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BRIEF ORIGINAL

Acute Q fever and the risk of developing endocarditis☆

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KEYWORDS
Q fever;
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Prevention

Abstract
Objectives: Assess clinical and serological data as parameters indicative of a possible evolution to endocarditis after an episode of acute Q fever.
Patients and methods: Retrospective cohort study of evolution to endocarditis after an acute Q fever episode, analyzing the clinical and serological evolution and the antibiotic treatment administered.
Results: Eighty patients were recruited, 20% of whom had phase I IgG antibody levels ≥ 1:1024 in the first 3 months. Only 44% of the patients underwent antibiotherapy in the acute phase; only 2 patients underwent extended antibiotherapy. Fifteen percent of the patients underwent an echocardiogram. None of the patients had symptoms suggestive of chronic infection or progressed to endocarditis after a median follow-up of 100 months, regardless of the early increase in phase I IgG antibodies.
Conclusions: The early increase in phase I IgG antibodies in asymptomatic patients is not associated with progression to endocarditis despite not undergoing prolonged antibiotic treatment.

PALABRAS CLAVE
Fiebre Q;
Coxiella burnetii;
Endocarditis;
Serología;
Ecocardiograma;
Prevención

Fiebre Q aguda: riesgo de desarrollo de endocarditis

Resumen
Objetivo: Valorar los datos clínicos y serológicos como parámetros indicativos de posible evolución a endocarditis tras un episodio de fiebre Q aguda.
Pacientes y métodos: Estudio de cohortes retrospectivo de la evolución a endocarditis tras un episodio de fiebre Q aguda, analizando evolución clínica, serológica y tratamiento antibiótico recibido.

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Resultados: Se reclutó a 80 pacientes, presentando el 20% niveles de anticuerpos IgG de fase I ≥ 1:1.024 en los primeros 3 meses. Solo el 44% recibió antibioterapia en la fase aguda; únicamente 2 enfermos recibieron antibioterapia prolongada. Se realizó ecocardiograma al 15%. Ningún paciente presentó síntomas indicativos de infección crónica ni evolucionó a endocarditis tras una mediana de seguimiento de 100 meses, independientemente de la elevación precoz de anticuerpos IgG de fase I.

Conclusiones: La elevación precoz de anticuerpos IgG fase I no se asoció a evolución a endocarditis a pesar de no haberse realizado tratamiento antibiótico prolongado en pacientes asintomáticos.

Background

Q fever is a zoonosis caused by *C. burnetii* whose acute phase clinical presentation varies between asymptomatic forms in 50–90% of patients to manifestations as variable as fever of intermediate duration, hepatitis and pneumonia.[1] This considerable variability appears be related to the strains prevalent in each geographical area.[2] In the south of Spain, 90% of symptomatic patients present with fever of intermediate duration, which is accompanied by hypertransaminasemia in 60% of patients.[3] The most severe clinical forms are endocarditis, vascular prosthesis infections of and aortic aneurysms, which require surgery in 15–73% of patients and cause mortality in 5–65%, depending on whether appropriate treatment is administered.[4–7]

Endocarditis and endovascular infections develop after an episode of acute Q fever at rates that vary between 0% and 1.5%,[3,7–9] reaching rates of up to 7% in specialized centers.[10] The presence of prior valvular heart disease constitutes the main risk factor, although it can be asymptomatic and go unnoticed.[11] Due to this risk, a number of authors recommend performing transthoracic echocardiography (TTE) for all patients with acute Q fever and transesophageal echocardiography (TEE) if the phase I IgG antibodies titers are >1:800 in the first 6 months. In addition, the authors recommend starting treatment with doxycycline plus hydroxychloroquine for 1 year if valvular heart disease (bicuspid aortic valve, valvular prosthesis, moderate to serious mitral regurgitation and mitral valve prolapse) is detected.[12–14] However, after an outbreak in The Netherlands, other authors found that none of the 134 patients diagnosed with acute Q fever progressed to endocarditis, despite the fact that many of them (59%) showed valvular heart disease and that none of them had undergone antibiotherapy. As a result, these authors do not recommend the systematic implementation of TTE.[9,15]

This study evaluated the progression to endocarditis and the prognostic value of serology for predicting the evolution of a cohort of patients with acute Q fever.

Patients and methods

A retrospective study was performed at a reference hospital for cardiac surgery in the province of Cadiz, which treats a mainly urban population of 222,515 inhabitants.

The patients were selected based on the positive serological results for *C. burnetii* between the 2000 and 2010 (indirect immunofluorescence; Q Fever IFA IgG/M, Focus Diagnostics, Cypress, CA, USA). A polymerase chain reaction (PCR) analysis for *C. burnetii* was not available. The patients had been initially treated in either hospital units or outpatient clinics. There was no specific established protocol for the treatment and follow-up of patients with Q fever. The use of antibiotherapy, the implementation of serological tests, echocardiography and the periodicity of checkups were therefore performed according to the individual discretion of each attending physician.

Cases of acute Q fever were considered those that presented a compatible clinical condition (fever, hepatitis, pneumonia), demonstrating a pattern indicative of seroconversion in 2 successive serological measurements (initial negative serology with the presence of positive phase I or II IgM antibodies in the second reading) or a positive phase I or II IgM with an increase in at least 4 dilutions of the phase II IgG antibodies in the second reading. Cases of chronicity to endocarditis were considered those that met the modified Duke criteria (phase I IgG antibody levels ≥ 1/800). Given that our study technique employed a double dilution method such that the value following 1:512 was 1:1024, the latter was the titer considered indicative of progression to chronicity,[16] as long as it was accompanied by a compatible clinical condition.

The assessment of progression after the acute Q fever episode was conducted using an analysis of the medical history to 2013, so that at least 24 months had elapsed after the episode of acute Q fever in all patients. The patients included in the study only had electronic medical histories, which included all episodes of hospitalization, emergency care and primary care. We assessed data regarding febrile episodes, prolonged asthenia, increased transaminase levels, pneumonia and symptoms consistent with valve or cardiac failure, as well as data indicative of peripheral embolisms and the microbiological results (blood cultures and serology).

We excluded patients who lacked medical assessments in their medical history, those who had only a single serological reading, those diagnosed with endocarditis by Q fever but with no prior episode of acute Q fever and patients with previous non-acute infections (phase I IgG antibodies titers < 1:1024, with negative IgM antibodies and with no clinical condition compatible with acute Q fever).

We recorded epidemiological variables (age, sex, residence), previous diseases (immunosuppression secondary to human immunodeficiency virus [HIV] infection, hematological neoplasms, treatment with steroids or