

SUDDEN VESTIBULAR AND HEARING LOSS IN MEDITERRANEAN SPOTTED FEVER: THE FIRST CASE REPORT

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ABSTRACT

Mediterranean spotted fever is an infection disease caused by Rickettsiae and transmitted by tick puncture; the diffusion of such disease is wide in countryside of the Mediterranean regions. The disease may be complicated by several organ failure due to a vasculitis, and also the inner ear can be involved although rarely. We report the first documented case of total involvement of inner ear with sensorineural hearing loss and acute vestibular impairment. The patient was treated with medical therapy and resolution of the infection, but the inner ear damage was not reversible with persistent loss of all functions, documented by instrumental vestibular analysis.

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1. Introduction

Mediterranean spotted fever is an infection disease caused by representatives of Rickettsiaceae family. Rickettsiae are intracellular Gram-negative bacilli transmitted by ticks, but fleas, lice and mites can also transmit them. The dog tick (*Rhipicephalus sanguineus*) is both the vector and the main reservoir of Rickettsiae; the tick usually becomes infected during a blood meal from an infected animal and in the same way may occasionally transmits the infection to humans¹. The disease has a seasonal pattern, with the highest incidence of cases occurring from July to September, which is the period of highest circulation of ticks. The infection is more frequent in rural areas, especially in southern Europe, Africa and the Middle East. Sicily is the most affected region in Italy². The incidence of the disease is higher in males and in young adults³. The bacteria penetrate the organism through the skin injuries caused by the vector's bites and subsequently disseminate through the lymphatics and blood circulation entering the endothelial cells and vascular muscle cells thanks to special surface proteins and a specific phospholipase. Rickettsiae reproduce itself rapidly in those target cells and induces a direct cytopathic effect.

The result is a generalized vascular damage, particularly of the microcirculation, with consequent activation of coagulation factors, plasma extravasation, due to alteration of vascular permeability, and tissue hypo-perfusion. The incubation period is from 2 to 14 days with an average of 7 days. The classic clinical symptoms of fever, rash and recent exposure to infected ticks is present in less than 18% of patients. A small ulcer covered with a black crust at the site of a tick bite is characteristic of several tick-borne rickettsial diseases. Most patients initially present fever often accompanied by headache and report recent tick bite occurs in 80% of patient. The skin rash occurs within 2 or 3 days after the onset of fever, first as small confluent maculae that quickly become petechiae; the rash occurs first on the skin of the ankles and wrists and then extends to the trunk and on the palmoplantar region. In severe cases the lesions tend to become confluent causing large areas of ecchymosis. Nausea and vomiting are frequent symptoms. There may be long-term complications of the disease, mostly neurological and always related to microvascular damage: peripheral neuropathy, sphincter disorders, language abnormalities and cerebellar dysfunction are the most common. In adults there is a relatively high percentage of abnormal and severe clinical presentation.

The prognosis of the disease is indeed favourable in case of early diagnosis and appropriate therapy; in some cases, the prognosis may be severe, and death occurs after 8-15 days from the clinical onset. The inner ear involvement is almost rare with some report of sensorineural hearing loss during the infection course; we report the first case of documented total inner ear failure with acute vestibular loss in a patient with Mediterranean spotted fever.

2. Case report

In July 2018, a 79 years old male patient reported hearing loss, vertigo, intense fatigue, vomiting and fever (TC 39.9 ° C) for about 3 days. A blood sample was taken and analysed: WBC 4.60x10³ (85%), Hb 14.5 g / dl, PLT 174.000, PCR 60 mg / dl, creatinine 1.44 mg / dl, sodium 134mEq / l, GOT / GPT 46/81 U / THE. The objective clinical examination showed a fine and diffuse micropapular rash on the palms and soles area and absence of lymphadenopathy. The patient presented a severe imbalance in standing position. The clinical vestibular examination showed a spontaneous third-degree spontaneous nystagmus directed to the right side with a predominantly horizontal component; in supine position a geotropic reinforcement was highlighted with the head swirled to the right and an apogeotropic reduction with the head swirled to the left. The clinical Head Impulse Test (HIT) was positive with catch-up saccade in the left swirl. The pure tone audiometric examination showed a left sensorineural hearing loss with an average threshold on the 500 1000 2000 4000 frequencies of 60 dB HL and a ski slope curve. Instrumental examinations were then carried out: video HIT showed a multicanalar left deficit (Figures 1-2) and no response to the left ocular and cervical vestibular evoked myogenic potentials (VEMPs). The patient reported to live in the countryside, a close contact with domestic animals and frequent presence of ticks, and for this reason, although no site of insect puncture was identified, the serological evaluation for Rickettsia and the Weil Felix test were therefore performed: the exams were both positive and a diagnosis of Mediterranean spotted fever was made. Antibiotic therapy with Doxycycline 100mg x 2 was started for 10 days. After 3 days since antibiotic therapy both the fever and the skin rash disappeared as well as the spontaneous nystagmus, but the hearing loss was still unchanged. To manage the inner ear failure intratympanic dexamethasone was started with injection of 0,5 ml of 8mg/ml dexamethasone every 3 days for 5 injection. The hearing loss was present until last audiometric test without improvement. The vestibular evaluation after the end of the therapy showed a persistent left labyrinthine failure, and the patient was addressed to vestibular rehabilitation program. After 12 months of follow-up, the hearing loss persisted without recovery, and the balance improved despite the total persistent failure of left vestibular system.

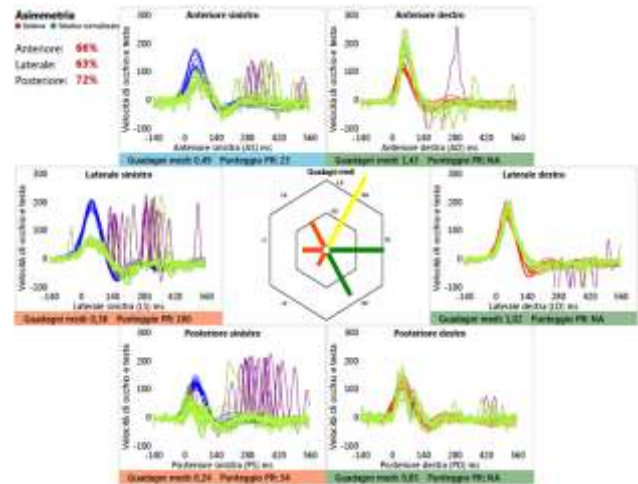


Figure 1. Multicanalar left deficit at video HIT.

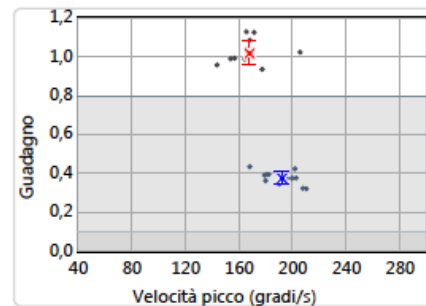


Figure 2. Response to the left ocular and cervical vestibular evoked myogenic potentials (VEMPs).

3. Discussion and conclusions

We reported a typical case of Mediterranean spotted fever complicated by a rare phenomenon: a complete sudden inner ear failure. This is the first case described in literature in which a patient complained unilateral sensorineural hearing loss and sudden peripheral vestibular loss on the same side.

The central nervous system (CNS) is generally involved in 2% to 5% of cases either during the acute or chronic phases of the Mediterranean spotted fever. The involvement of CNS is caused by a direct invasion of CNS by the bacteria that provokes aseptic meningitis, encephalitis, myelitis, Guillan-Barrè Syndrome and facial nerve paralysis⁴.

The most appropriate laboratory methods for the diagnosis of Rickettsiosis are: indirect immunofluorescence on serum, immunoenzymatic method; and direct immunofluorescence on biopsy samples. The Weil-Felix test, based on the serum agglutination of Proteus strains Ox19, Ox2, or OxK, is both not very sensitive and very specific; however, it can be used for diagnostic confirmation of rickettsiosis⁵. The antibiotic treatment should be started based on the clinical diagnosis, without waiting for laboratory confirmation.

Tetracyclines are the first-choice antibiotics: doxycycline 200 mg in single administration, followed by 100 mg for seven days until the clinical condition of the patient improves and no fever is present for at least 24-48. In patients with poor clinical conditions, intravenous therapy is recommended. Chloramphenicol 500 mg for seven days is the second-choice antibiotic.

The pathophysiology of the acute damage of the neural structures is linked to the bacterial action to the endothelial cells by mean direct cytopathic effect and development of a vasculitis as well. On the other hand, the delayed damage of CNS is presumably due to immune-mediated mechanisms secondary to bacterial antigens expression⁶.

Some cases of CNS involvement associated with hearing loss in patients with Mediterranean spotted fever were described in literature, but never with contextual acute vestibular failure and instrumental confirmation^{2,7}.

In our patient both the sudden hearing loss and the vestibular impairment were immediate complications of Rickettsia infection and, despite the therapy with proper antibiotics and steroids for inner ear failure⁸, any recovery of inner ear function was recorded during follow-up.

All the receptors of the vestibular system were analysed with instrumental test to assess the function: cervical and ocular VEMPs showed absence of activity of macular receptors and vHIT showed the absence of semicircular canals response to head rotational impulse; both branches of vestibular nerve were without activity. The instrumental tests were important for both the diagnostic pathway and the follow-up⁹. The resolution of dizziness and vertigo was obtained with medical treatment and with a rehabilitation of vestibular-ocular reflex and a balance training with dynamic posturography¹⁰.

In conclusion we underscore the importance of vestibular assessment in patients with acute impairment of inner ear function in course of some infective disease.

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