Introduction

Rickettsial infections are a group of tick borne acute diseases caused by *Rickettsia* spp and they could have a wide range of clinical manifestations with possible systemic and multi-organ involvement. The vector of *Rickettsia* injects the rickettsiae in the blood vessels during a blood meal, with haematogenous and lymphatic spread of bacteria [1]. After the puncture, the tick leads to a typical cutaneous lesion called *tache noire*, with a necrotic eschar area, fever and maculopapular rash [2]. Nevertheless, the infection often does not show all typical features. Some cases never develop rash (spotless). The spectrum of the disease is quite variable, from asymptomatic to fulminant forms, but it is almost only diagnosed after the typical purpuric rash presentation in a patient with a history of tick bites [3]. Thus Rickettsial infection requires a high level of clinical suspicion to be diagnosed, especially when poor clinical data are available.

Among Rickettsial infections, Mediterranean Spotted Fever (MSF) is an acute febrile disease caused by *Rickettsia conorii*, transmitted to humans by the brown dog tick *Rhipicephalus sanguineus* [4]. Number of cases in Italy, as such in other countries, appears to be increased in the last twenty years, although the real incidence of MSF remains unknown, because of lack of epidemiologic surveillance programs in many countries [4, 5].

Case Report

An 84-year-old man was presented to our hospital Emergency Room after an episode of collapse when he was at home. The patient was living in very poor hygienical conditions; and no relatives could be contacted, due to lack of information. After asking to his family doctor, we were informed that the patient was treated with betametasone and amoxicillin/clavulanic acid for dyspnea and dysphagia arisen that morning. The patient was admitted to the Internal Medicine Department. At clinical examination, the patient showed signs of uncontrolled chronic obstructive pulmonary disease and hypercholesterolemia. He also presented oliguria, fever and abdominal pain. A blood sample was then performed. The haematology was indicative of neutrophilic leukocytosis (10.160 BC/mmc, 92.4% N), hyperglycaemia (139 mg/dL), hyperazotemia (84 mg/dL), hypernatremia (156 mEq/L) and increase in aminotransferase levels (58 UI/L). A treatment consisting with ceftriaxone (2 g iv), beclometasone (8 mg) and anticholinergics for suspected upper respiratory obstructive disease was then immediately started. However, a new episode of loss of consciousness occurred with bradypnea and bradycardia. The Intensive Care Department was then contacted for a possible emergency cardiopulmonary resuscitation. The patient was then put on oxygen face mask, assisted with Auxiliary Manual Breathing Unit (AMBU) and, as soon as all the vital signs where in the range of normality, an ECG examination was then performed showing evidence of a supraventricular tachycardia. The man was then transported to the CT scan unit for...
a head scan which did not reveal evidence of ischemic or haemorrhagic damage. The chest X-ray was not indicative of abnormalities on the lung parenchyma.

After nasogastric tube placement, the patient became asphyxiated and presented supraventricular tachycardia and hemodynamic instability. An uvula oedema was then noticed and an otorhinolaryngologist was contacted for the management of the airways. The results of the examinations were compatible also with epiglottis oedema and the patient was transferred into the Intensive Care Unit, then intubated and ventilated. A sample for bacteriology was collected. No bacterial infection was found and the results of the procalcitonin marker were unremarkable (0.3 ng/mL). A new biochemical panel was then performed showing an increase in CPK (1085 UI/L), LDH (494 UI/L), amylase (142 UI/L), BNP (634 pg/mL), D-dimer (3972 ng/L), myoglobin (579.8 ng/mL), troponin I (0.15 ng/ml), CPK-MB (27.7 ng/mL).

At ICU clinical examination, the patient also presented fever, hypertension and oliguria. After 12 hours, a further otorhinolaryngology examination by fibrobronchoscopy showed reduction in the epiglottis oedema, probably due to steroid therapy. During the following days, the patient was still presenting episodes of tachy/bradycardia (Figure 1), hyperthermia (T 39°C) and hypertensive crisis (Figure 2) partially responding to treatment.

Five days later ICU admission, a neurological examination revealed hypertone of lower limbs associated with non-recovery state of consciousness despite interruption of sedation (propofol).

Figure 1 - Heart rate during admission in ICU.

Figure 2 - Changes in blood pressure during the ten days of hospitalization.
A new CT scan of the head was then performed to rule out the possibility of an ischemic lesion. The results of the scan were unremarkable. Samples for Tetanus, Borrelia, Rickettsia and Toscana virus infections were also collected. The patient deteriorated even more and showed diffuse muscle stiffness, signs of meningismus (Kernig, Brudzinski, and Laségue+++), haemodynamic instability, desaturation with oliguria and hyperthermia. In few days he was lead to the exitus. The post mortem results of the samples collected confirmed the suspect of Rickettsial infection (R. conorii, serological IFA IgM ≥64, IgG ≥256).

**DISCUSSION**

The vector of Rickettsia conorii is a particular type of tick called *Rhipicephalus sanguineus*, regarded as the most common tick in Mediterranean area [1]. The main hosts are dogs and rodents [6]. After puncture, the tick leads to a typical cutaneous lesion called *tache noire*, with a necrotic eschar area, fever and maculopapular rash [2]. Even if Rickettsia conorii is supposed to be the aetiologial agent of MSF, in the last years the molecular biology techniques allowed to identify new species and sub-species of Rickettsia causing diseases similar (but even not) to the classical MSF [4]. Moreover it has been reported that MSF is a benign and self limiting disease in children, but severe complications often arise in adults [4]. Some authors found that elderly patients, often with underlying chronic diseases, could commonly present severe general symptoms, complications, and delayed recovery [7].

Regarding the case discussed above, the upper respiratory condition consisting in an uvula oedema required an empiric anti-inflammatory and antibiotic therapy which, in terms of probability, masked the clinical features usually seen in case of Rickettsia, cutaneous rash in particular. Skin, muscles, heart, lungs and CNS are usually involved [8]. Also pulmonary involvement has been frequently reported in severe human Rickettsial infection, even leading to ARDS, in rare isolated cases [3].

The clinical complications occurred could find a physiopathological explanation in Rickettsia intracellular invasion of endothelium cells, with perivasal inflammation, which leads to vasculitis with multi organ damage: renal hypoxic and ischemic damage clinically manifested with oliguria/anuria, cardiac arrhythmias and increase in myocardic specific biomarkers, loss of consciousness related with impaired CNS activity, caudo-rostral muscular stiffness of the lower limbs [4]. The very first clinical sign reported, consisting in oedema of the upper respiratory airways, led the doctor in charge to start a symptomatic steroid treatment, which was later also carried out in hospital at the time of hospitalization. The symptom made the staff of the Intensive Care Unit start with a symptomatic treatment for the respiratory infection, at the moment non indicative of Rickettsial infection. The upper respiratory condition was at the time considered a life threatening situation and interfered with the diagnostic process resulting in a delayed diagnosis. The extended state of sedation in which the patient was put on also reduced the reliability of the neurological assessment. In case of haematological parameters abnormalities and CNS involvement, diseases involving tick as vector have to be considered [9].

Rickettsial diagnosis is based on epidemiologic, clinical and serologic features. Serological antibodies detection with indirect immunofluorescence assay (IFA) is the most frequently used method for confirming spotted fever worldwide. But serological evidence of infection occurs no earlier than 7 to 10 days after the onset of illness [10]. Thus, PCR should be considered the gold standard in the early course of disease. Nevertheless we have to remark that diagnosis must be based on clinical and epidemiological grounds, because the delay of specific treatment with doxycycline or macrolides increases the risk of severe or fatal outcomes [10, 11].

In fact, Rickettsia and other conditions related with possible tick bite have to be considered in the list of differential diagnosis especially in case of severe systemic or localised disease particularly when the only suspicious sign is a clinical history indicative of patient living in poor conditions of hygiene.

*Keywords*: Rickettsia, Intensive Care Unit.
SUMMARY

We report the case of an 84-year-old man admitted to ICU with symptoms/signs occurring after upper respiratory airways disease. The upper respiratory condition consisting in an uvula oedema required an empiric anti-inflammatory and antibiotic therapy which masked the clinical features usually seen in the case of rickettsial infections, especially cutaneous rash. Although the patient subsequently presented unexplained cardiac and neurological involvement, the starting treatment interfered with the diagnostic process, resulting in a delayed diagnosis. Rickettsia and other conditions related with a possible tick bite have to be considered in the list of differential diagnosis especially in the case of severe systemic or localised disease, particularly when the only suspicious sign is a clinical history indicative of a patient living in poor conditions of hygiene.

REFERENCES