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Reminder of important clinical lesson

Q fever: a case with a vascular infection complication

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Summary

The most common clinical presentation of chronic Q fever is endocarditis with infections of aneurysms or vascular prostheses being the second most common presentation. Here, the authors report a case of vascular chronic Q fever. In this patient, a renal artery aneurysm was discovered by abdominal and pelvic CT during a systematic investigation to identify predisposing factors to chronic Q fever because of high antibody titres in a patient with valve disease.

BACKGROUND

Chronic Q fever is detected by an increase in phase I antigen-specific antibodies against *Coxiella burnetii*. It has been recommended to test serum samples 3 and 6 months after acute Q fever both to detect the progression to chronic Q fever and to investigate cardiac valve lesions using echocardiography.

The infection of aneurysms and vascular prostheses is the second most common form of chronic Q fever. Chronic Q fever is potentially fatal and therefore needs be diagnosed early to enable adequate treatment and avoid more severe complications. If chronic Q fever is suspected, a systematic search may allow for the discovery of small aneurysms.

CASE PRESENTATION

A 72-year-old man was admitted to the Jacques Coeur Hospital in Bourges, France, on September 1, 2008, for polyarthralgia associated with biologic inflammatory syndrome. The symptoms had started 3 weeks earlier. On examination, he complained of shoulder pain, myalgia and neck stiffness. He was afebrile, asthenic and reported a weight loss of a few kilograms. Cardiopulmonary and neurological examinations were normal.

INVESTIGATIONS

The patient's leukocyte count was 6.5 g/l. The erythrocyte sedimentation rate and C-reactive protein were elevated at 95 mm, first hour and 54 mg/ml, respectively. Moreover, polyclonal hypergammaglobulinaemia (17.3 g/l) and hyper-α2globulinaemia (11.6 g/l) were detected. The serum level of liver enzymes was normal. Because a diagnosis of polymyalgia rheumatica was suspected, treatment with 40 mg per day of prednisone was started on September 4, 2008. Concomitantly, Q fever serology was found to be positive, both for immunoglobulins to phase II (1:800, 1:200 and 1:100 for IgG, IgM and IgA, respectively) and to phase I antigens (1:400, 1:100 and 1:50, respectively). Such titres were consistent with acute Q fever. Upon subsequent questioning, the patient acknowledged that he was in frequent contact with farm animals, the usual source of *C burnetii*, the aetiologic agent of Q fever. Treatment with doxycycline, 200 mg per day orally, was prescribed for 14 days, and the prednisone was decreased to 5 mg every 14 days. One month later, new serology showed increasing antibody titres consistent with chronic Q fever, with the titres of phase I antigen-specific antibodies being 1:6400, 1:100 and 1:50 for IgG, IgM and IgA, respectively (table 1). No *C burnetii* could be detected in the serum using a previously described PCR-based protocol.[1] In our patient, both transthoracic and transoesophageal echocardiography ruled out the diagnosis of endocarditis, or pre-existing valvulopathy. Radiologic exploration was completed with abdominal and pelvic CT, and as part of our systematic investigation of patients with chronic Q fever, a small, right-renal-artery aneurysm measuring 13 mm in diameter was detected. On the basis of these findings, the diagnosis of chronic vascular Q fever was made.

Table 1 Evolution of Q fever serology (indirect immunofluoresence assay) and PCR in our patient

	Phase I			Phase II			PCR
	IgG	IgM	IgA	IgG	IgM	IgA	
17/09/2008	400	100	50	800	200	100	
18/10/2008	6400	0	50	12,800	0	100	Negative
18/12/2008	6400	0	50	12,800	0	100	Negative

Ig, immunoglobulin.

TREATMENT

Treatment with a combination of doxycycline (200 mg per day) and hydroxychloroquine (600 mg per day) was started for a minimum of 18 months. Surveillance of this treatment consists of both drugs dosages on serum samples and an ophthalmologic examination every 6 months to detect possible ocular toxicity due to hydroxychloroquine. Surgery was planned for the patient shortly after diagnosis.

DISCUSSION

Q fever is an ubiquitous zoonosis caused by *C burnetii*. Infected aerosols generated by farm animals are the usual source of human infection.[2] Our patient reported frequent contact with farm animals, specifically goats. *C burnetii* is an obligate intracellular bacterium that may cause acute and chronic infections in humans. Although most acute infections (60%) are asymptomatic, frequently observed symptoms include isolated fever, atypical pneumonia and hepatitis.[3] Recovery is spontaneous in most cases. However, acute Q fever may evolve to chronic infection, that is, an infection persisting for more than 6 months, in 1 to 5% of patients.[4] Such a progression occurs most frequently in patients with a valve disease, a vascular prosthesis or aneurysm, immunocompromised patients or in pregnant women.[5] Serologically, chronic Q fever is characterised by an IgG titre to phase I antigen greater than 1:800. Clinically, chronic Q fever presents as endocarditis, vascular infections, osteoarticular infections and chronic hepatitis.[6] Infective aneurysms and infection of vascular prostheses account for 9% of chronic Q fever cases.[7] The risk of progression from acute to chronic infection is estimated to be 40% in patients with valvular defects,[5] but it is as yet undetermined in patients with arterial diseases.

The delay between acute and chronic infection is variable. In 2007, Landais *et al*[8] demonstrated that 50% of patients developed chronic Q fever within 3 months of acute infection, and 75% within 6 months. Here, the development of chronic Q fever may have been facilitated by the use of corticosteroids for polymyalgia rheumatica. Indeed, exacerbation of chronic Q fever with corticosteroid therapy has been previously reported.[9] Despite the severity of chronic Q fever, its diagnosis is often delayed due to the absence of specific clinical symptoms and because the initial infection is often asymptomatic.[10]

Q fever is mainly diagnosed through serology with the reference method being the indirect immunofluorescence assay.[11] In our laboratory in Marseille (Southern France), the French National Reference Centre for Rickettsial Diseases, we use a microimmunofluorescence technique. Chronic Q fever was defined by a cut-off titre of phase I antigen-specific IgG greater than 1:800. The serological diagnosis of chronic Q fever should encourage the search for valve disease by echocardiography. Transthoracic echocardiography is recommended in the first instance; however, in the case of a normal transthoracic echocardiograph, transoephageal echocardiography should be performed in order to detect a bicuspid aortic valve or mitral regurgitation[12] if the antibody titre increases. Indeed minor valvulopathies, such as minor valvular insufficiency, mitral valve prolapse or a bicuspid aortic valve, are a predisposing factor for Q fever endocarditis.[13] If a valvular lesion is ruled out, abdominal and pelvic CT should be performed to search for an arterial

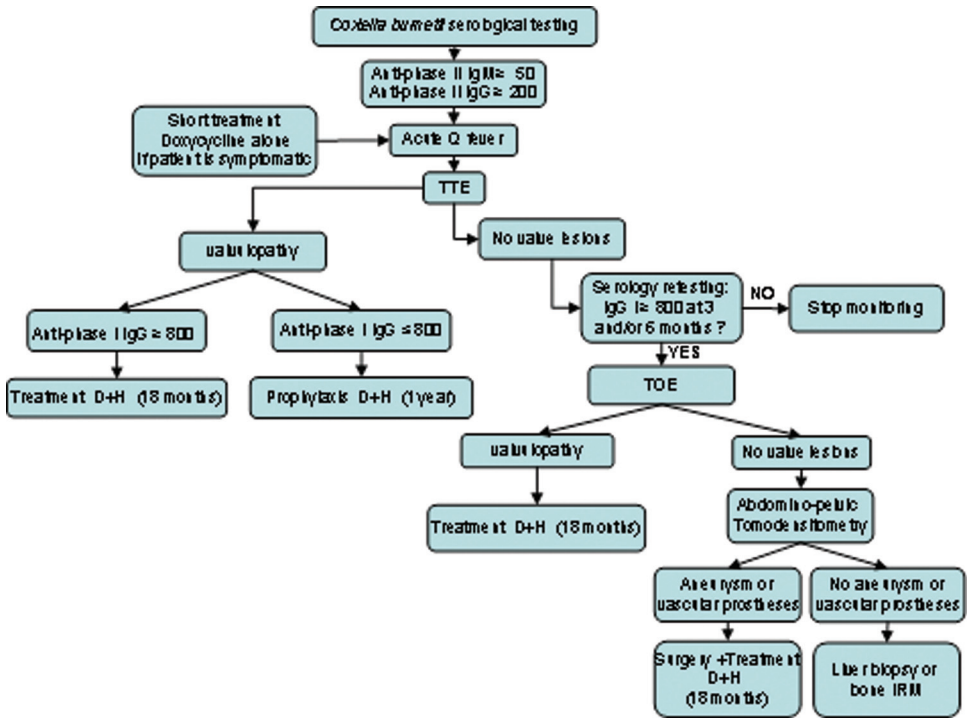

Figure 1 Strategy and management of chronic Q fever diagnosis.
TTE: Transthoracic echocardiography
TOE: Transoesophageal echocardiography
D: doxycycline
H: hydroxychloroquine

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aneurysm.[14] (figure 1). The diagnosis of an aneurysm infection can be established by serology with the same profile as endocarditis.[6] The documentation of cardiac or arterial abnormalities is crucial to improve the management and prognosis of chronic Q fever. The management of chronic Q fever is complex. Prolonged antibiotic therapy with both doxycycline (200 mg per day) and hydroxychloroquine (600 mg per day) should be administered for a minimum of 18 months.[10]

C burnetii vascular infection has a poor prognosis. An early diagnosis is necessary to enable early treatment and avoid severe complications. In a recent study of 30 cases of *C burnetii* infected aortic aneurysms or vascular grafts, vascular surgery was significantly associated with recovery but the associated mortality rate was high (25%). Because rupture of infected aneurysms is the main complication of *C burnetii* aortic infections, surgery is required in most *C burnetii* vascular infections.[15]

It is recommended that serological testing be performed 3 and 6 months following the diagnosis of acute Q fever to allow for the early detection of chronic infection. Delays in diagnosis have been shown to have a significant negative impact on prognosis.[8] When phase I antigen-specific antibody titres are increasing rapidly and when echocardiography is negative, we suggest performing a CT scan to identify any arterial aneurysms.

Learning points

- Radiologic examinations, notably echocardiography and CT, have as important a place in chronic Q fever diagnosis as serology because management of Q fever infection depends on the presence or absence of valve disease or vascular infection.
- These vascular infections have a poor prognosis, which is why early management of this infection is fundamental, especially because diagnosic delays have a significant impact on prognosis.

Competing interests None.

Patient consent Obtained.

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