

# Severe Rickettsiosis with Neuromeningeal Involvement : about a case with review of the literature

## ABSTRACT

Mediterranean spotted fever (MSF) is a rickettsial disease of the spotted group caused by rickettsia conorii. This zoonosis is known to have a benign course but can be complicated in severe forms by neurological damage, which sometimes makes it so serious. We report an observation of a 45-year-old female patient, who presented with headaches, vomiting evolving in a febrile context, in whom the clinical examination showed an inoculation chancre associated with diffuse skin lesions, a sub-stiff neck, the lumbar puncture showed a lymphocytic meningitis, after the administration of doxycycline the evolution was favorable.

*Keywords: rickettsiosis, skin rash, inoculation chancre, fever, meningitis.*

## 1.INTRODUCTION

Rickettsial diseases are infectious, re-emergent, polymorphic, potentially fatal in case of delayed diagnosis [1]. We present a clinical case of a severe rickettsial disease caused by rickettsia conorii with neurological involvement. The rapid clinical diagnosis and the introduction of empirical treatment represent the key element of the management.

## 2.CASE REPORT

Patient aged 45 years, without any particular history, who had headaches and vomiting for one week, evolving in a context of fever and chills, resistant to antipyretic treatments, the clinical examination finds a febrile patient at 39°C, obtunded, with a Glasgow score of 14/15, pupils equal and reactive, without sensitivomotor deficit, nor clinical convulsions, a slight stiffness of the neck, a blood pressure of 130/80 mmHg, a heart rate of 110 beats per minute, Pulse oxygen saturation was 98% on room air, cardio-pulmonary auscultation was unremarkable, the abdomen was soft and depressed, The skin and mucous membrane examination showed small, diffuse, round maculo-papular skin lesions that faded on in vitro pressure (Fig.1), sparing neither the palms nor the soles of the feet, and respecting the face, with a black spot showing a chancre of inoculation in the left inguinal fold (Fig.2).

The biological work-up showed hyperleukocytosis at 12000/mm<sup>3</sup> with neutrophilic predominance, thrombocytopenia at 100 000/mm<sup>3</sup>, functional renal failure with a urea level at 0.7 g/l, creatinine at 11 mg/l with creatinine clearance at 55 ml/ min, moderate hepatic cytolysis with aspartate amino transferase (AST) at 120 IU/l and alanine amino transferase (ALT) at 115 IU/L, Hepatitis A, B and C serologies were negative, prothrombin level was 80%, PCR covid 19 was negative, blood ionogram was normal, CRP was 120 mg/l, procalcitonin was 5. The brain scan was without abnormality. The lumbar puncture showed a meningitis with white blood cells at 13 elements/mm<sup>3</sup>, predominantly lymphocytic, normoglycorachic with a moderate hyperproteinorachy at 0.5 g/l. A blood sample for rickettsial serology was taken.

The diagnosis of rickettsiosis complicated by lymphocytic meningitis was retained on the basis of several arguments : a febrile syndrome, skin lesions, an inoculation chancre with an infiltrated base, and the Mediterranean endemic context.

The patient was put under rehydration with saline, antibiotic treatment with doxycycline 200 mg / day for 15 days, preventive anticoagulation with enoxaparin 40mg / day subcutaneously, the evolution was favorable with disappearance of fever after 03 days, and attenuation of skin lesions, improvement of renal function and biological parameters of the infection. The result of the serology was obtained one week after the sampling, which came back positive to the rickettsiosis type Rickettsia conorii.



**Fig.1.**round, diffuse maculo-papular skin lesions



**Fig.2.**Inoculation canker with infiltrated base

### 3.DISCUSSION

Mediterranean spotted fever (MSF), secondary to *Rickettsia conorii*, is an infectious pathology endemic to countries around the Mediterranean. It is a benign pathology. However, severe forms of rickettsiosis represent 6 to 10% and neurological damage can occur in nearly 28% of severe cases. It is a zoonosis caused by *Rickettsia conorii* subsp. *conorii*. The transmission of this bacterium is by the dog tick of the genus *Rhipicephalus sanguineus*, which has little affinity for hosts other than dogs. This explains the sporadic character and the occurrence in urban and peri-urban areas. This infection is mainly encountered in summer when ticks are active. It is endemic in the Mediterranean basin and in sub-Saharan Africa [2,3].

The onset is insidious with fever, chills, headache and sometimes the presence of a black spot. A generalized maculo-papular rash, most often involving the palms and soles, usually appears after four days [4,5]. Severe forms with perimyocarditis, multi-organ failure, severe neurological manifestations occur in 5 to 6% of cases, with a mortality of 2.5%, the meningeal syndrome with clear fluid meningitis with hyper albuminorachia represents the most common neurological involvement [6,7]. Risk factors for poor outcome include advanced age, hepatic cirrhosis, alcoholism, diabetes, glucose-6-phosphate dehydrogenase deficiency, and delay in appropriate antibiotic treatment [8,9]. The diagnosis of rickettsiosis in our patient was based on the clinical findings, including skin lesions, chance of

inoculation and fever, the delay in appropriate antibiotic treatment explains the severe form with neurological involvement and renal and hepatic failure.

Diagnosis is based initially on epidemiological, clinical (fever, headache, rash) and paraclinical (thrombocytopenia and hepatic cytolysis) criteria. The microbiological test of reference in most laboratories is serology, but it only allows a retrospective diagnosis. The average time to seroconversion is 16 days and this time may be even longer in cases of African tick fever (average time 25 days) [10]. PCR and immunohistochemistry allow diagnosis during the acute phase of the disease (before seroconversion) by detecting rickettsiae in biopsies (skin, lymph node, liver, kidney...), and arthropods. PCR can remain positive even after a few days of antibiotic treatment. The black spot is the ideal site to biopsy because it contains a large number of rickettsiae. Indeed, PCR has a sensitivity of 68% and a specificity of 100%. 24 If the black spot is absent, the skin rash can also be biopsied for diagnostic purposes [11]. In our case, the result of the Rickettsian serology is obtained only after one week of the diagnosis allowing a retrospective confirmation of the diagnosis.

If rickettsial disease is suspected, empirical treatment should be started without waiting for diagnostic confirmation to avoid potentially fatal complications. Doxycycline is the treatment of choice [12,13]. Clarithromycin, azithromycin and ciprofloxacin could be alternatives respectively in children and in cases of allergy to tetracyclines [14,15]. Also levofloxacin seems to have a bacteriostatic effect on rickettsia conorii, in a study carried out in Israel, it was equal or twice as active as ofloxacin. Such in vitro results are promising and clinical trials are warranted [16].

Our patient was put on doxycycline immediately after the suspected diagnosis with a dramatic improvement in symptomatology.

#### **4.CONCLUSION**

Rickettsial diseases can often be life threatening. The diagnosis must be evoked in front of any cutaneous rash with fever occurring in an endemic area. Preventive measures and early diagnosis of rickettsiosis allow to decrease the morbidity and mortality of these infections whose frequency is constantly increasing.

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

#### **CONSENT**

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

#### **Ethical Approval:**

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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