Case Report

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Tache Noire in a Patient with Acute Q Fever

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Significance of the Study

- Tache noire is the pathognomonic sign of Mediterranean spotted fever (MSF), caused by *Rickettsia conorii*, and of MSF-like illness, but it is not a clinical feature of Q fever. We report a rare case of Q fever with tache noire.

Keywords
Tache noire · Q fever · Mediterranean spotted fever

Abstract

Objective: To describe a rare case of acute Q fever with tache noire. ***Clinical Presentation and Intervention:*** A 51-year-old man experienced acute Q fever showing tache noire, generally considered a pathognomonic sign of Mediterranean spotted fever (MSF) and MSF-like illness, but not a clinical feature of Q fever. The patient was treated with doxycycline 100 mg every 12 h. ***Conclusion:*** In the Mediterranean area, tache noire should be considered pathognomonic of MSF but it should not rule out Q fever. Clinical diagnosis should be supported by accurate laboratory diagnostic tests to guide proper management.

Introduction

Coxiella burnetii is an obligate, intracellular gram-negative bacterium which infects several vertebrate species. In humans, it is the causative agent of Q fever. Q fever may be transmitted via inhalation of contaminated aerosols and ingestion of contaminated milk. The possibility of *C. burnetii* also being transmitted to humans via ticks was reported in 1947 [1]. Q fever is endemic in large parts of Europe, and studies conducted between 1970 and 2009 showed that 10–30% of rural populations in different countries have antibodies against *C. burnetii*, as highlighted by the ECDC technical report in 2010 [2]. Acute Q fever has a sudden onset, with fever, headache, chills, cough, and myalgia being the most common symptoms. The clinical picture includes flu-like illness, pneumonia, and hepatitis.

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Table 1. Serology tests performed on a patient with tache noire during acute Q fever

Serology test	First evaluation (at time of first visit)	Second evaluation (after 2 weeks)
Rickettsia spp.[1]	IgM <1:64 IgG <1:128	IgM <1:64 IgG <1:128
Anaplasma phagocytophilum[2]	IgM <1:20 IgG <1:40	IgM <1:20 IgG <1:40
Ehrlichia canis[3]	IgM <1:20 IgG <1:40	IgM <1:20 IgG <1:40
Bartonella henselae[4]	IgM <1:20 IgG <1:40	IgM <1:20 IgG <1:40
Coxiella burnetii[5]	IgM 1:50 phase I antigen IgG: 1:50 phase II antigen	IgG 1:320 phase II antigen IgG 1:80 phase I antigen

[1] Cut-off: IgM 1:64, IgG 1:128; [2] cut-off: IgM 1:20, IgG 1:40; [3] cut-off: IgM 1:20, IgG 1:40; [4] cut-off: IgM 1:20, IgG 1:40; [5] cut-off: IgM and IgG: 1:50 phase I and II antigens.

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Fig. 1. a Tache noire at the lower medial surface of the right leg surrounded by circular erythema. **b** Complete remission after 14 days of doxycycline treatment.

Tache noire is considered a pathognomonic sign of Mediterranean spotted fever (MSF) and MSF-like illness, which are transmitted by ticks, but it is not considered a clinical feature of Q fever.

Case Report

We report a case of acute Q fever with tache noire in a 51-year-old man from Sassari, Northwestern Sardinia, where Q fever represents 8% of acute febrile illnesses in the spring/summer period [3].

The patient lived in a periurban area, and was referred to the Infectious Disease Unit of the University of Sassari in June 2012, with a low fever (37.5°C), headache, general malaise, myalgia, and a nonproductive cough which had started 7 days before. Physical examination revealed a dark crusty skin lesion compatible with inoculation eschar, surrounded by edema and a circular erythema (Fig. 1). No maculopapular rash was present. The patient recalled a tick bite. Cardiopulmonary and abdominal physical examinations were normal. Laboratory results showed a relative lymphomonocytosis and a slight increase in C-reactive protein. The remaining parameters were within the normal range. Based on a clinical suspicion of MSF-like illness, the patient was started on doxycycline 100 mg every 12 h.

Serological analyses for all *Rickettsia* spp., *Anaplasma phagocytophilum*, *Ehrlichia canis, Bartonella henselae*, and *C. burnetii* were performed by immunofluorescence antibody assay (IFA) at the first clinical evaluation, and then repeated after 2 weeks. Enzyme-linked immunosorbent assay (ELISA) for *Rickettsia conorii* and *Borrelia* spp. was also performed. The first sample showed anti-*Coxiella* IgG phase II and I antibody titer of 1:50, but the second test was clearly positive, with an antibody titer >6 times higher than in the previous test (anti-*Coxiella* IgG phase II = 1:320 and phase I = 1:80). The search for other antibacterial antibodies was negative in both samples (Table 1), as were the ELISA for *R. conorii* and *Borrelia* spp.

Additionally, a skin biopsy of the tache noire collected in PBS buffer and a whole-blood sample were obtained prior to antibiotic therapy. DNA was extracted for genomic detection of *Rickettsia*, using molecular methods based on real-time PCR. The primers (forward) TCGCAAATGTTCACGGTA CTTT and (reverse) TCGTGCATTTCTTTCCATTGTG were used to identify the genus *Rickettsia* that includes the spotted fever group (SFG) and the typhus group (TG), and to amplify the gene *gltA* which codes for the citrate synthase enzyme [4]. All of these tests were negative.

The patient completed a 14-day course of doxycycline at home, with complete clinical remission (Fig. 1).

Discussion

Our case suggests that *C. burnetii* was the etiological agent in a patient with tache noire and suspected MSF-like illness. This finding has important clinical implications. Rickettsioses are endemic in Sardinia, where MSF is a common summertime fever mostly caused by *R. conorii*, and sometimes by *R. monacensis* [5]. Thus, Q fever was, to some extent, an unexpected diagnosis in a patient with fever and tache noire. In particular, this case suggests

that tache noire, generally considered to be the pathognomonic sign of *Rickettsia* infection, may also be seen in acute Q fever.

Differential diagnosis is important, as infections due to *C. burnetii* have a different clinical management from other Rickettsioses in terms of the duration of therapy, particularly if complicated. In our case, a misdiagnosis of Q fever would have led to a shorter antibiotic treatment, with the possible occurrence of further complications and the potential risk of developing a chronic infection.

Q fever is not usually considered as being a tick-borne disease; however, several published studies suggest that *C. burnetii* may indeed be found in ticks in Mediterranean countries, including Italy. For example, in a study conducted in Algeria, 268 ticks were evaluated, using real-time PCR, standard PCR, and sequencing, for the presence of *Bartonella* spp., *Rickettsia* spp., *Borrelia* spp. and *C. burnetii*. DNA from *C. burnetii* was identified in 3/19 (15.8%) *Ixodes vespertilionis* ticks [6], and a study conducted in Sardinia found evidence of *C. burnetii* infection in ticks from mammal hosts [7].

Finally, ticks seem to play a fundamental role in the spread of *C. burnetii* among various vertebrates, such as rodents, lagomorphs, and wild birds, as reviewed by Porter et al. [8], highlighting, again, the need for more knowledge about the role of these arthropods in the natural cycle of *C. Burnetii*, particularly concerning the possible transmission of Q fever to humans.

Q fever is considered to be an airborne zoonotic disease, but ticks such as *Rhipicephalus microplus* or *R. sanguineus* are also suspected to be involved in Q fever epidemiology as potential vectors [9]. We do not know what species of tick was involved in our case, but given its countrywide distribution, we speculate that *R. sanguineus* may have been responsible.

In conclusion, in the Mediterranean area tache noire should be considered pathognomonic of MSF, but its presence should not rule out a diagnosis of Q fever, and the possibility of concomitant or consecutive infections should also be considered [10]. Of course, clinical diagnosis should be supported by accurate laboratory diagnostic tests in order to rapidly differentiate between possible pathogens and to guide a proper management.

Disclosure Statement

The authors report no conflicts of interest.

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