A case of spotted fever rickettsiosis in a human immunodeficiency virus-positive patient

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Introduction

Mediterranean spotted fever (MSF) due to Rickettsia conorii conorii is an acute febrile disease endemic in Italy, where about 400 cases are reported every year, transmitted to humans by the brown dog tick. Nearly half of Italian MSF cases occur in Sicily (Colomba et al., 2006). However, in recent years other tick-borne spotted fever group rickettsiae such as Rickettsia conorii israelensis, Rickettsia conorii caspia, Rickettsia slovaca, Rickettsia massiliae, Rickettsia aeschlimannii, Rickettsia akari and Rickettsia sibirica mongolitimonae have been documented to cause infection in humans in the Mediterranean basin. All of these agents, although causing milder illnesses than R. conorii, cross-react with R. conorii, thus requiring care in interpretation of serological tests. MSF in an immunocompetent host is typically characterized by fever, skin rash and a black eschar at the site of the tick bite (‘tache noire’). Here, we describe a case of spotted fever rickettsiosis with a benign course in a human immunodeficiency virus-positive patient.

Case report

A 49-year-old Italian male with longstanding human immunodeficiency virus (HIV)/hepatitis C virus (HCV) co-infection was admitted to the Infectious Disease Unit of the University Hospital of Palermo, Palermo, Italy, in May 2012 with a 5-day history of continuous remittent fever, severe headache and arthromyalgia, and with skin rash presenting 24 h before admission.

At the time of admission, he was taking darunavir, ritonavir, raltegravir and etravirine. His most recent HIV RNA viral load was undetectable and his CD4+ cell count was 235 μl⁻¹ (16.64%). His plasma HCV RNA level was 2 370 000 IU l⁻¹. His body temperature was 38 °C, blood pressure 140/90 mmHg and heart rate 94 beats min⁻¹. Physical examination showed hepatomegaly and a maculopapular skin rash over his whole body but especially on the palms, and some of these lesions were petechial; an eschar was detected on his right leg. No tick was found. An electrocardiogram and chest X-ray were normal. Laboratory examination demonstrated normal white and red blood cell counts and a normal haemoglobin value, with a low platelet count (91 000 cells ml⁻¹); serum creatinine was in the normal range (0.73 mg dl⁻¹), aspartate aminotransferase was 54 U L⁻¹, alanine aminotransferase was 51 U l⁻¹ and lactate dehydrogenase was 605 IU l⁻¹. C-reactive protein was 26.77 mg dl⁻¹. Coagulation parameters were within normal limits.

Clinical diagnosis of MSF was made, and the patient started therapy with oral doxycycline (100 mg twice daily) from the day of admission for 10 days. The patient improved within 72 h, and 6 days after admission had recovered completely. A Rickettsia conorii serological test performed on day 2 was negative, but rickettsial DNA was detected from both full blood and buffy coat samples with a highly sensitive real-time PCR assay for the detection of spotted fever and typhus group rickettsiae (Stenos et al., 2005). An immunofluorescent antibody test for R. conorii performed after a 2-week interval showed both IgM (1 : 320) and IgG (1 : 1280).

Discussion

MSF is a benign disease in children, while severe complications can arise in adults (Colomba et al., 2006, 2008; Giammanco et al., 2005; Saporito et al., 2010). Diagnosis is based on epidemiological, clinical and laboratory criteria. The mortality rate of MSF is usually estimated at around 2.5% and risk factors for severe forms include elderly patients, diabetes, cardiovascular illness, chronic renal failure, glucose 6-phosphate dehydrogenase deficiency and chronic alcoholism (Brouqui et al., 2007; Schmulewitz et al., 2008; Sousa et al., 2008). Complicated forms of the disease have also been described in patients without risk factors (Colomba et al., 2008, 2011; Giammanco et al., 2005; Saporito et al., 2010). A single case of MSF was described in an immunocompromised patient after liver transplantation and the illness was lethal.
(Barrio et al., 2002). Sometimes primary HIV infection can mimic MSF presentation (Segura et al., 2002).

Our patient exhibited a typical MSF clinical picture, including a maculopapular rash and a black eschar at the site of the tick bite. In Sicily, R. conorii is the most common agent of MSF (Giammanco et al., 2005), but other spotted fever group (SFG) rickettsiae cannot be excluded to have caused the infection, as not sufficiently long PCR product could be used for sequencing and serological tests for R. conorii cannot exclude cross-reactions with other SFG rickettsiae. The course and outcome of the disease were favourable. Although the agent responsible for the illness was not identified precisely, this case could either be a milder-than-expected MSF or a severe clinical picture caused by a less pathogenic SFG rickettsia.

The immune mechanisms by which the host controls rickettsial infection are highly dependent on cellular immunity, with a critical role identified for CD4+ T lymphocytes. T lymphocytes are a potentially rich source of gamma interferon, which plays an important role in controlling spotted fever rickettsioses by activating endothelial cells, the major target cells of rickettsial infections, to kill intracellular organisms (Barrio et al., 2002). However, in mice, depletion of CD4+ cells has no observed effect on the course or outcome of infection (Mansueto et al., 2012). In contrast, CD8+-depleted mice, infected with sublethal doses of R. conorii, remain persistently infected and ill, and a high proportion of these animals die of uncontrolled rickettsial infection (Walker et al., 2001).

In our case, the CD4+ T-lymphocytes count was not strikingly low and apparently did not play a crucial role in worsening the prognosis of the disease. Possibly, the awareness of the disease in this endemic area, its prompt recognition and timely antibiotic administration may have shortened the symptomatic period and prevented the appearance of severe complications of MSF in our immunocompromised patient. However, whether or not a less pathogenic SFG agent was involved, the presence of petechiae and significant thrombocytopenia would indicate that HIV-positive patients could be prone to develop more severe presentations than expected. In both cases, routine use of molecular biology tools might shorten the time to laboratory diagnosis and allow administration of treatment without delay.

References


