

Mediterranean spotted fever presenting as an acute pancreatitis

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Abstract

Mediterranean spotted fever (MSF) is an infectious disease, caused by *Rickettsia conorii*. It can have a serious course, even deadly, with many types of complications. Described is a case of a 70-year-old man, hospitalized for fever, abdominal pain, amylase and lipase elevation, and ultrasound hypoechoic pancreas. The working diagnosis at admission was acute pancreatitis. 2 days after admission, the patient developed signs of MSF: fever, maculopapular rash, and "tache noire". Treatment with oral doxycycline was started. After 5 days of therapy, there was complete remission of epigastric pain and fever. Gastrointestinal and hepatic complications are described in association with Mediterranean spotted fever. Much more rare is pancreatic involvement. (Acta gastroenterol. belg., 2011, 74, 91-92).

Key words: mediterranean spotted fever, rickettsiosis, boutonneuse fever, *rickettsia conorii*, pancreatitis.

Introduction

Mediterranean spotted fever (MSF), also called boutonneuse fever, is an infectious disease due to *Rickettsia conorii*. It is usually characterized by the symptomatologic triad: fever, maculo-papular rash, and "tache noire", the typical eschar at the site of the tick bite. Other frequent symptoms are myalgia, arthralgia, and headache. This illness is transmitted by the dog tick *Rhipicephalus sanguineus*, and is endemic in the Mediterranean area, especially in southern Europe and northern Africa. MSF is an emerging or a reemerging disease in several countries: Italy, Portugal, southern France, Malta, Cyprus, India, central and southern Africa, eastern Europe, Black Sea area (1). Climatic changes taking place in the world were suspected of favoring the MSF, through increased activity and spread of ticks (2). MSF usually runs a mild course. However, it can have a severe course, being able to reach, in some cases, high mortality rates (1,3,4).

Case report

A 70-year-old man was admitted to a hospital of Calabria, South Italy, in 2007, because of fever, abdominal pain, and headache. On examination, his blood pressure was 130/80 mm Hg, heart rate 80 beats per minute, and temperature 38.2°C. The cardiac examination was significant for chronic atrial fibrillation, already reported by the patient in his medical history, for which he took aspirin and digoxin. The pulmonary examination was normal. There was epigastric tenderness on palpation,

but no rebound tenderness. Laboratory test results were: WBC 7,900/ μ L, without alterations of the leukocyte formula; amylase 353 U/L (normal values 28-100 U/L); lipase 1026 U/L (normal values 13-60 U/L); AST 31 U/L (normal values 15-40 U/L), ALT 30 U/L (normal values 10-40 U/L); calcium 2.2 mmol/L (normal values 2.2-2.6 mmol/L); glycemia 6.7 mmol/L (normal values 3.8-6.3 mmol/L); triglycerides 1.1 mmol/L (normal values < 2.2 mmol/L); total bilirubin 22 mmol/L (normal values 5.1-17.0 mmol/L), direct 4.6 mmol/L (normal values 1.7-5.1 mmol/L). Serological screening: Hepatitis A Viral Antibody IgM negative, Hepatitis B Virus surface antigen negative; Hepatitis C Virus Antibody negative (normal values < 0.9), IgG anti-virus capsid antigen of Epstein-Barr Virus < 20 U/L, (normal values < 20 U/L), IgM anti-virus capsid antigen of Epstein-Barr Virus < 20 (normal values < 20 U/L); Cytomegalovirus antibody 9.65 IU/mL (normal values < 0.5); Cytomegalovirus antibody IgM 0.5 RU/mL (normal values < 1.0); parotitis virus antibody IgM 0.1 IU/L (normal values < 0.20 IU/mL). Serology for type 1 Herpes Simplex Virus, *Toxoplasma gondii*, *Salmonella typhi* and *paratyphi* O and H antibody was negative. Stool culture was also negative. An ultrasound of the abdomen showed: hepatomegaly, no gallstones, normal common bile duct, and pancreas with a diffusely hypoechoic parenchyma. The patient denied any alcohol intake. He, with diagnosis at admission of acute pancreatitis, was treated with gabexate mexilate, and analgesics, with partial remission of abdominal pain, but persistence of headache and fever. Two days after admission, the patient developed maculopapular rash. A careful examination revealed the "tache noire" on the inguinal fold. The indirect immunofluorescence showed a *Rickettsia conorii* IgM antibody degree > 1:64 (value 1:128; negative value < 1:64). Patient was given 200 mg/day of doxycycline. After 5 days of therapy, there was complete remission of epigastric pain and fever. At discharge the amylase was 175 U/L, and lipase 236 U/L.

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Discussion

Mediterranean spotted fever is characterized by the association of fever, "tache noire", and maculopapular rash. *Rickettsia conorii*, after its entrance into the organism through the dermis, gains the circulation and the vascular endothelial cells. Here it causes a vasculitis, responsible for the clinical and laboratory manifestations, with an increase of vascular permeability, edema, and immunity mediated reaction by Natural Killer cells, Interferon-gamma, antibodies, Tumour Necrosis Factor-alpha, and cytotoxic T lymphocytes. In most cases of MSF, there are generally focal lesions in various organs, but they are not able to determine a severe organ dysfunction (5). Furthermore, the infection and injury to endothelial cells lead to a procoagulant state, with a wide spectrum of phenomena, from a reduction in the platelet count, to severe coagulopathies, such as deep venous thrombosis and disseminated intravascular coagulation (6). Usually, MSF has a benign course. However, forms of MSF have been described with a more severe course in 5-6% of cases (7,8). Fatal cases of MSF are also described, with a mortality rate up to 32.3%, reported in Beja, Portugal, in 1977 (4). The number of cases of serious or fatal MSF varies depending on the years and also the geographical region considered. The reasons for these variations are still unknown (9). The predisposing factors for severity of illness are identified as: old age, heavy smoking, glucose-6-phosphate dehydrogenase deficiency, respiratory failure, diabetes, cardiac disease, chronic alcoholism, end stage kidney disease (4,10). Gastrointestinal complications are relatively frequent and involve up to 30% of patients (11). Most frequent manifestations are: nausea, vomiting, diarrhea, gastrointestinal bleeding. Hepatic involvement in MSF is very frequent, albeit mild, consisting of hepatomegaly, and abnormal liver function tests. However, in a few cases, the increase of transaminases could be serious and the recovery delayed (12,13). More rare is pancreatic involvement, described in literature in few cases (14,15). In the first case (14), the pancreatic involvement was mild, with a prompt response to antibiotic therapy. However, the second case describes a serious multiorgan involvement, including the pancreas, in three South African patients infected by *Rickettsia conorii* (15). In a study, based on paraffin blocks of pancreatic tissue, obtained from patients with a fatal form of Rocky Mountain spotted fever (another similar form of rick-

ettsiosis, caused by *Rickettsia rickettsii*), the pancreatic lesions were vasculitis, hemorrhage, thrombi (16). This case demonstrates that MSF is a disease that gastroenterologists should always consider in the differential diagnosis. Indeed, the disease involves the gastrointestinal tract and liver frequently. More rare is instead the involvement of the pancreas, but it can be the mode of onset of the disease.

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