Cureus
Part of SPRINGER NATURE

Open Access Case Report

Mediterranean Spotted Fever With Central Nervous System Involvement

Etiandro Moura [1], Karen Moura [1], Danilson Caetano [2]

1. Family Medicine, Hospital Garcia de Orta, Lavradio, PRT 2. Family Medicine, Hospital de São Bernardo, Seixal, PRT

Corresponding author: Etiandro Moura, etiandromoura84@hotmail.com

Review began 10/15/2026
Review ended 11/11/2026
Published 11/15/2026

© **Copyright** 2026
Moura et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.119701

Abstract

Mediterranean spotted fever (MSF), caused by *Rickettsia conorii*, is an endemic tick-borne disease in the Mediterranean region. Although generally self-limiting when treated promptly, severe complications, including central nervous system (CNS) involvement, may occur. We report the case of a 66-year-old woman with hypertension, type 2 diabetes mellitus, and dyslipidemia who presented with fever, vomiting, and asthenia, followed by progressive clinical deterioration. She was admitted for fever of unknown origin. Clinical examination revealed a macular erythematous rash involving the trunk, lower limbs, and palms, as well as an inoculation eschar ("tache noire") on the left thigh. Neurological manifestations included dizziness and horizontal nystagmus. Based on the clinical and epidemiological findings, empirical doxycycline was initiated for suspected rickettsiosis, resulting in rapid clinical improvement. The diagnosis was confirmed by PCR for *Rickettsia conorii*. Brain magnetic resonance imaging revealed multiple recent ischemic lesions and a cortical hemorrhage, suggesting cerebral vasculitic involvement secondary to rickettsial infection. This case highlights a severe manifestation of MSF with CNS involvement and emphasizes the importance of early clinical recognition, particularly in primary care settings, to facilitate timely treatment and prevent serious complications.

Categories: Family/General Practice
Keywords: by rickettsia conorii, fever with central nervous system involvement, mediterranean spotted fever, tache noire, zoonotic disease

Introduction

Mediterranean spotted fever (MSF) is a zoonotic disease caused by *Rickettsia (R.) conorii* and transmitted by infected ticks. It is endemic in southern Europe, with Portugal reporting one of the highest incidences in the Mediterranean basin, estimated at 9.8 cases per 100,000 inhabitants [1,2]. Environmental factors, including higher mean temperatures and lower precipitation, have been proposed as potential contributors to increased tick activity and transmission, and may influence the number of vector life cycles completed annually [1]. These factors may therefore contribute to the epidemiology of MSF in Portugal, although their specific contribution to disease incidence remains uncertain.

Rickettsia conorii conorii is the predominant subspecies responsible for MSF in this region [1,2]. Two main strains of *R. conorii* have been predominantly associated with MSF: the *R. conorii* Malish strain, which has been isolated from both human samples and the dog tick Rhipicephalus sanguineus, and the Israeli tick typhus strain, which has been isolated exclusively from human samples [2].

The typical clinical manifestations of MSF include fever, maculopapular rash, inoculation eschar (tache noire), headache, and gastrointestinal symptoms. However, the initial presentation may be nonspecific, which can make early diagnosis challenging [2]. Severe disease may progress to multiorgan involvement, including neurological complications, such as encephalitis and cerebral vasculitis, which are associated with increased morbidity and mortality [3,4].

Primary healthcare plays a key role in the early recognition of MSF, as it is often the patient's first point of contact with the healthcare system. Early clinical suspicion, based on the combination of clinical and epidemiological findings, is essential for the timely initiation of appropriate treatment and the prevention of severe complications. Recognizing MSF in primary care is therefore particularly important in endemic areas, where nonspecific febrile illness may precede the development of more characteristic clinical manifestations.

Case Presentation

A 66-year-old woman was initially evaluated in primary care for several hours of left hip pain without systemic symptoms. Bursitis was suspected, and naproxen was prescribed. Approximately five weeks later, she presented to the emergency department with fever up to 39 °C, vomiting, anorexia, and asthenia. She received symptomatic treatment and was discharged. Approximately one week later, she was reassessed in primary care because of worsening bilateral hip pain and progressive functional limitation. Analgesic

therapy was adjusted, and outpatient follow-up was advised. The following day, she returned to the emergency department with persistent fever and intractable vomiting and was admitted for fever of unknown origin.

Laboratory studies revealed leukocytes of 6,700/µL, lymphopenia (660/µL), thrombocytopenia (147,000/µL), and elevated C-reactive protein (31.4 mg/dL). Mild hyponatremia (132 mmol/L), elevated transaminases (aspartate aminotransferase (AST) 66 U/L, alanine aminotransferase (ALT) 55 U/L), and increased lactate dehydrogenase (LDH; 461 U/L) were also noted. Renal function was preserved (Table *1*).

Laboratory parameter	Patient value	Unit	Reference range
White blood cell count	6,700	/µL	4,000-11,000
Lymphocyte count	660	/µL	1,000-4,000
Platelet count	147,000	/µL	150,000-400,000
C-reactive protein	31.4	mg/dL	<0.5
Sodium	132	mmol/L	135-145
Aspartate aminotransferase (AST)	66	U/L	<35
Lactate dehydrogenase (LDH)	461	U/L	120-250
Creatinine	0,9	mg/dL	0,5–1,1
Urea	30	mg/dL	15–45

TABLE 1: Laboratory findings at hospital admission

Chest and abdominal radiographs and an abdominopelvic computed tomography scan showed no significant abnormalities. Viral screening was negative.

During hospitalization, physical examination revealed a non-pruritic, macular erythematous rash involving the trunk, lower limbs, and palms, together with an eschar on the left thigh consistent with a “tache noire.” Neurological symptoms included dizziness and horizontal nystagmus. Further epidemiological history revealed rural exposure, contact with domestic animals and vegetation, and a reported tick bite approximately one month before symptom onset.

Given the clinical suspicion of rickettsiosis, empirical doxycycline therapy was initiated. Molecular testing was performed on blood and an eschar biopsy specimen.

The patient showed a rapid clinical response, with resolution of fever and rash and normalization of inflammatory markers. However, vestibular symptoms persisted during hospitalization. Cranial computed tomography was unremarkable, whereas brain magnetic resonance imaging (MRI) demonstrated multiple small cortical and subcortical ischemic lesions with diffusion restriction, together with a small cortical hemorrhage (Figure *1*). These findings were considered suggestive of cerebral vasculitic involvement associated with Rickettsia infection.

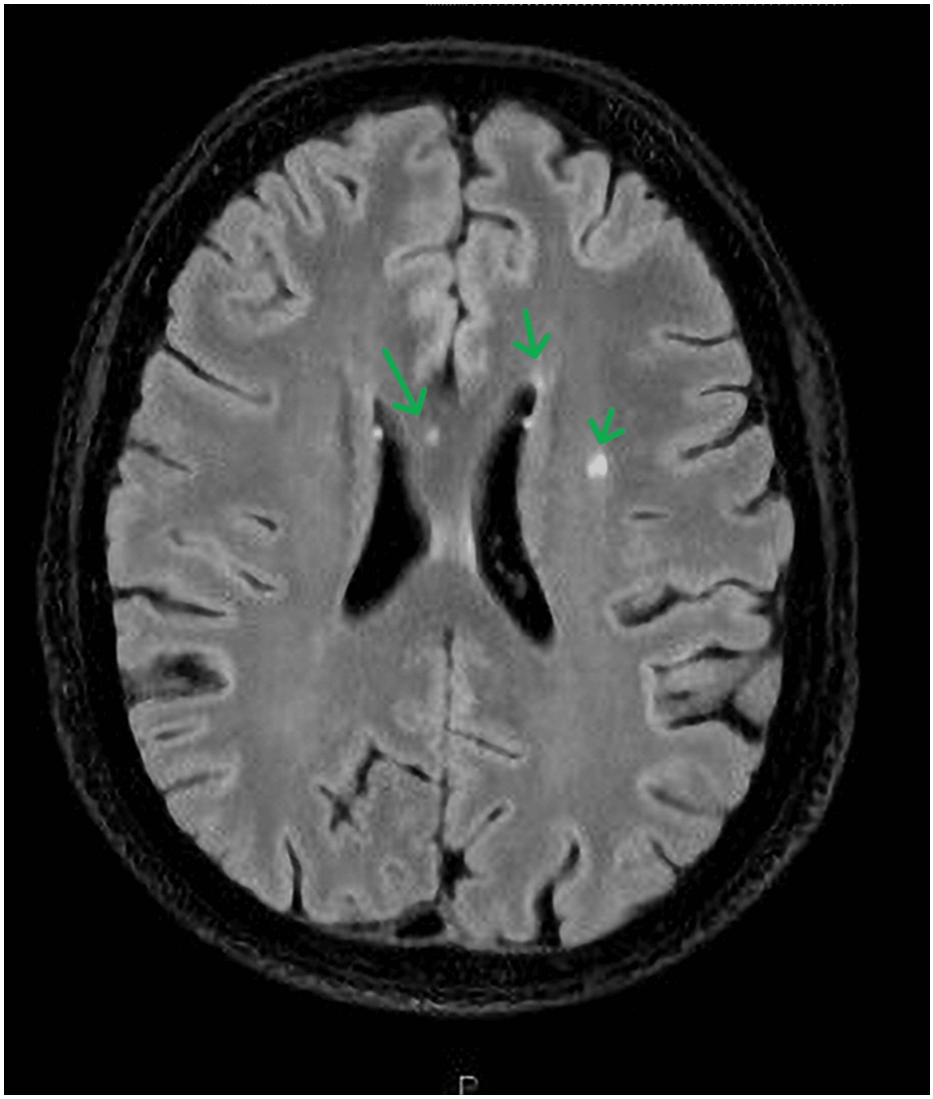


FIGURE 1: Brain magnetic resonance imaging (MRI) demonstrated multiple small cortical and subcortical ischemic lesions with diffusion restriction, together with a small cortical hemorrhage.

Cerebrospinal fluid analysis was normal. Serological testing showed strongly positive IgM antibodies against Rickettsia. Other infectious causes, including HIV, hepatitis C, syphilis, *Borrelia*, *Mycoplasma*, and *Coxiella*, were excluded (Table *2*). The patient had no neurological sequelae during follow-up.

Investigation	Result	Interpretation
Cerebrospinal fluid	Normal	No findings suggestive of CNS infection
Rickettsia serology	Strongly positive IgM	Consistent with Rickettsia infection
HIV	Negative	No evidence of infection
Hepatitis C	Negative	No evidence of infection
Syphilis	Negative	No evidence of infection
Borrelia	Negative	No evidence of infection
Mycoplasma	Negative	No evidence of infection
Coxiella	Negative	No evidence of infection

TABLE 2: Investigations performed during hospitalization confirmed strongly positive IgM for Rickettsia, with exclusion of other infectious causes including HIV, hepatitis C, syphilis, Borrelia, Mycoplasma, and Coxiella.

Discussion

MSF is usually a self-limited disease when diagnosed and treated promptly; however, severe complications, particularly neurological involvement, may occur [3,4]. Rickettsial infections typically present with fever, an inoculation eschar, and a generalized rash, although nonspecific manifestations, including gastrointestinal, musculoskeletal, and neurological symptoms, may also occur [5]. In the present case, the initial presentation with osteoarticular pain, fever, vomiting, and anorexia was nonspecific and contributed to a delay in diagnosis. The subsequent identification of an inoculation eschar, together with the history of tick exposure and contact with rural vegetation, was crucial for raising clinical suspicion.

Rickettsial vasculitis is characterized by endothelial cell infection, inflammatory activation, microthrombosis, and vascular injury, which may result in ischemic and hemorrhagic cerebral lesions [3]. In this patient, persistent vestibular symptoms prompted neurological investigation, and brain magnetic resonance imaging revealed multiple small cortical and subcortical ischemic lesions associated with a small cortical hemorrhage, supporting cerebral vascular involvement. Although neurological manifestations are uncommon, other *Rickettsia* species, including *Rickettsia felis*, have also been associated with neurological disease, including meningoencephalitis [5,6].

The clinical severity of rickettsial infections may vary according to pathogen virulence and host-related factors, including older age, delayed diagnosis, organ dysfunction, and central nervous system involvement [5]. The patient's age and multiple comorbidities may therefore have contributed to the severity of her presentation. Early treatment with doxycycline remains the cornerstone of therapy and is associated with favorable outcomes when initiated promptly [3,4]. In this case, antimicrobial therapy was followed by rapid clinical improvement, with resolution of fever and rash and normalization of inflammatory markers.

This case highlights the importance of maintaining a high index of suspicion for MSF in endemic regions, particularly when nonspecific febrile illness is accompanied by an inoculation eschar, rash, and relevant epidemiological exposure. Primary care plays an important role in early recognition, as subtle clinical findings and epidemiological information may precede disease progression [3,4]. Early diagnosis and treatment are essential to reduce the risk of severe complications, including neurological involvement.

Conclusions

Mediterranean spotted fever should be considered in patients presenting with nonspecific febrile illness in endemic areas, particularly when accompanied by rash, an inoculation eschar, or relevant epidemiological exposure. Early recognition and prompt treatment are essential to prevent severe complications, including neurological involvement. Primary health care plays a pivotal role in early diagnosis and timely management, as careful assessment of subtle clinical and epidemiological findings may significantly improve outcomes.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the

work.

Concept and design: Etiandro Moura, Karen Moura, Danilson Caetano

Acquisition, analysis, or interpretation of data: Etiandro Moura, Karen Moura, Danilson Caetano

Drafting of the manuscript: Etiandro Moura, Karen Moura, Danilson Caetano

Critical review of the manuscript for important intellectual content: Etiandro Moura, Karen Moura, Danilson Caetano

Supervision: Etiandro Moura, Karen Moura, Danilson Caetano

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Meireles M, Magalhães R, Guimas A: Mediterranean spotted fever: retrospective review of hospitalized cases and predictive factors of severe disease [Article in Portuguese]. Acta Med Port. 2015, 28:624-31. 10.20344/amp.5992
2. Sousa R, Nóbrega SD, Bacellar F: Mediterranean spotted fever in Portugal. Risk factors for fatal outcome in 105 hospitalized patients. Acta Med Port. 2008, 16:429-39. 10.20344/amp.1216
3. Sahni A, Fang R, Sahni SK, Walker DH: Pathogenesis of rickettsial diseases: pathogenic and immune mechanisms of an endotheliotropic infection. Annu Rev Pathol. 2019, 14:127-52. 10.1146/annurev-pathmechdis-012418-012800
4. Fisher J, Card G, Soong L: Neuroinflammation associated with scrub typhus and spotted fever group rickettsioses. PLoS Negl Trop Dis. 2020, 14:e0008675. 10.1371/journal.pntd.0008675
5. Zeng Z, Wang C, Liu C, Wang B, Meng X, Chen Y, Guo S: Follow-up of a Rickettsia felis encephalitis: some new insights into clinical and imaging features. Int J Infect Dis. 2021, 104:300-2. 10.1016/j.ijid.2020.12.090
6. Sekeyová Z, Danchenko M, Filipčík P, Fournier PE: Rickettsial infections of the central nervous system . PLoS Negl Trop Dis. 2019, 13:e0007469. 10.1371/journal.pntd.0007469