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Case Report

Case report: Infectious cerebral vasculitis due to rickettsiosis ☆

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ABSTRACT

Rickettsiosis is a widespread infection throughout the world and in Africa, it covers a wide range of infectious diseases caused by Rickettsia species. Rickettsial infections, with the exception of Q fever, typically present with fever, rash, and vasculitis. The central nervous system (CNS) can be affected by all rickettsial diseases and is an important target for several of them.

Clinical manifestations are suggestive of rickettsial infection, but serology and skin biopsy provide confirmation.

Although the presence of abnormal neuroimaging is rare, its presence is associated with a worse clinical prognosis. Computed tomography (CT) and magnetic resonance imaging (MRI) scans mainly show signs of vasculitis, which may be reversible if appropriate treatment is initiated early in the course of the disease.

We present here a case of infectious cerebral vasculitis due to rickettsiosis with some MRI features.

Introduction

Rickettsiae are small gram-negative bacteria that are generally obligate intracellular parasites. They are generally transmitted from animals to humans by an arthropod vector, with the exception of Q fever, which is transmitted by direct inhalation of the organism. Rickettsiae can cause vasculitis by infecting the endothelium of small arteries, veins, and capillaries. The central nervous system (CNS) can be affected by all rickettsial diseases and is an important target for many of them [1].

We report the case of a woman who presented to the emergency department with a febrile meningeal syndrome. The diagnosis of rickettsiosis was suspected clinically and confirmed by serological results, with MRI showing cerebral vasculitis of rickettsial origin. We will discuss the clinical

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and radiological findings of this disease and a review of the literature.

Case report

A 56-year-old woman, living in the countryside, with no remarkable medical history. The patient was admitted to the emergency department with a febrile meningeal syndrome. Symptoms began 7 days earlier with a high fever associated with coughing, vomiting and headache, followed a day later by a diffuse, nonitchy rash over the whole body, prompting the patient to consult a general physician 2 days later, who administered oral antibiotics (penicillin) and symptomatic treatment.

As the fever did not improve and her general condition worsened, the patient consulted the emergency department, where a neurological examination revealed meningeal stiffness, leading the doctors to institute emergency treatment for purpura fulminans, and the patient received 3 doses of cephalosporin (third generation) meningeal dose, intravenously.

A thorough skin examination revealed a diffuse maculopapular exanthema over the trunk, upper and lower limbs and face, purpuric in places with palmoplantar involvement, with the presence of a black eschar on the medial surface of the arm correlating with an eschar patch. The diagnosis of rickettsial disease with neurological involvement was made on the basis of these observations.

Biological assessment revealed a normal Hb of 13.2 g/L, an elevated leukocyte count of 13,6 × 109/L with a predominance of neutrophils, a low platelet count of 121,000/ mm^3 and an elevated C-reactive protein of 215, with normal liver and renal function tests.

The patient was initially negative for rickettsial serology.

A CT scan was performed, showing 2 bilateral frontal cortico-subcortical hypodense areas, and ill-defined hypodensities in the subcortical area and at the white matter-gray matter junction, unchanged after contrast injection, possibly related to foci of encephalitis. It also showed a right basifrontal porencephalic cavity of similar density to that of the CSF, with a sequellar ischemic appearance (Fig. 1).

A lumbar puncture was also performed, showing an increased white blood cell count and protein level.

The patient was then admitted to the dermatology department, where oral antibiotic therapy was started; doxycyclin (2nd-generation cyclins) at a dose of 200 mg/d with local treatment of the eschar.

The patient began to improve clinically and biologically, with regression of the rash and headache and improvement of the infectious work-up.

Given the CT abnormalities, an MRI was performed 8 days after the CT images and showed multiple punctiform lesions, rounded in shape, involving the deep white matter, white matter-gray matter junction, subcortical, and periventricular region, at frontoparietal level bilaterally. These lesions are described in hypersignal T2 and FLAIR, nonrestrictive and not enhanced after contrast injection. It also showed a right basifrontal porencephalic cavity, similar in signal to the CSF, with a sequellar ischemic appearance. All these lesions are related to micro-infarcts caused by infectious vasculitis in the context of rickettsial disease. In contrast, there was complete resolution of the frontal cortico-subcortical areas described on CT (Fig. 2).

The patient was discharged from the hospital 4 days later, continued antibiotic treatment at the same dosage for 10 days, and repeated rickettsial serology after 2 weeks, which proved positive.

Discussion

Rickettsiosis is a widespread infection throughout the world and in Africa [2]. In fact, it covers a wide range of infectious diseases caused by different etiological agents that share the rickettsia genus. Rickettsiae are small gram-negative bacteria that are generally obligate intracellular parasites, usually transmitted from animal to human via a contaminated arthropod vector. The exception is Coxiella burnetii, responsible for Q fever, which is transmitted by inhalation and has an endospore form capable of surviving in an extracellular environment [1,3].

Rickettsiae are able to invade and develop in a wide variety of host cells from different species and organs. In humans, the rickettsial pathogen is inoculated either by a tick or mite bite, or by scratching the skin after infected flea or louse excrement has been deposited on the skin [4]. They spread into the bloodstream, proliferating, and damaging the endothelium of small arteries, veins and capillaries and, in some cases, vascular smooth muscle cells, causing damage to the microcirculation of virtually every organ [3]. This anatomical distribution determines the fundamental similarity of the pathology (vasculitis) and pathophysiology (increased vascular capacity) of rickettsial diseases [5].

Diagnosis of CNS rickettsial diseases is difficult and often delayed due to the non-specific clinical presentation of the disease. The neuroinvasion of rickettsia occurs during the systemic phase of the disease, usually after dissemination of the bacteria into the bloodstream. Once rickettsiae reach the blood-brain barrier, they can cross it transcellularly (intracellular mode), which may be explained by bacterial replication in endothelial cells [6].

Rickettsial species are classified into 4 groups: the spotted fever group, the transitional group, the typhus group, and the ancestral group [6]. The most common rickettsial infections are Rocky Mountain spotted fever, epidemic typhus, and Q fever. Rickettsial infections, with the exception of Q fever, generally present with fever, rash, and vasculitis [3].

The clinical spectrum of rickettsial diseases can range from mild fever to high-risk, life-threatening complications. Spotted fever group rickettsioses typically present with a clinical triad consisting of high fever, an inoculation lesion (eschar), and a diffuse rash. However, other symptoms such as isolated fever, nonspecific flu-like symptoms, cough, myalgias, abdominal pain, lymphadenopathy, and various neurological symptoms may also be observed [6].

The severity of rickettsial disease varies from patient to patient and has been linked to differences in pathogen vir-

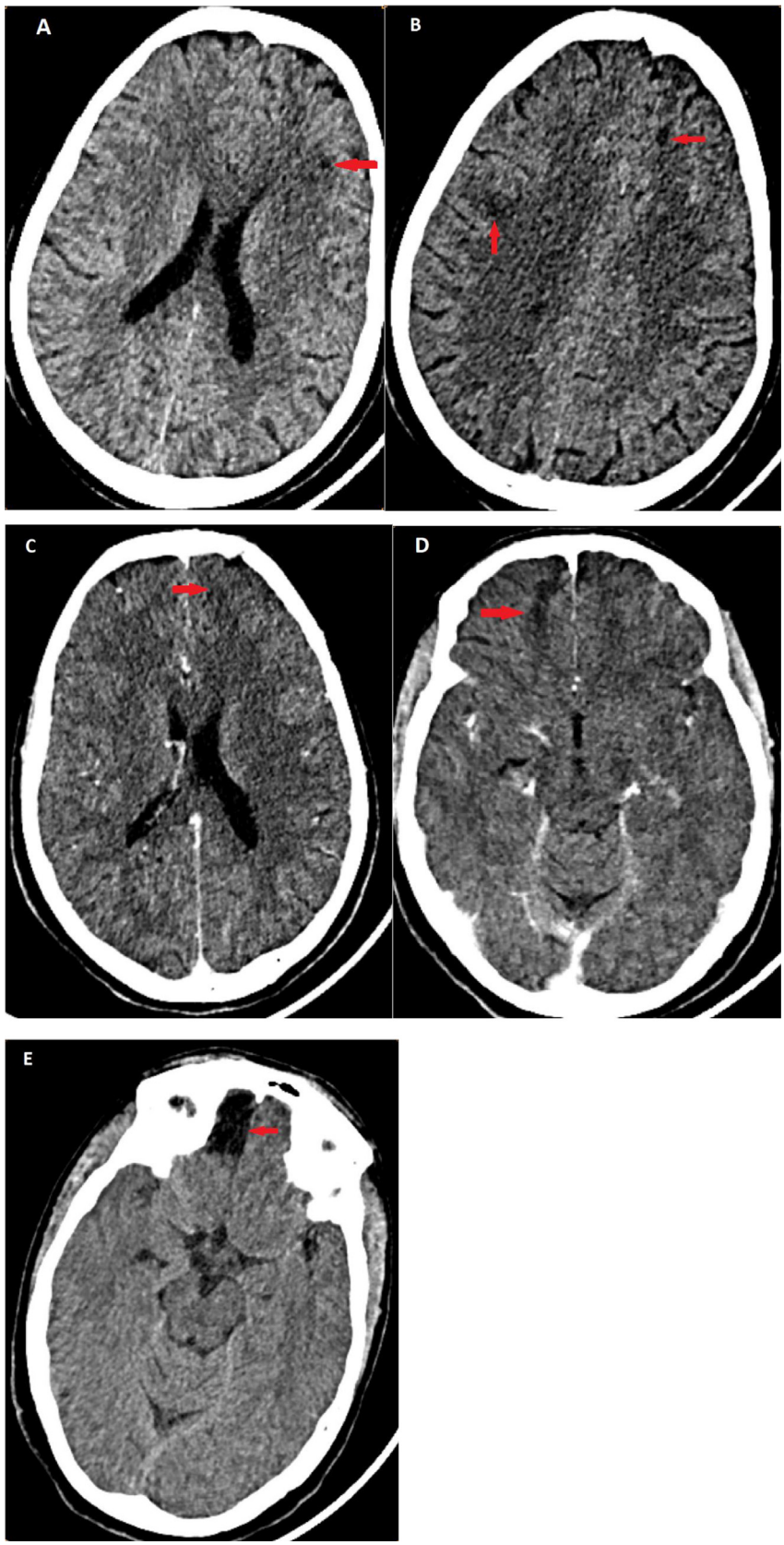

Fig. 1 – Axial CT with and without contrast: shows some subcortical hypodensity in the frontal region bilaterally (A, B) and 2 bilateral frontal cortico-subcortical low attenuation areas (C, D), poorly limited for most of them, unchanged after contrast injection, possibly related to foci of encephalitis. It also shows a right basifrontal porencephalic cavity, similar in density to the CSF, with a sequellar ischemic appearance (E).

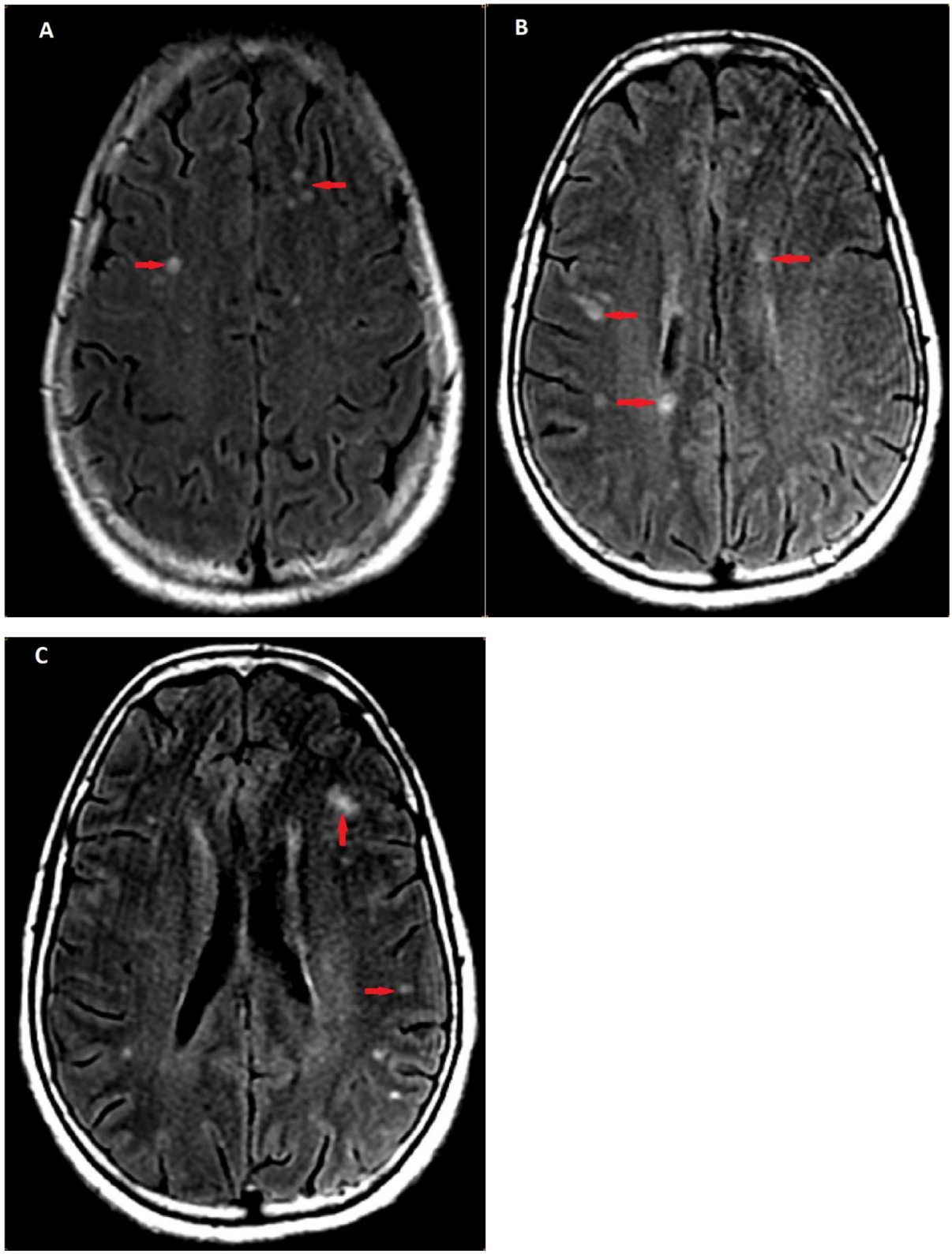

Fig. 2 – MRI with axial FLAIR sequences (A-C): shows multiple lesions of increased signal (red arrow), mostly punctiform and rounded in shape, involving the deep white matter, the white matter-gray matter junction, subcortical and periventricular regions, at frontoparietal level bilaterally. All these lesions are related to micro-infarcts caused by infectious vasculitis in the context of rickettsiosis.

ulence and host factors (e.g. age, late diagnosis, liver and kidney dysfunction, CNS, and lung involvement) [6]. All rickettsial diseases can affect the central nervous system (CNS), considered an important target for many of them [1]. The most frequently reported neurological manifestations of rickettsial infections are encephalitis, meningitis, and acute disseminated encephalomyelitis. However, some studies have reported other manifestations, such as unilateral facial nerve paralysis and cerebral infarction [6].

Early recognition of CNS involvement is essential, as it is often the cause of increased mortality. Imaging techniques are extremely useful in highlighting the various aspects of neurorickettsiosis. Although the presence of abnormal neuroimaging is rare, it is associated with a poorer clinical prognosis [3]. In fact, the changes observed in neurorickettsiosis are more frequent on MRI than on CT [7].

Computed tomography (CT) and magnetic resonance imaging (MRI) primarily reveal and detect signs of vasculitis. Abnormalities observed on brain CT and MRI mainly consist of a characteristic pathological sign known as a typhoid nodule. These nodules are essentially perivascular infiltrates of lymphocytes, macrophages and polymorphonuclear leukocytes. They may show rim enhancement after contrast injection on injected MRI, and are generally characteristic of spotted fever group rickettsia and scrub typhus [7].

Other pathological lesions include white matter and periventricular micro-infarcts (hyperintensities on FLAIR and T2-weighted images), cerebral edema, meningeal enhancement, and prominent perivascular spaces. The predominant involvement of periventricular and deep white matter is also compatible with the disease's predilection for small vessels, as in our case [7].

Neuroimaging findings are potentially reversible with complete resolution if appropriate treatment is initiated early in the course of the disease [3].

The main differential diagnosis is disseminated meningococcal infection (meningococcemia), whose rash is a manifestation of disseminated intravascular coagulation, making it difficult to distinguish between meningococcal and rickettsial disease in the early stages of the patient's presentation [1].

The diagnosis of rickettsial fever is confirmed by both serology and immunostaining of skin biopsies. Although the sensitivity and specificity of the Weil-Felix test are low, it is still widely used to diagnose rickettsial infections. This test attempts to diagnose rickettsial disease by identifying antibodies that cross-react with 2 Proteus antigens (OX-19 and OX-2) [8].

Treatment of rickettsial vasculitis consists of 100 mg doxycycline every 12 hours for at least 7 days, and for at least 2 days after apyrexia. Doxycycline is the drug of choice for rickettsial infections, and treatment should be started as soon as the diagnosis is suspected; indeed, the mortality rate is significantly lower in patients treated within the first 5 days of illness than in those treated later [1–8].

Conclusion

Rickettsiosis covers a wide range of infectious diseases caused by Rickettsia species [2]. The central nervous system (CNS) can be affected by all rickettsial diseases, and is an important target for many of them [1]. Definitive diagnosis of clinically suspected rickettsial infections is confirmed by serology and skin biopsy [1]. Neuroimaging abnormalities are rare and reveal signs of vasculitis, which may be reversible if appropriate treatment is initiated early in the course of the disease [3].

Patient consent

I, the author of the article: "Case report: Infectious Cerebral Vasculitis due to Rickettsiosis" approve that the patient gives his consent for information be to published in radiology case reports.

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