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Neurological Involvement during Rickettsiosis in 4 Cases: A Review of Mechanisms, Clinical Manifestations and Therapeutic Implications

Hachad Salma[1*], Ouggane Inas[1], Badi Hanane[1], Marhoum El Filali Kamal[1]

[1]Department of Infectious Diseases, Ibn Rochd University Hospital Casablanca, Morocco

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***Corresponding author:** Hachad Salma
Department of Infectious Diseases, Ibn Rochd University Hospital Casablanca, Morocco

Abstract **Review Article**

Mediterranean spotted fever (MSF), caused by Rickettsia conorii, is an endemic zoonosis in Mediterranean regions. Although cutaneous and systemic manifestations are well described, neurological involvement remains an underestimated but potentially serious complication. This article explores the pathogenic mechanisms, clinical manifestations, diagnostic tools and therapeutic options for neurological involvement in BMF, based on recent data.

Keywords: Mediterranean Spotted Fever, Rickettsioses, Rickettsia Conorii.

INTRODUCTION

Mediterranean spotted fever (MSF), secondary to Rickettsia conorii, is an infectious disease endemic to countries around the Mediterranean. It is characterised by the classic triad of fever, maculopapular rash and inoculation sore. However, neurological complications can occur, ranging from mild symptoms (headache, confusion) to severe disease (meningoencephalitis, peripheral neuropathy). Severe forms of rickettsial disease account for 6-10% of cases, with a mortality rate of 32%, and neurological damage accounts for 28% of severe cases, with a guarded prognosis requiring rapid treatment.

RESULTS

The study involved 4 cases of confirmed severe MBF with neurological involvement. The average age was 51 years and there was a 100% male predominance. The average duration of the disease was one week. Clinical signs were dominated by a generalised maculopapular rash that spared neither the palms nor the soles, occurring alongside fever in three patients. Inoculation sores were present in two cases (see Figure 1). Symptoms were complicated by meningeal syndrome in all cases, presenting as heaviness in the left hemisphere and involuntary hand movements in one patient, and confusion in another.

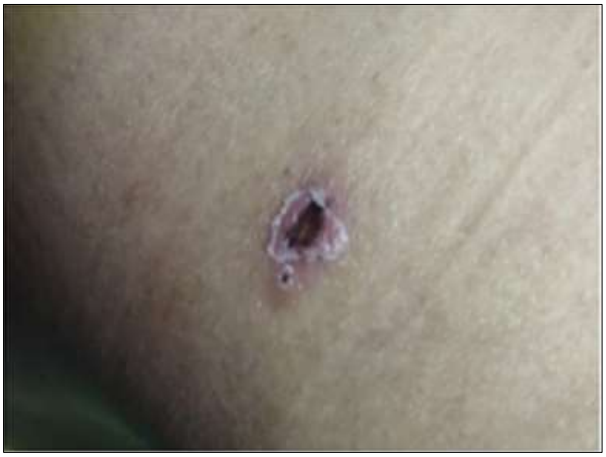

Figure 1: Shows an inoculation eschar in one of our patients

Cerebral CT scans showed no abnormalities in all four patients, while cerebral MRI angiography revealed a left deep sylvian ischaemic stroke in one patient. Biological tests showed elevated C-reactive protein (CRP), hyperleukocytosis and inflammatory anaemia in all four patients. Hepatic work-up showed hepatic cytolysis in two patients and renal work-up showed normal results in three patients and functional renal failure in one patient, which was corrected by rehydration. Viral serologies (hepatitis B and C, HIV) and syphilis serologies were negative. Lumbar punctures were normal in three patients and abnormal in one patient, showing lymphocytic meningitis. Blood cultures were sterile in all patients.

Confirmation of conorii type rickettsiosis was by indirect immuno-fluorescence serology in all 4 cases.

Treatment consisted of doxycycline and phenicols in 3 patients and ciprofloxacin in 1 patient for ten days.

The outcome was favourable in all 4 cases, with clear clinical improvement after 2 weeks.

DISCUSSION

Mediterranean spotted fever (MSF) is an infectious disease caused by an obligate intracellular bacterium, Rickettsia conorii. This bacterium is transmitted to humans via a brown dog tick, Rhipicephalus sanguineus, which plays a dual role as a vector and reservoir of infection.

Endemic to the Mediterranean region, BMF occurs in summer epidemics. Its incidence is estimated at 50 cases per 100,000 inhabitants per year in this region. In Morocco, although the exact prevalence is not yet well defined, it appears to be relatively high in these climates. The infection affects both men and women, and can occur at any age, with a predominance in children and people over 60.

Diagnosis is based on epidemiological and clinical criteria, including fever, the presence of an eschar (black spot) at the site of inoculation and a maculo-papular rash. Diagnosis is confirmed by serology (direct immunofluorescence, with evidence of seroconversion), molecular biology, etc.

Although generally benign, BMF can lead to systemic complications, particularly neurological manifestations, which are observed in around 1% of cases. These neurological disorders are varied and include:

- Meningitis and meningoencephalitis: cases of lymphocytic meningitis with frequent meningeal signs and often normal cerebrospinal fluid (CSF) have been reported. Encephalitis may cause impaired alertness, convulsions or a cerebellar syndrome.
- Peripheral neurological disorders: cranial nerve paralysis, particularly facial paralysis, as well as myelitis and acute polyradiculoneuritis have been described.
- Strokes: although rare, ischaemic strokes have been documented in patients with MBF. One notable case involved a 49-year-old female patient who developed massive right hemiplegia during hospitalisation for rickettsial disease. However, cerebral infarctions linked to rickettsiosis remain exceptional.

The diagnosis of neurological involvement is based on the association of neurological symptoms with fever and rash. It is confirmed by serology (anti-Rickettsia IgM and IgG), PCR on CSF, and cerebral MRI, which may reveal inflammatory or ischaemic lesions. CSF analysis frequently reveals lymphocytic pleocytosis and hyperproteinorachia.

Cerebral infarcts of infectious origin have complex pathophysiological mechanisms. The main factor involved is a vasculitis resulting from inflammation of the arterial wall in response to the presence of the pathogen. This inflammation leads to endothelial damage, local thrombosis and sometimes vascular rupture, explaining the occurrence of infarction and haemorrhage, or a combination of the two.

Early treatment is essential to reduce the duration of symptoms and prevent complications. The mainstay of treatment is appropriate antibiotic therapy to control infection and reduce morbidity and mortality.

The first-line treatment is doxycycline, administered at a dose of 200 mg per day in adults and 5 mg/kg per day in children. For pregnant women and children, josamycin is an alternative. If contraindicated, azithromycin or chloramphenicol may be used. The use of fluoroquinolones in the treatment of BMF is controversial: some authors recommend them for severe forms, particularly neurological, or in cases of allergy to cyclins, for a period of seven days. However, others recommend avoiding them, given recent studies suggesting an association between these antibiotics and worsening of the disease.

Finally, adjuvant treatment, including anticonvulsants or corticosteroids, may be necessary in severe forms.

CONCLUSION

Neurological involvement in BMF, although rare, is a serious complication that requires early recognition and early, appropriate management. A better understanding of the pathogenic mechanisms and modern diagnostic tools will help to improve patient management.

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