

## INFECTIOUS DISEASES

### Editorial

Dear colleague,

The Mediterranean exanthematous fever, endemic disease in the countries bordering the Mediterranean Sea, is the most common rickettsiosis in Tunisia. It is a seasonal infection which appears during the hot season. During this period, an important reproduction of dogs' ticks occurs. These ticks transmit the disease by bites. The clinical diagnosis is easy, in the presence of the characteristic clinical triad. The treatment is based on the prescription of antibiotics with good intracellular diffusion, which permits a rapid favorable outcome.

The objective of this clinical presentation is to remind to physicians to evoke this diagnosis in all eruptive fever occurring during the hot season, the means to confirm the diagnosis and the rules of antibiotherapy.

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# CIPRO

CIPROFLOXACINE



IN THE HEART  
OF THE INFECTION

### Clinical data

Mr. AB, 28 years old, without particular pathologic history, was admitted on July, 15, 2007, for an eruptive fever associated to frontal headaches. He reports the presence of dogs in his environment.

The physical examination :

- Fever at 39°5 C
- Heart rate at 86/min
- A generalized, non pruriginous, extended to hands' palms and plantas , but sparing the face maculo-papulous eruption
- The rest of physical exam did not show meningeal syndrome or cardio-pulmonary anomalies

The biological exams :

- Leucopenia at 3800/mm<sup>3</sup>
- Hemoglobin at 13.2g/dl
- Platelets at 119 000/ mm<sup>3</sup>
- A hepatic cytolysis (ASAT = 98 IU, ALAT= 112 IU)

- CRP at 20mg/l

The chest radiography showed a discreet interstitial syndrome.

## What is your diagnosis?

### Solutions and comments

#### Response 1 :

The diagnosis is : a Mediterranean exanthematous fever

The Mediterranean exanthematous fever is the most common rickettsiosis in Tunisia. It is caused by rickettsiae conori and transmitted by the brown ticks of dogs, *Rhipicephalus sanguineus*. This disease is more common during the hot season and in the rural milieu.

**The interrogatory** should search the notion of dogs in the entourage and, eventually, the presence of ticks in the dogs.

**The functional symptomatology** includes a sudden fever associated to headaches, arthralgia and myalgia .

#### The physical exam :

- Fever, generally around 39°C  
- Macula-papulous eruption with, sometimes, marked reliefs (exanthematous). This eruption is generalized, reaches hands, palms and feet plants (It can be purpuric and this constitutes a gravity sign)

- A black spot or inoculation bed sore : it corresponds to the inoculation point and can be localized at any part of the body, particularly in the folds (groin, armpit) or the scalp, especially in children. It should be carefully searched by a meticulous physical exam. The black spot is not painful, red or black and can be confounded with a furuncle or an excoriation. It is observed in 50 to 75% of cases and can be replaced by unilateral inoculation conjunctivitis

#### Biological exam, commonly observed :

- Leucopenia and thrombopenia
- Elevation of transaminases
- The diagnostic is based on the indirect immune-fluorescence (IFI) serology : a seroconversion, an IgM presence or an IgG level at 4 times the normal, permit to confirm the diagnosis;

#### Question 2 : What would be your therapeutic approach?

#### Response 2 :

The treatment of Mediterranean exanthematous fever is based on **antibiotics** acting on rickettsiae and having a good **intra-cellular diffusion**.

The antibiotics responding to these criteria are cyclins, fluoroquinolones and macrolides.

Currently, the most prescribed therapeutic schemes in the non complicated forms are:

- Fluoroquinolones:

**Ciprofloxacin 500mg (CIPRO 500)** : 1 tablet x 3/day during 2 to 5days

Or,

**Ciprofloxacin 750mg (CIPRO 750)** : 1 tablet x 2/day during 2 to 5days

Or,

Ofloxacin 200mg : 1 tablet x 2/day during 2 to 5days

- Cyclines:

Oxytetracycline 250mg: 2 tablets x 4/day during 7days



Brown ticks of dogs, *Rhipicephalus sanguineus*



A black spot or inoculation bed sore



Maculopapular eruption evoking a Mediterranean exanthematous fever



Retinal damages during Mediterranean exanthematous fever

Or,

Doxycycline 200mg, short treatment: a unique taking or 2 takings with a 12 hours interval.

- Macrolides:

Azithromycin, short treatment : 2 capsules at 250mg in 2 takings with a 12 hours interval.

#### Question 3 : What are the possible complications?

#### Response 3 :

With an efficient antibiotherapy, the outcome is the more often favorable. Apyrexia is generally obtained in 48 hours. The eruption and the black spot disappear in 8 to 10 days. The convalescence takes a long time and is marked by an asthenia.

Lethality is weak, about 2,5% and is related to the less common complications which can occur in the severe forms.

The major complications are:

- Renal insufficiency
- Hepato-splenomegalia, mainly in children
- Digestive hemorrhages, following gastric ulcerations : rare but serious
- A meningeal syndrome : acute lymphocytic meningitis, with an often benign outcome
- Central neurological complication : usual during the severe forms. It includes confusional syndrome, sometimes coma and convulsive seizures
- The cardiac complication includes electric myocarditis, and sometimes bradycardia
- Thrombo-embolic complications : thrombophlebitis or pulmonary embolism
- Symptomatic interstitial pneumopathies
- Retinal damages often asymptomatic

Serious or malignant forms are rare, they occur in the elderly, alcoholic or immunodepressive patients and those presenting a G6PD deficiency. These forms include a poly-visceral damage with coma, a respiratory distress and a renal insufficiency. The evolution is more severe in the absence of an early treatment and the lethality is more important.

#### Highlights:

- The triad : fever + eruption + black spot is very characteristic of the Mediterranean exanthematous fever
- The observation of this triad during summer or associated to the presence of dogs in the patient's entourage should strongly evoke the diagnosis of Mediterranean exanthematous fever and make starting an antibiotherapy acting on rickettsiae
- The diagnosis will be confirmed later with serology

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