

Mediterranean spotted fever and peripheral facial nerve palsy: a rare neurological complication

Hayet Bouchaib, Achour Amrane, Jacques Sevestre, Idir Bitam, Phillipe

Parola

► To cite this version:

Hayet Bouchaib, Achour Amrane, Jacques Sevestre, Idir Bitam, Phillipe Parola. Mediterranean spotted fever and peripheral facial nerve palsy: a rare neurological complication. International Journal of Infectious Diseases, 2022, 117, pp.15-17. 10.1016/j.ijid.2022.01.050. hal-03678997

HAL Id: hal-03678997 https://amu.hal.science/hal-03678997v1

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Version of Record: https://www.sciencedirect.com/science/article/pii/S1201971222000601 Manuscript_9929ea2635d0be189a40bdedcdc7d21d

1 Mediterranean spotted fever and peripheral facial nerve palsy: a rare neurological

- 2 complication
- 3 BOUCHAIB Hayet^a, AMRANE Achour^b, SEVESTRE Jacques^{c,d}, BITAM Idir^e, PAROLA
- 4 Phillipe^{c,d*}
- 5 ^a Université Mouloud Mammeri, Maladies Infectieuses, Tizi-Ouzou, Algeria
- ⁶ ^b EHS El Kettar, Service B, Alger, Algeria
- ^c Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, Marseille, France
- 8 ^d IHU-Méditerranée Infection, Marseille, France
- ^e Ecole supérieure en Sciences de l'Aliment et des Industries Agro-Alimentaires, Alger,
- 10 Algeria
- 11 *Corresponding author: Professor Philippe PAROLA, Institut Hospitalo-Universitaire
- 12 Méditerranée Infection, 19-21 Boulevard Jean Moulin, Marseille 13385 Cedex 05, France.
- 13 Electronic address: philippe.parola@univ-amu.fr.
- 14 Keywords: Mediterranean spotted fever, *Rickettsia conorii*, peripheral facial nerve palsy

Abstract: Mediterranean spotted fever (MSF) caused by the bacterium *Rickettsia conorii* conorii is one of the oldest known tick-borne diseases. It is transmitted by the brown dog tick *Rhipicephalus sanguineus* and occurs mainly in the Mediterranean area. MSF usually presents with a skin rash, high fever, and a characteristic eschar at the tick bite site. The course of this disease may be benign or life threatening. Focal neurological manifestations are unusual. We

20 report the case of a patient who presented with an isolated peripheral facial nerve palsy
21 complicating *R. conorii conorii* infection.

22 **1. Introduction**

Mediterranean spotted fever (MSF) is a zoonosis caused by Rickettsia conorii conorii, a tick-23 borne pathogen belonging to the spotted fever group (SFG) rickettsiae. It is transmitted by the 24 25 brown dog tick Rhipicephalus sanguineus. MSF is endemic in North Africa including Algeria and Southern Europe countries bordering the Mediterranean Sea (Rovery and Raoult 2008). 26 MSF may present as benign or life threatening conditions. It is characterized by fever, rash 27 and a black eschar ("tache noire") at the site of the tick bite, a hallmark of many SFG 28 rickettioses (Rovery and Raoult 2008). Focal neurological manifestations are unusual. We 29 report the case of a young female patient who presented with peripheral facial nerve palsy 30 complicating R. conorii infection. 31

32 **2.** Case Report

A 12 year old girl with no significant medical history presented to the infectious diseases 33 outpatient unit with a six-day history of febrile maculopapular rash associated with arthralgia. 34 Patient history was notable for contacts with dogs. Physical examination revealed fever 35 (39°C), tachycardia (95bpm) and tachypnea (26/min). Cutaneous examination revealed a 36 generalized maculopapular rash, more prominent on the lower limbs. The rash consisted in 37 erythematous indurated lesions, a few millimeters in diameter (Figure 1). Routine laboratory 38 findings showed leukocytosis (13,000 leukocytes/mL and C - reactive protein (CRP) 39 elevation at 76 mg/L. All other parameters were within normal range. Chest radiography did 40 not retrieve abnormalities. Serum samples and a dry swab obtained from the eschar were also 41

42 sent to the Reference Center for Rickettsial diseases in Marseille, France for specific43 diagnosis.

The patient was started on oral doxycycline 200 mg/day for seven days. On the second day 44 after admission, the patient presented sudden left peripheral facial palsy (Fig. 1). Physical 45 examination revealed asymmetry at rest and onset drooping of left eye. No ocular pain or 46 redness was noted. Otoscopic examination showed a normal tympanum on both sides. Head 47 48 and neck examination did not retrieve any parotid lesion. Neurological examination did not reveal any other abnormality. Contrast-enhanced CT scan of the brain including orbital cuts 49 was normal. Cerebrospinal fluid examination was normal. The patient received oral 50 51 prednisone at a dosage of 2 mg/kg per day of for seven days, and gradually tapered within seven days. The outcome was favorable, with apyrexia after 3 days of treatment. One month 52 later, on a follow up evaluation, the girl had retrieved normal left facial nerve function. 53

Serum samples and the dry swab were secondarily studied in Marseille, France. A Rickettsia 54 serological assay was performed. Indirect immunofluorescence (IFI) testing was positive for 55 *R. conorii*, with an Ig G titre of 1:2048 [normal range < 1:128] and IgM titre of 1:256 [normal 56 range < 1:64]) (Rovery and Raoult 2008). DNA extraction was obtained from the dry swab 57 sample, and the eluate was screened in real-time quantitative PCR (qPCR) with genus-specific 58 primers and probes targeting a fragment of the gltA gene of all spotted fever group Rickettsia 59 species (Renvoisé et al. 2012) using a CFX Connect[™] Real-Time PCR Detection System 60 (Bio-Rad, Hercules, CA, USA) and the Eurogentec Takyon qPCR kit (Eurogentec, Seraing, 61 Belgium). Since the sample was positive, it was tested with species-specific R. massiliae and 62 63 R. conorii qPCR, targeting fragments of an hypothetical protein and the putative acetyltransferase genes, respectively (Renvoisé et al. 2012). DNA extract from cultures of R. 64 massiliae and R. conorii were used as qPCR positive controls. The specific assay for R. 65 66 conorii was positive, confirming the diagnosis of MSF.

67 **3. Discussion**

We reported the case of a young female patient who presented with a typical MSF associated 68 with peripheral facial nerve palsy. Although rare, some neurological complications have been 69 described in MSF: meningoencephalitis, myelitis, Guillain-Barré syndrome as well as facial 70 nerve paralyses (Bitsori et al. 2001). Facial nerve paralysis in MSF has been seldom reported 71 72 in the literature (Bitsori et al. 2001; Mert et al. 2006; Cascio et al. 1998). In a Turkish series of R conorii infection cases, one case only of facial nerve palsy was noted (Mert et al. 2006). 73 Two cases developing facial paralysis as a complication of MSF were reported by Sicilian 74 authors (Cascio et al. 1998). Moreover, Bitsori reported two teenage girls with facial nerve 75 palsy and serological evidence of *R. conorii* infection (Bitsori et al. 2001). 76

77

78 FBM is a systemic disease, with symptoms caused by vasculitis, which results from proliferation of rickettsiae in vascular endothelial cells. Direct rickettsial invasion of the 79 nervous system has been described in patients with acute neurological complications 80 (Sekeyová et al. 2019). However, cranial nerve palsies occurring in the absence of clinical, 81 laboratory or imaging evidence of meningoencephalitis, are thought to be a consequence of 82 83 selective vasculitis affecting the respective nerves (Sekeyová et al. 2019). In our report, the diagnosis has been definitely documented using reference methods including direct molecular 84 85 detection on swab eschar sample and indirect serological IFA assay and, performed in an 86 international referral centre for Rickettsioses (Rovery and Raoult 2008; Renvoisé et al. 2012). 87 The use of molecular tools or cell culture on a skin biopsy specimen from an eschar has been a widespread method to identify Rickettsia spp (Parola et al. 2013). However, this technique 88 89 is invasive and painful for patients, and may be difficult to perform on certain areas of the body (Parola et al. 2013). Swabbing of an eschar is much less painful and invasive than 90 performing a biopsy from the eschar. This sample requires a dry sterile swab that must be 91

rotated vigorously to the base of the eschar, right after the crust has been withdrawn (Parola et 92 93 al. 2013). In the case of a dry eschar lesion, a wet compress previously soaked with sterile water should be placed on the inoculation eschar for 1 minute before swabbing, to increase 94 the quantity of material swabbed. Moreover, the crust can also be used for rickettsial 95 diagnosis (Parola et al. 2013). Thus, this technique may be performed rapidly, either at the 96 bedside or in outpatient settings. As soon as the samples are sent to a laboratory where qPCR 97 diagnosis is feasible, results can be obtained quickly. This method has shown encouraging 98 results for the detection of different Rickettsia species infecting humans in several countries 99 (Bechah et al. 2011; Socolovschi et al. 2012; Khrouf et al. 2016). 100

Therapeutic management in patients presenting neurological complications in MSF relies on
antibiotic and corticosteroid therapy (Bitsori et al. 2001; Mert et al. 2006; Cascio et al. 1998).
The reference treatment of rickettsial diseases remains doxycycline, including in severe forms
of childrens (Parola et al. 2013). Although corticosteroids were administered in our case, as in
facial nerve palsy of other or unknown origins, its use remains nowadays discussed (Arican et
al. 2017).

107 **4.** Conclusion

108 The reemergence of rickettsial infections is occurring in many regions of the world due to 109 human travel and environmental changes, thus clinicians should know the complications 110 related to the disease.

111 This case emphasizes the importance of considering MSF in the differential diagnosis of a 112 patient with fever, rash and facial nerve palsy in endemic areas. A prompt diagnosis is 113 fundamental since early antibiotic treatment significantly improves the outcome of the 114 disease.

115 Figure Legends

116	Figure 1, Panel A: Picture of the patient's face showing peripheral facial palsy with loss of the
117	nasolabial fold.

118 Figure 1, Panel B: Picture of the anterior view of the patient's legs, showing generalized

119 erythematous maculopapular rash.

Figure 1, Panel C: Picture showing the dark-brown inoculation eschar on the site of the tick'sbite.

Aknowledgements: The authors wish to thank the patient's family for accepting publicationof this case report.

Funding information: This research did not receive any specific grant from funding agencies

125 in the public, commercial, or not-for-profit sectors.

126 Ethics: Written informed consent was obtained from the patient's family for publication of127 this case report.

References

- Arican, Pinar, Nihal Olgac Dundar, Pinar Gencpinar, and Dilek Cavusoglu. 2017. "Efficacy of Low-Dose Corticosteroid Therapy Versus High-Dose Corticosteroid Therapy in Bell's Palsy in Children." *Journal of Child Neurology* 32 (1): 72–75. https://doi.org/10.1177/0883073816668774.
- Bechah, Yassina, Cristina Socolovschi, and Didier Raoult. 2011. "Identification of Rickettsial Infections by Using Cutaneous Swab Specimens and PCR." *Emerging Infectious Diseases* 17 (1): 83–86. https://doi.org/10.3201/eid1701.100854.
- Bitsori, M., E. Galanakis, C. E. Papadakis, and S. Sbyrakis. 2001. "Facial Nerve Palsy Associated with Rickettsia Conorii Infection." *Archives of Disease in Childhood* 85 (1): 54–55. https://doi.org/10.1136/adc.85.1.54.
- Cascio, A., P. Dones, A. Romano, and L. Titone. 1998. "Clinical and Laboratory Findings of Boutonneuse Fever in Sicilian Children." *European Journal of Pediatrics* 157 (6): 482–86. https://doi.org/10.1007/s004310050859.
- Khrouf, Fatma, Hanene Sellami, Emna Elleuch, Zouhour Hattab, Lamia Ammari, Moncef Khalfaoui, Jihed Souissi, et al. 2016. "Molecular Diagnosis of Rickettsia Infection in Patients from Tunisia." *Ticks and Tick-Borne Diseases* 7 (5): 653–56. https://doi.org/10.1016/j.ttbdis.2016.02.010.
- Mert, Ali, Resat Ozaras, Fehmi Tabak, Muammer Bilir, and Recep Ozturk. 2006.
 "Mediterranean Spotted Fever: A Review of Fifteen Cases." *The Journal of Dermatology* 33 (2): 103–7. https://doi.org/10.1111/j.1346-8138.2006.00021.x.
- Parola, Philippe, Christopher D. Paddock, Cristina Socolovschi, Marcelo B. Labruna, Oleg Mediannikov, Tahar Kernif, Mohammad Yazid Abdad, et al. 2013. "Update on Tick-Borne Rickettsioses around the World: A Geographic Approach." *Clinical Microbiology Reviews* 26 (4): 657–702. https://doi.org/10.1128/CMR.00032-13.
- Renvoisé, Aurélie, Pascal Delaunay, Elea Blanchouin, Isabelle Cannavo, Eric Cua, Cristina Socolovschi, Philippe Parola, and Didier Raoult. 2012. "Urban Family Cluster of Spotted Fever Rickettsiosis Linked to Rhipicephalus Sanguineus Infected with Rickettsia Conorii Subsp. Caspia and Rickettsia Massiliae." *Ticks and Tick-Borne Diseases* 3 (5–6): 389–92. https://doi.org/10.1016/j.ttbdis.2012.10.008.
- Rovery, Clarisse, and Didier Raoult. 2008. "Mediterranean Spotted Fever." *Infectious Disease Clinics of North America* 22 (3): 515–30, ix. https://doi.org/10.1016/j.idc.2008.03.003.

- Sekeyová, Zuzana, Monika Danchenko, Peter Filipčík, and Pierre Edouard Fournier. 2019. "Rickettsial Infections of the Central Nervous System." *PLoS Neglected Tropical Diseases* 13 (8): e0007469. https://doi.org/10.1371/journal.pntd.0007469.
- Socolovschi, Cristina, Aurélie Renvoisé, Philippe Brouqui, Philippe Parola, and Didier Raoult. 2012. "The Use of Eschar Swabs for the Diagnosis of African Tick-Bite Fever." *Ticks and Tick-Borne Diseases* 3 (5–6): 361–63. https://doi.org/10.1016/j.ttbdis.2012.10.018.

