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CASE REPORT

A case of multifocal chronic Q fever osteomyelitis

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Abstract Chronic Q fever can be difficult to diagnose because of a variety of non-specific clinical presentations. Chronic Q fever osteoarticular infections have rarely been reported in the literature. We describe here an unusual multifocal osteomyelitis due to *Coxiella burnetii* in an adult.

Keywords Bone infection · Chronic Q fever · *Coxiella burnetii*

Introduction

Q fever is a worldwide zoonosis caused by an intracellular bacterium named *Coxiella burnetii*. This disease is reportable in the USA, but not in France. It is responsible for acute and chronic forms distinguished by their clinical expression, temporal course and serological profiles [1–3]. Due to host factors, infection may become chronic in 1–5% of the cases [3, 4]. The most frequent chronic form (60–70%) is endocarditis, followed by vascular infections, osteoarticular infections, hepatitis and pulmonary infections [3, 5]. The suspicion of chronic Q fever is confirmed by the positivity of antibodies directed against the phase I antigen of *C. burnetii*. In the French national reference laboratory based in Marseille, a phase I immunoglobulin G (IgG) titre $\geq$1:800 is recommended as a cut-off value for the diagnosis of chronic Q fever with a positive predictive value of 98% [3]. Recommended therapy for chronic Q fever endocarditis consists of doxycycline associated with hydroxychloroquine, acting as an alkalinising substance, allowing the rise of the lysosomal pH and restoring the bactericidy of the doxycycline. Treatment is recommended for at least 18 months [2–4]. Only 19 cases of chronic Q fever osteoarticular infections (13 in adults and six in children) have been reported in the literature, including osteomyelitis, spondylodiscitis and some cases of tenosynovitis [6, 7]. We describe a new case of osteoarticular chronic Q fever, presenting as an unusual multifocal osteomyelitis.

Case report

A 49-year-old man was admitted to hospital in December 2008 with a 3-week history of night fever associated with inflammatory articular pain of both knees, left elbow and humerus, maximum during the febrile peaks. He had no past medical history, but lived in the countryside, with young cats and sheep in his neighbourhood. On physical examination, his temperature was normal during the day

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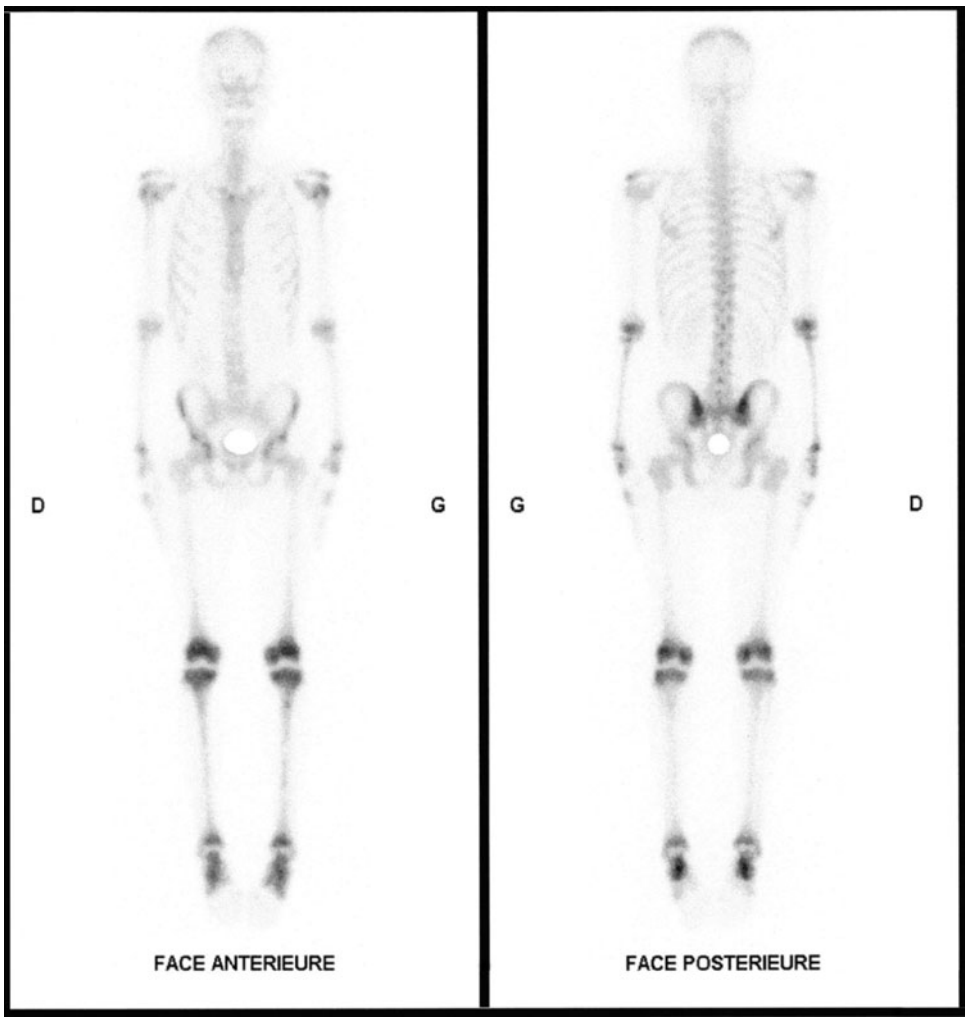

Fig. 1 Tc-99m scintigraphy showing a hyperfixation of the metaphyso-epiphyseal long bones

and around 39°C in the evening. No cardiac murmur was noted.

Laboratory tests showed a normal leukocyte count, an elevated erythrocyte sedimentation rate (77 mm/h), an elevated C-reactive protein (167 mg/L for a normal <5 mg/L) and isolated liver cholestasis twice the normal value (gamma-glutamyl transpeptidase [gamma-GT] and phosphatasis alkaline 137 U/l for a normal <67 U/l) with normal transaminase levels. Blood and urine cultures were sterile. *C. burnetii* serology revealed titres significant for the diagnosis of chronic Q fever (phase I: IgG 1:6,400, IgM 1:100, IgA 1:100; phase II: IgG 1:12,800, IgM 1:200, IgA 1:200; indirect immunofluorescence assay performed in the national reference centre in Marseille). *C. burnetii* polymerase chain reaction (PCR) from serum was negative. Endocarditis was ruled out by a trans-oesophageal echocardiography. Computed tomography showed emphysaema secondary to smoking but no sign of pneumonia, no hepatosplenomegaly nor lymphadenopathy. A multifocal osteoarticular form of chronic Q fever was suspected, given that phase I immunoglobulin G (IgG) titre was over 1:800, even if the symptoms had been lasting for just a little more than one month at this stage [2].

Radiographs of the painful joints were normal, but Tc-99m scintigraphy showed a hyperfixation of the metaphyso-epiphyseal long bones (Fig. 1). Magnetic resonance imaging of the lower limbs revealed a bilateral tibio-femoral osteomyelitis. HIV serology was negative and immunological investigations showed IgG lambda dysglobulinaemia without hypogammaglobulinaemia, a decreased CD4/CD8 ratio, but with 608 CD4/mm^3, type 2 cryoglobulinaemia and positive anti-smooth muscle antibodies. Osteo-medullar biopsy, performed mainly to rule out lymphoma, showed doughnut granulomas with fibrin rings, classically associated with Q fever but not specific for the disease.

A combination of doxycycline (200 mg/day bid) and hydroxychloroquine (600 mg/day tid) was started in January 2009. One month later, despite the treatment, the patient remained febrile and reported increased bilateral inflammatory bone pain. Serology titres had decreased by half. Doxycycline and hydroxychloroquine serum levels were measured and the doses were adapted accordingly.

Rifampicin (1,200 mg/day bid) was added given the absence of clinical response and the radiological confirmation of the suspicion of osteoarticular chronic Q fever. In March 2009, doxycycline was replaced by ofloxacin (400 mg/day bid), given its documented bone penetration and the absence of clinical improvement. Significant clinical and biological improvements were obtained after 6 months of antibiotic therapy. Antibiotic therapy was stopped after 18 months. The patient was asymptomatic, with a normal C-reactive protein level and an anti-phase I IgG titre of 1:200 with no detection of anti-phase I IgA.

Discussion

Among the 19 osteoarticular infections due to chronic Q fever published in the literature, nine are osteomyelitis, including four chronic multifocal recurrent infections in children [6, 7]. The case we report here is, to the best of our knowledge, the first multifocal osteomyelitis due to *C. burnetii* described in an adult.

Chronic Q fever is usually diagnosed by serological investigation, which is an easy-to-perform diagnostic tool; symptoms also usually last for more than one month, which was the case in our patient [2]. Serum PCR has a low sensitivity, whereas PCR is highly sensitive on tissue samples [2, 8]. Histological identification of a doughnut-ring granuloma can help in establishing a presumptive diagnosis but it implies an invasive liver or bone marrow biopsy [2, 3]. While the therapy of Q fever endocarditis is well established, consisting of doxycycline and hydroxychloroquine, adapted to serum levels [9], for at least 18 months, the treatment of the osteoarticular forms is not consensual [6]. Antibiotics with documented good bone penetration, such as rifampicin or fluoroquinolones, could be added to doxycycline and hydroxychloroquine [6, 10].

It is thought that anti-phase I IgG titres $<$1:800 18 months after the start of therapy are indicative of cure and allow the discontinuation of therapy [2, 3]. Evaluation of therapeutic success in patients with chronic Q fever requires prolonged clinical and serological follow-up because of the possibility of later relapse [2, 3].

Conclusions

Because of its non-specific clinical presentation, Q fever osteoarticular infection is difficult to diagnose. Clinicians should consider this diagnosis in endemic areas, and order Q fever serological screening when appropriate.

Conflict of interest None.

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