International Journal of Infectious Diseases 35 (2015) 34–36

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Mediterranean spotted fever and hearing impairment: a rare complication

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ARTICLE INFO

Article history:
Received 7 March 2015
Accepted 10 April 2015

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:
Rickettsia conorii
Mediterranean spotted fever
Neurological complication
Hearing loss

SUMMARY

Mediterranean spotted fever (MSF) is caused by *Rickettsia conorii* and transmitted by the brown dog tick *Rhipicephalus sanguineus*. It is prevalent in southern Europe, Africa and central Asia.

The disease usually has a benign course and is characterized by fever, myalgia and a characteristic papular rash with an inoculation eschar ('tache noir') at the site of the tick bite. Severe forms of disease can have cardiac, neurologic or renal involvement. Nervous system complications are unusual and may develop in the early phase of disease or as a delayed complication. Neurological symptoms include headache and alterations of the level of consciousness, and some cases of meningoenchefalitis and Guillain-Barrè syndrome have been also reported. Peripheral nerve involvement is reported only in a limited number of case reports.

We describe a case of *Rickettsia conorii* that was complicated with hearing loss and did not respond to specific treatment. Hearing loss is a rare event, but clinicians should be aware of this complication.

1. Introduction

Mediterranean spotted fever (MSF), also known as boutonneuse fever, is a zoonosis caused by *Rickettsia conorii* and is occasionally transmitted to humans through the bite of an infected tick (*Rhipicephalus sanguineus*).

It is a member of the spotted fever group of rickettsiae and it is widely distributed throughout southern Europe, Africa, and the Middle East. In Italy the most affected region is Sicily. Most cases occur during the period from July to September, when the tick vectors are active.

Diagnosis is often made with the following symptoms: fever, a popular and purpuric skin rash involving palms and soles, and a black eschar (tache noire) that can be found at the site of the thick bite and represents local endothelial invasion by rickettsiae.

Severe forms of the disease have been reported, especially in adults with the following conditions: diabetes, cardiac disease, chronic alcoholism, glucose-6-phosphate dehydrogenase deficiency, end-stage renal kidney disease. Another relevant factor is prior prescription of delayed and/or inappropriate antibiotic.[1]

Diagnosis of the disease is based on epidemiologic, clinical and laboratory criteria. Doxycycline is considered the drug of choice.

Neurological manifestations described in the literature are rare, and the most common are encephalitis and Guillain–Barré syndromes.[2] Rarely has the involvement of peripheral nerve also been reported.

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http://dx.doi.org/10.1016/j.ijid.2015.04.005

Herein, we report a case of Mediterranean spotted fever complicated by irreversible hearing loss.

2. Case Report

In September 2014, a 74-year-old Italian woman was admitted to the Ospedale Maggiore Policlinico in Milan, Italy, because of high fever, diarrhea, arthralgia and a cutaneous rash that persisted for seven days. She had returned a week before from holiday in Sicily, South Italy. Her medical history included: hypertension, type II diabetes mellitus and dyslipidemia.

On examination, the patient showed a non-itching maculopapular rash most notably on the trunk, also involving her legs and arms, and the remaining physical examination was unremarkable.

Laboratory tests revealed a pathological value for C-reactive protein (20 mg/dl normal value < 0,5 mg/dl), mild neutrophil leucocytosis (white blood cell count 10,2 X 10^9/l, 80% polymorphonuclear neutrophils), and abnormal liver function tests (alanine aminotransferase 64 IU/l and aspartate aminotransferase 51 IU/l). The chest x- ray was normal.

Blood, stool and urine samples were sent for culture analysis. An empiric antimicrobial agent, ceftriaxone 2 g/day was prescribed without improvement, and meanwhile the cutaneous rash worsened.

On her third day of hospital stay, the dermatological picture of the patient was characterized by a widespread maculopapular rash with palmoplantar involvement. The lesions were pink, blanchable macules of 3-5 mm in diameter, evolving over a few days to mildly infiltrated papules sometimes with a purpuric or haemorragic aspect. An erythematous, indurated lesion with a diameter of 12 mm with a central necrotic eschar was found on the posterior aspect of her right leg (Fig. 1).

A careful re-evaluation of the patient's history revealed that she had gone trekking in the woods during her vacation in Sicily. Based on clinical symptoms, history, and laboratory results, a diagnosis of Mediterranean spotted fever was made and treatment with doxycycline 100 mg twice a day was started ten days after the onset of symptoms. After the administration of doxycycline, fever subsided and inflammatory values started to decrease, the skin rash gradually resolved and her general conditions were improved.

Unfortunately, three days after the admission, the patient complained about her hearing.

She had no vertigo or tinnitus, both tympanic membranes were observed intact on otoscopy. The audiometric test showed a profile of right anacusis without any vocal discrimination, and a mild sensorineural hypoacusis on acute tones involving the left ear. Magnetic resonance imaging examination of the brain revealed phlogistic bilateral impairment of the mastoid, most pronounced on the right side, and a barrier alteration involving cochlea on the right side suggesting a meningogenic relevance. Auditory evoked potentials confirmed sensorineural hearing loss.

Therefore the otolaryngologist recommended adding citicoline and hyperbaric oxygen therapy to the ongoing treatment. The patient was discharged with a diagnosis of Mediterranean spotted fever, receiving doxycycline for a total of nine days.

Treatment with citicoline, steroids and hyperbaric oxygen therapy were started, but subsequent to eight sessions she had no improvement. On the tenth day after discharge the patient ended the therapy with citicoline and steroids. Later, the patient underwent eight sessions of oxygen therapy. In November the audiometric test after the sixteenth cycles did not show any improvement in her hearing impairment.

An immunofluorescent antibody test was performed two months after the onset of symptoms, showing elevated IgM and IgG titers to *Ricketsia conorii* (IgG titer:1: 4000 [normal value < 1:64] and IgM titer 1:512 respectively [normal value < 1:16]). The serological tests were consistent with a recent infection of *R. conorii.*

Currently, three months after the acute infection, the patient has an irreversible hearing loss.

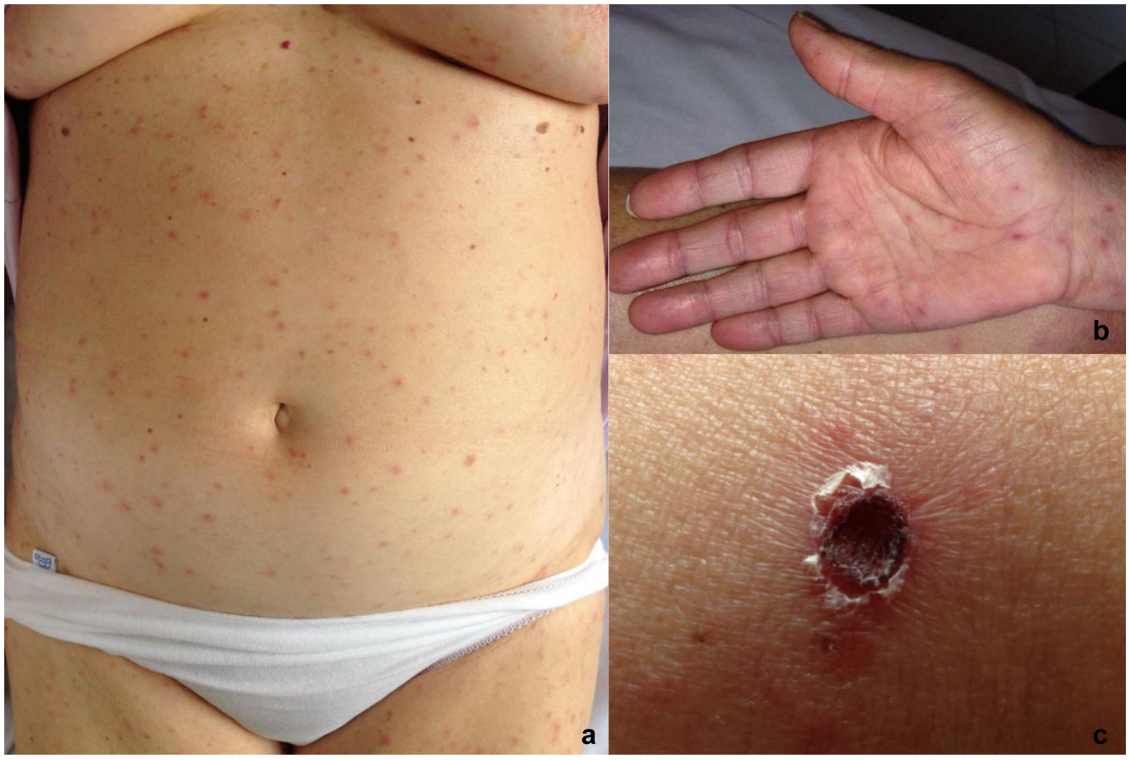

Figure 1. Erythematous papules with purpuric aspects disseminated on patient's trunk (A) Palmar involvement (B). Detail of the tache noire at the site of the mite bite (C).

3. Discussion

In this report we presented a case of a typical MSF with hearing loss, a rare neurological complication. The patient had the typical clinical features of Mediterranean spotted fever, with fever, a characteristic maculopapular and purpuric rash with palmoplantar involvement, and the presence of 'the tache noire', the small eschar representing the site of the tick's bite, which is the cutaneous hallmark of this disease. Headache, myalgia and diarrhoea were present.

Neurological involvement in rickettsial infections is described in a minority of reported cases with severe systemic manifestations. Meningoenchefalitis, myelitis, Guillain-Barrè syndrome and facial nerve paralysis also have been reported.[3]

Rickettsioses are systemic diseases with symptoms caused by vasculitis, which results from proliferation of rickettsiae in vascular endothelial cells. Direct rickettsial invasion of the nervous system has been described in patients with acute neurological complications, but subacute involvement of rickettsiosis is believed to be secondary to immune-mediated mechanisms, because also Guillan-Barrè polyneuropathy has been described after infection with *Rickettsia conorii* and *Rickettsia rickettsii*.[4]

Cases of hearing loss related to rickettsial diseases have been more rarely described in the literature. Hearing loss can be unilateral or bilateral and can be a long term sequela as in Rocky Mountain spotted fever or a transient alteration. One third of patients with scrub typhus are known to develop deafness, which is considered to be a diagnostic feature. Rare association between murine typhus and hearing loss is documented. Only a case of transient subacute hearing loss associated with *Ricketssia conorii* is described.[5]

In our patient hearing loss was a delayed complication and we have not observed an improvement using doxycycline, steroid therapy and hyperbaric oxygen therapy. The few cases reported in the literature showed that antibiotic therapy is necessary, whereas use of corticosteroids is a controversial treatment.

To our knowledge, this is the first case of nonreversible hearing impairment in a patient with rickettsial infection. The reemergence of rickettsial infections is occurring in many regions of the world due to human travel and environmental changes, thus clinicians should know the complications related to the disease. This case emphasizes the importance of considering Mediterranean spotted fever in the differential diagnosis of a patient with fever and rash, especially in people with a history of travel in endemic areas.

A prompt diagnosis is fundamental since early antibiotic treatment significantly improves the outcome of the disease. Moreover in this report we want to underline the importance of neurological complications in patients with rickettsial infection.

List of abbreviations

MSF= Mediterranean spotted fever.

Acknowledgements

We have not received contributions from non-authors.

Competing interests: The authors declare they have no competing interests

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