



Case report

Mediterranean spotted fever as a cause of septic shock

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ABSTRACT

Mediterranean spotted fever is a generally benign disease but with the potential of serious manifestations.

We report a case of Mediterranean spotted fever in a 56-year-old woman, with pet dog exposure, who presented with a septic shock pattern. Based on clinical symptoms, history, and laboratory results, the diagnosis of Mediterranean spotted fever was suspected and the outcome was favorable with doxycycline treatment.

Although rickettsiae remain an uncommon cause of the sepsis syndrome, it is important to consider it, especially as people are now traveling to endemic areas more frequently.

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Introduction

Mediterranean spotted fever (MSF) is a zoonotic disease. The causative agent, *Rickettsia conorii* (*R. conorii*), is transmitted to man by the bite of the brown dog tick, *Rhipicephalus sanguineus* [1]. MSF is an endemic disease present in many countries, especially in the Mediterranean region including Tunisia (Fig. 1) [2], with summer seasonality. It presents with various non-specific symptoms, including fever, headache, maculopapular rash, myalgia, diarrhea and vomiting. A black eschar at the tick-bite site is characteristic but not present in all cases. The course of MSF is usually mild and it has long been considered as a benign disease. The association with septic shock is rare but the disease can lead to serious and potentially fatal presentation.

We report a case of Mediterranean spotted fever in a 56-year-old woman, with pet dog exposure, who presented with a septic shock pattern.

Case report

In September 2018, a 56-year-old, previously healthy woman presented to the emergency department with a 4 days of fever associated with headache, asthenia, generalized myalgia, nausea and vomiting. The physical examination in the emergency room revealed a fever of 39 °C, tachycardia (120 pulse/min), hypotension (80/55 mmHg), a petechial and macular rash (Fig. 2), on the trunk

and the limbs and an eschar (Fig. 3), on the abdominal region. No neurological signs were found. Her blood pressure remained low despite fluid resuscitation.

Laboratory tests revealed an elevated C-reactive protein (163.71 mg/L normal value < 8 mg/L), an increased blood lactate level 2.6 mmol/L, leukopenia 2150/mm³, polymorphonuclear neutrophils count 1548/mm³, thrombocytopenia 30,000/mm³, anemia, hyponatremia with sodium level 127 mmol/L, renal impairment (creatinine 1.29 mg/dL) and abnormal liver function tests (alanine aminotransferase 61 IU/L, aspartate aminotransferase 92 IU/L and gamma-glutamyl transpeptidase 186 IU/L). The chest x-ray was normal.

The patient was stabilized by fluid resuscitation, inotropic drugs, ciprofloxacin and gentamicin. Further questioning of the patient revealed a history of a tick-bite in the abdominal region a week before the onset of symptoms. Based on clinical symptoms, history, and laboratory results, the diagnosis of Mediterranean spotted fever was suspected, the patient was transferred to the infectious disease department and treatment with doxycycline 200 mg per day was started. A complete ophthalmic examination, including dilated biomicroscopic fundus examination was performed and revealed no associated ocular symptoms. After four days of treatment with doxycycline, she was afebrile, her general condition improved and the skin rash gradually resolved. The lactate and serum creatinine rapidly normalized. The other laboratory abnormalities improved more slowly. The patient was discharged from hospital after 8 days with one more week of doxycycline. *Rickettsia conorii* serology by indirect immunofluorescence retrospectively confirmed the diagnosis with positivity of immunoglobulin G at 1:200 and immunoglobulin M at 1:100.

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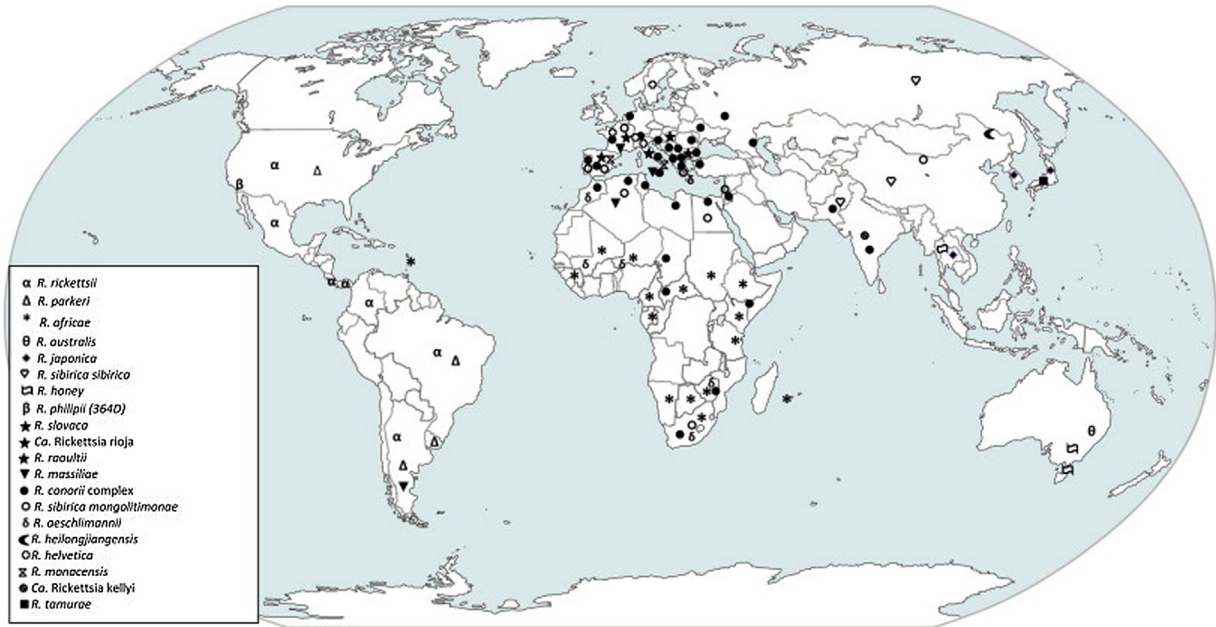


Fig. 1. The distribution of human tick-borne rickettsioses.



Fig. 2. Maculopapular rash in the leg of the patient.



Fig. 3. Eschar in the abdominal region of the patient.

Discussion

Mediterranean spotted fever is often considered as a benign disease but in fact, severe forms and fatalities have been frequently described [3]. It was estimated that about 5–10% of MSF cases were

serious with a mortality rate that could reach 35% [4]. Identified risk factors for severe forms are: advanced age (≥ 50 years), immunosuppression, diabetes, cardiac insufficiency, respiratory insufficiency, chronic alcoholism, G6PD deficiency, delay in treatment and inadequate antimicrobial therapy [5]. In this patient, the only predisposing factor to a severe form of MSF was age greater than 50 years.

Septic shock and multiorgan failure were reported in many of the severe cases of MSF [6] and were most often associated with neurological manifestations and high fatality rate [7]. These patterns result from a diffuse vasculitis process, with an increase in microvascular capillary permeability, which results from the proliferation of rickettsiae in vascular endothelial cells. Necropsies of fatal cases of MSF showed disseminated vascular infection, including meningoencephalitis, and vascular lesions in kidneys, lungs, gastrointestinal tract, liver, pancreas, heart, spleen, and skin [8]. This ubiquitous process explains the wide spectrum of complications according to the predominantly injured organs.

There is no reliable test to diagnose the infection in its early stages and the diagnosis must be made on the basis of

epidemiological, clinical and biological features, as was done for this patient. The European Guidelines for the diagnosis of MSF [9], based on epidemiologic, clinical, and laboratory data, can be used to establish the positive diagnosis if the overall mark is greater than or equal to 25, and in our case the score was 28. In case of septic shock, physicians may be careful to these particularities to avoid unnecessarily broad spectrum antimicrobials. The most specific method for the diagnosis of *R. conorii* infection is the identification of the agent, either by immune staining in tissue specimens or by PCR [10]. However, the detection of antibody to *R. conorii* by immunofluorescence (IFA) is the most available laboratory method to diagnose Mediterranean spotted fever. It is necessary to take two sera in seven or ten days apart (considered positive if greater to or = 1/128); a seroconversion, a presence of IgM or a significant increase ($\times 4$) of the titer of antibodies to establish the diagnosis. For the treatment, doxycycline should be used upon suspicion of MSF, without awaiting laboratory confirmation. Fluoroquinolones are not recommended and recent studies have revealed a worse outcome with their use. Alternatives to doxycycline should be proposed for pregnant women, and clarithromycin seems to be a safe alternative [11].

Conclusion

MSF presented a wide range of manifestations from benign to life-threatening diseases. This case illustrates the importance of taking a careful travel history and performing a thorough clinical examination. Although rickettsiae remain an uncommon cause of sepsis, it is important to consider it, especially as people are now travelling to endemic areas more frequently.

Authorship contributions

A. Meriam and H.Sakly: Drafting the manuscript
 W.Marrakchi, I.Kooli and A.Aouam: managing the patient
 C.Loussaif and A.Toumi: interpretation of data
 H. Ben Brahim and M. Chakroun: Critical revision

Conflict of interests

None.

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Ethical approval

We have read and complied with policy of the journal on ethical consent, as stated in the Guide to authors.

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