

A Rare Complication of Rickettsiosis: Thrombophlebitis

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ABSTRACT

AIM: Rickettsiosis is an endemic anthroponosis, especially around the Mediterranean. Although it is reputed to be benign, it can have several complications including vascular which can be serious and sometimes fatal. We report the case of a patient who had rickettsiosis complicated by deep vein thrombosis.

CASE REPORT: A 77-year-old patient, without any particular pathological history, was admitted for acute fever and confusion. On clinical examination, he had altered consciousness and a maculopapular rash. Rickettsial serology was in favor of a recent infection with *Rickettsia conorii*. The patient was treated with ciprofloxacin and preventive anticoagulation. During hospitalization,

he developed a rapid atrial fibrillation at 140 cycle per minute with inflammatory signs of the left lower limb, which was edematous. Venous Doppler ultrasound showed the presence of left iliofemoral thrombophlebitis. He received curative anticoagulation therapy but the outcome was fatal after a respiratory distress related to pulmonary embolism.

CONCLUSION: The vascular complications of rickettsiosis are due to endothelitis caused by these bacteria. The location of these vascular damage conditions the patient's vital prognosis. It is important to diagnosis of these complications for better therapeutic management.

Key words: Rickettsiosis; Vasculitis; Thrombophlebitis

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INTRODUCTION

Mediterranean spotted fever (MSF) is an acute febrile, zoonotic disease caused by *Rickettsia conorii* and transmitted to humans by the brown dog tick^[1]. MSF is endemic across southern Europe and North Africa. Its diagnosis is frequently based on clinical manifestations^[2]. Mostly, this disease follows a benign course, but some cases present with a severe form that may lead to death^[3]. Thrombophlebitis is one of the rare and severe complications of MSF exceptionally reported in the literature. We report a rare case of thrombophlebitis complicating a severe form of MSF.

CASE REPORT

A previously healthy 77-year-old patient was admitted in our department for 3-day history of fever and confusion. In the clinical examination, the patient was febrile and Glasgow score was 11/15. He had a maculopapular rash affecting the palms and soles with a stiff neck. Biologically, he had thrombocytopenia at (57,000 / mm³),

lymphopenia (900 / mm³) and renal failure (serum creatinine at 240 µmol / l). Serologies performed 10 days apart showed seroconversion, which confirmed the rickettsial aetiology. Lumbar puncture confirmed meningeal involvement and rickettsial meningoenzephalitis was the diagnosis retained. The patient received ciprofloxacin and preventive anticoagulation. At the seventh day, we noted the installation of a rapid atrial fibrillation at 140 cycle per minute with inflammatory signs of the left lower limb, which was edematous. Venous Doppler ultrasound showed the presence of left ilio-femoral thrombophlebitis. A curative anticoagulation was started with regression of the edema after 9 days. However, the subsequent course was fatal at day 18 after a respiratory distress related to pulmonary embolism.

DISCUSSION

Mediterranean spotted fever (MSF) is a tick-borne infection caused by *Rickettsia conorii*, Gram-negative obligate intracellular bacteria^[4]. The main clinical signs and symptoms of MSF are: a skin eschar at the site of tick bite, fever and flu-like manifestations such as headache, asthenia, anorexia, myalgia, emerging 3-5 days before the onset of papular or maculopapular rash over the trunk and extremities, involving the hands and feet^[5]. In most cases, the clinical course is benign with a slow recovery, but in about 6 % of the cases, it may be complicated by involvement of multiple organs, with a mortality of 2.5-5 %^[4]. MSF may also follow a severe course in diabetics, alcoholics, people with glucose-6-phosphate dehydrogenase deficiency and the elderly. Neurological complications are the most common and are associated with a high mortality rate that reached 54.5% in hospitalized patients with neurological manifestations and multiorgan involvement^[5]. Cardiovascular complications are less common including thrombophlebitis, which is rarely reported in the literature. In a series of 376 cases reported by Raoult and all, five cases of peripheral venous thrombosis of the lower limbs were noted^[6]. Rickettsial infections is primarily known to affect endothelial cells that normally have a potent anticoagulant function. As a result of endothelial cell infection and injury, the hemostatic system is perturbed and shows changes that vary widely from a minor reduction in the platelet count (frequently) to severe coagulopathies, such as deep venous thrombosis and disseminated intravascular coagulation (rarely)^[7]. The anticoagulant effects of the endothelial cells prevent the initiation and the propagation of the coagulation process. In addition, the cell surface of endothelial cells displays a repellent effect on platelets and other blood cells^[8]. The severe injury or death of endothelial cells, particularly by apoptosis, enhances the exposure of membrane phosphatidylserine and concomitantly enhances the rate of activation of factor X by factor IX. In addition, apoptosis or necrosis of endothelial cells may expose substantial areas of highly procoagulant subendothelial matrix, with or even without cell detachment, probably through cell retraction. Moreover, apoptotic leukocytes and endothelial cells may circulate as procoagulant bodies in a platelet-like manner. Spotted fever rickettsia-infected endothelial cells have been observed to circulate in the blood after detachment. It is evident that changes in endothelial cells after infection may be associated with activation of the coagulation system, such changes have been reported in hospitalized patients with bacterial sepsis^[9]. The MSF clinical forms associated

with thrombophlebitis are generally severe and the mortality rate is high^[10]. Pulmonary embolism is a complication frequently observed in these situations. That would explain the poor outcome even when curative anticoagulation therapy is initiated.

CONCLUSION

Activation of the hemostatic system seems to be a relevant aspect of MSF. Though different mechanisms could be involved in the pathogenesis of these disturbances, vasculitis should be considered as an important component and could account for anomalies in the hemostatic parameters seen during this rare and often fatal complication of MSF. Special clinical awareness should be attributed to this complication in order to initiate adequate treatment as early as possible to avoid the fatal outcome.

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