Case Report

Myocarditis in Mediterranean spotted fever: a case report and a review of the literature

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Introduction: Mediterranean spotted fever (MSF) is a tick-borne acute febrile disease caused by Rickettsia conorii. Most cases follow a benign course, with a case fatality rate of 3–7% among hospitalized patients. Complications are described mainly in adult patients and include hepatic, renal, neurological and cardiac impairment. Among cardiac complications, pericarditis, myocarditis and heart rhythm disorders are uncommon complications in MSF and only a few cases have been reported in the literature.

Case Presentation: We describe a new case of acute myocarditis complicating MSF in an immunocompetent adult patient without risk factors for severe MSF.

Conclusion: Myocarditis is an uncommon but severe complication of MSF. Clinicians should be aware of a possible cardiac involvement in patients with MSF. Close monitoring and an aggressive approach are essential to reduce mortality rates of MSF.

Keywords: myocarditis; rickettsia; conorii; Mediterranean; spotted; fever.

Abbreviations: CT, computed tomography; MSF, Mediterranean spotted fever.
lower lobe and mild pericardial effusion. Because of the multi-organ failure, the patient was transferred to the ICU, intubated, and given intravenous fluid therapy after the cranial CT results. Serological tests to detect *R. conorii* IgM and IgG (indirect immunofluorescence assay (IFI) and ELISA) were negative. *Rickettsia* PCR on blood was positive. Based on a presumptive diagnosis of MSF, the patient was promptly treated with chloramphenicol 3.5 g four times per day and ciprofloxacin 400 mg twice daily intravenously. A cardiology consultation suggested myocardial protection therapy with bisoprolol 1.25 mg orally once daily and ramipril 1.25 mg orally once daily. After two days the patient became afibrile, and after six days, the patient’s condition improved sufficiently that he was transferred to the Infectious disease unit.

The *R. conorii* IFI and ELISA were repeated after one week, showing elevated IgM and IgG titers (IFI IgM–IgG 1/320–1/640; ELISA IgM–IgG 1/200–1/800). After six days of chloramphenicol, antibiotic therapy was switched to doxycycline 100 mg orally twice daily until the patient was discharged on hospital day 16. A follow-up electrocardiogram performed after two weeks demonstrated T-wave normalization. Echocardiogram findings after two weeks and one month were unchanged. At the six-month follow-up the patient was in good clinical condition.

**Discussion**

Cardiac impairment is a rare complication of severe *Rickettsia* spp. infection. Myocarditis has been observed frequently at autopsy in fatal cases of Rocky Mountain spotted fever (Walker et al., 1980; Bradford & Hackel 1978; Nilsson et al., 2005). One case of Japanese spotted fever, one case of African tick-bite fever and very few cases of scrub typhus complicated with acute myocarditis have also been described (Fukuta et al., 2007; Sittiwangkul et al., 2008).

Regarding cardiac complication in MSF, several cases of pericarditis have been described. Few cases of myocarditis and very few cases of heart rhythm disorders have been reported. Only one case of coronary involvement has been described in Italy (Colomba et al., 2008; Grand et al., 1975). A scrupulous analysis of all publications resulted in five eligible articles describing five patients with cardiac involvement clearly related to *R. conorii* (Colomba et al., 2008; Cascio et al., 2011; Ben Mansour et al., 2014; Salvi et al., 1985). Data regarding clinical characteristics, therapy and outcome of these patients, along with our case, are analytically shown in Table 1. Cascio et al. (2011) describe the case of a 3-year-old boy with MSF who developed a transient right coronary artery teasias. The authors suggest that it is more likely that coronary ectasia was the result of the rickettsial vasculitis. The inflammatory response to rickettsial infections triggered the cascade of events that led to Kawasaki syndrome (KS) (Cascio et al., 2011). Considering the diagnosis of KS, treatment with intravenous immunoglobulin and aspirin was initiated while clarithromycin was continued to treat serologically confirmed MSF. Clarithromycin is considered one of the safest and most efficacious treatment (Cascio et al., 2001, 2002). Among the
only three cases of myocarditis related to R. conorii infection described in the literature, two were children and one a young adult (Ben Mansour et al., 2014; Salvi et al., 1985). Only in one case the diagnosis was performed with endomyocardial biopsy (Salvi et al., 1985). The histological finding of myocarditis in the course of MSF is diffuse vasculitis with disruption of the vessel wall by a predominantly mononuclear-cell infiltrate. The target cell of rickettsiae is the vascular endothelial cell where it multiplies. The result is a widespread vasculitis of capillaries, arterioles and small arteries that correlates with the presence of R. conorii (Mekhlofi & Ait-Abbas, 2001).

Even if a definitive diagnosis of myocarditis can be made only by endomyocardial biopsy, it is an invasive procedure that carries the risk of lethal complication and it is not recommended in the routine evaluation of patients with new-onset heart failure (Yancy et al., 2013). Consequently, in our case we did not request endomyocardial biopsy to confirm the diagnosis. However, in our opinion, the clinical syndrome, cardiac biomarkers, and electrocardiographic and echocardiographic findings provided strong evidence of acute myocarditis. Early diagnosis and treatment allowed favourable evolution.

Among MSF cardiac complications, arrhythmia has been rarely reported. Inflammation may play a role in the pathogenesis of atrial fibrillation. Inflammatory cells infiltrating the left atrial endocardium have been demonstrated in patients affected by this arrhythmia. Moreover, the pulmonary veins have a crucial role as one of the key trigger sites for the onset of atrial fibrillation. R. conorii could trigger atrial fibrillation because of its ability to invade endothelial cells and cause perivascular inflammation with activation of the acute phase response (Colomba et al., 2008). Besides a case we described (Colomba et al., 2008), another case of atrial fibrillation and one case of supraventricular tachycardia in a child have been described (Scaffidi et al., 1981; de Groot et al., 1984).

Myocarditis is an uncommon but severe complication of MSF. Clinicians should be aware of a possible cardiac involvement in patients with MSF. Close monitoring and an aggressive approach are essential to reduce mortality rates of MSF.

**References**


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