; blood pressure, 80/60 mm Hg; heart rate, 120 beats/min. He had stupor. His mucous membranes appeared normal. He had a purpuric rash on the trunk and extremities, including palms and soles, and an eschar on his left hip. No other signs or symptoms were observed on examination.

The main laboratory findings on admission were as follows: leucocytes, 7300 with 88.5% neutrophils; haematocrit, 36%; platelets, 44 000/L; elevated levels of lactate, 28 mg/dL (normal value, 5.7–22 mg/dL); and procalcitonin, 3.09 ng/mL (normal value, ≤ 0.5 ng/mL); as well as elevated serum creatinine, 1.51 mg/dL; aspartate aminotransferase, 388 IU/L; alanine aminotransferase, 62 IU/L; gamma-glutamyl transpeptidase, 89 IU/L; creatine phosphokinase, 553 IU/dL; lactate dehydrogenase, 900 IU/L; C reactive protein, 193 mg/L; arterial pH, 7.35; pO₂, 68 mm Hg; pCO₂, 22 mmHg; and O₂ saturation, 94%. Blood culture and urine culture were ordered. An EDTA-treated blood specimen was collected before antibiotic treatment to investigate the presence of *Rickettsia* spp. using polymerase chain reaction (PCR) assays for *gltA* and *ompB* rickettsial genes, as previously described [2]. A negative control (sterile water) and a positive control (DNA from *R. amblyommii*) were included in each test.

In addition, acute and convalescent sera specimens (collected a month after the onset of the illness) were tested by immunofluorescence assays (IFA) using *Rickettsia conorii* as antigen (BioMérieux, Marcy l'Etoile, France).

The chest radiograph did not show consolidation or other abnormality. The abdominal ecography did not reveal any abnormality.

Supportive therapy with fluids and inotropic agents, intravenous (IV) meropenem (1 g/8 h.), IV vancomycin (1 g/12 h.) and IV doxycycline (100 mg/12 h.) was started.

After 2 days of treatment he was afebrile, alert and oriented. His blood pressure was 100/60. His condition gradually improved, except for the purpuric rash, which was present during all hospitalization. The levels of lactate and procalcitonine were rapidly normalized. The other laboratory abnormalities improved more slowly. Blood and urine cultures were negative. DNA was extracted from blood

TABLE 1. Epidemiological and clinical data of patients reported after those described by Fournier et al. in 2005

Patient	1	2	3	4	5	6	7	8	9	Percentage (%)
Sex	Male	Female	Male	Male	Male	Male	Male	Male	Male	88.9 male
Age (years)	76	20	44	73	52	34	41	73	69	NA
Month of infection	December	June	August	August	September	September	June	August	September	NA
Tick-bite	Yes	No	No	No	No	Yes	Yes	Yes	No	NA
Country	Greece	France	Portugal	Portugal	Egypt	South Africa	Spain	Spain	Spain	NA
Temperature (°C)	38.2	38.5	38.7	39.6	38.0	38.5	39.0	39.0	39.9	NA
Myalgias	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100
Headache	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100
Eschar (number)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	No	Yes (1)	Yes (1)	88.9
Lymphadenopathy	Yes	Yes	Yes	No	No	Yes	No	No	No	44.4
Lymphangitis	No	Yes	Yes	No	No	Yes	No	No	No	33.3
Rash	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	66.7
Complications	No	Retinal vasculitis	No	No	No	No	No	No	Septic shock	NA

NA, not applicable.

using the DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany), according to the manufacturer's instructions. Rickettsial DNA was detected by PCR assays targeting *gltA* and *ompB* rickettsial genes. Nucleotide sequence analysis (300 and 382 bp, respectively) showed 100% identity with *gltA* and *ompB* from *R. sibirica mongolitimonae*. Partial sequences for *gltA* and *ompB* generated in this study were deposited in GenBank under accession Nos. JQ782656 and JQ782657, respectively. Percentages of identity with *R. conorii* were 99.3% for *gltA* (298/300) and 98.9%, for *ompB* (378/382). No IgG antibodies against *R. conorii* were found in the acute serum specimen, whereas they were detected at titre of 2048 in the convalescent one.

From January 1996 to June 2004, *R. sibirica mongolitimonae* infections were reported in nine patients from France and South Africa [1]. In these first descriptions, this tick-borne rickettsiosis showed several epidemiological and clinical differences with Mediterranean spotted fever (MSF). Many cases occurred in spring and the main distinctive features were the presence of enlarged lymph nodes in the territory draining the eschar in five patients (55%), or lymphangitis expanding from the eschar to the draining node in four of them (44%), and multiple eschars in two patients.

To date, nine more cases have been published: one each in South Africa, France, Greece and Egypt, two in Portugal, and three in Spain (including the one herein described) [2–9]. Unlike the previously published cases that occurred in spring, most cases of infection herein reviewed (6/9) were probably acquired in summer, during the seasonal peak of MSF in some areas (i.e. northern Spain), except for two patients that became ill in spring and one in winter. Lymphangitis, a clinical feature proposed as typical of *R. sibirica mongolitimonae* infection, was only present in one-third of patients (3/9). Multiple eschars, the other distinctive feature of this tick-borne rickettsiosis, were not observed in any

case. A half of patients (4/9) exhibited clinical signs and symptoms similar to MSF, and they occurred in 1 month with high incidence of MSF. Epidemiological and clinical data from these patients are shown in Table 1.

To our knowledge the vector is unknown, although *R. sibirica mongolitimonae* has been associated with *Hyalomma* spp. and *Rhipicephalus pusillus* ticks [4,5,10,11]. These ticks bite more commonly in spring, corresponding with most reported cases.

The patient herein described was originally diagnosed with a severe form of MSF and this is the only reported case of septic shock due to *R. sibirica mongolitimonae*.

It is not possible in rickettsiosis to implicate a rickettsia at the species level based only on clinical manifestations, because the same agent may cause different signs and symptoms. As for clinical presentation, patients with LAR have been reported in France, Portugal and South Africa. Nevertheless, although lymphangitis is a very specific sign allowing clinical diagnosis, it may be absent. Patients with *R. sibirica mongolitimonae* infection exhibit a broad spectrum of clinical syndromes with different degrees of severity. Furthermore, infections caused by different *Rickettsia* spp. may cause the same clinical syndrome. For instance, in Spain, in addition to *R. conorii*, which is the main agent of MSF, MSF-like symptoms may be, at least, caused by *Rickettsia monacensis* [12] or *R. sibirica mongolitimonae* [2].

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Transparency Declaration

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