

CASE REPORT

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# Q fever endocarditis of the tricuspid valve transmitted in an urban setting with no livestock exposure: Case report

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## Abstract

**Background** *Coxiella burnetii* is a bacterium with extreme tenacity and contagiousness that is mainly transmitted by inhalation of contaminated aerosols. Nevertheless, a transmission by ticks is under discussion. We report a case of Q fever in an urban environment and far away from sheep breeding that caused a rare right-sided endocarditis.

**Case presentation** A 55-year-old man who was in good health before the event developed a *C. burnetii*-endocarditis of the tricuspid valve. He had no contact with sheep and no recent travel in a rural or even endemic area. The infection originated in a strictly urban environment, and the patient's occupation as a cemetery gardener in Berlin, coupled with the close temporal and local exposure to wild boar, made a transmission by these animals a plausible hypothesis. The infection was confirmed by the German Reference Laboratory, and the patient recovered completely after treatment with doxycycline and hydrochloroquine.

**Conclusions** The specialities of this case report are the right-sided endocarditis and the transmission of *C. burnetii* in a metropolitan area without sheep contact. We think that this case should serve to increase awareness of the potential for Q fever infection even in non-rural areas.

**Keywords** Q fever, *Coxiella burnetii*, Tricuspid valve, Right heart, Infective endocarditis, Wild boar, *Sus scrofa*, Transmission, Non-rural area, *Dermacentor marginatus*, *Ixodes ricinus*

## Case presentation

A 55-year old man, hitherto in good health, experienced a rapid increase in inspiratory left-sided chest pain accompanied by severe bilateral headache. He developed fever between 39.2 and 39.6 °C, shivered and

sweated profusely, and lost 2 kg of weight within four days. Despite self-medication, the headache and fever persisted, and the patient proceeded to our emergency unit. Here, we saw a muscular man (190 cm, 94 kg) with an unremarkable clinical status, particularly lacking any signs of meningism, palpable lymph nodes or heart murmurs. The chest X-ray, ECG and urinary status were all normal. After sampling of blood cultures, intravenous analgesic and antipyretic medication and rehydration, the patient was admitted to our normal ward. The diagnostic procedures were stepwise extended and delivered unremarkable results in cerebral computed tomography (CT), cerebral magnetic resonance imaging (MRI) including angiographic reconstruction, lumbar puncture, transthoracic echocardiography, duplex-sonography of temporal and carotid arteries, and -apart from splenomegaly of 13

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x 6 cm- abdominal ultrasound. Laboratory values indicated on more viral inflammation although they lacked specificity. These included an elevated C-reactive protein CRP of 22 mg/dL (reference value 0.5 mg/dL), a normal procalcitonin (PCT, 0.3 ng/mL), and a mild leucopenia (nadir at day 2 with 3.1 / nL), and mild anemia (hemoglobin 12.4 mg/dL, reference  $\geq 14.0$  mg/dL). The following serological markers were within the reference values: For diseases of the liver (transaminases, gamma-glutamyltransferase, alkaline phosphatase, bilirubin, protein, albumin), kidney (creatinine kinase, electrolytes), plas-matic coagulation (international normalised ratio, partial thromboplastin time), thyroid gland (thyroid-stimulating hormone TSH), myocardium (high-sensitive troponin, creatine kinase) and rheumatic diseases (rheumatic factor, antibodies against double-stranded DNA, cardiolipin(2.6 U/L; reference value 10 U/L), and plas-matic and cytosolic ANCA).

Transesophageal echocardiography (TEE) revealed the presence of a 9 x 5 mm mobile structure at the septal cuspid of the tricuspid valve with consecutive degree 1 regurgitation (Fig. 1, video in eSupp). However, all eleven blood cultures remained sterile, prompting the search to be extended to serological prove of viruses or atypical bacteria. There was no evidence of antibodies in serum (s) or cerebrospinal fluid (c) against *Brucella abortus* (s), *Borrelia burgdorferi* (s,c), *Treponema pallidum* (s,c), Herpes simplex (s,c), Ebstein-Barr-virus (c), Spring-summer-encephalitis virus (c), Enterovirus (c), Influenza A and B (s), Hepatitis A and C (s), Human immunodeficiency virus HIV (s). Positive antibodies against the Hepatitis B surface antigen indicated the effective protection by former vaccination. At day 11 after submission, a positive phase II IgM (qualitative test) and an elevated phase II IgG (262 U/mL; reference value 30 U/mL) antibody titre against *Coxiella burnetii* provided sufficient evidence to diagnose Q fever endocarditis. A confirmation sample

was sent at day 17 to the German national reference laboratory on Q fever (Landesgesundheitsamt Baden-Württemberg). The laboratory found antibody titres of phase I IgM 1:64 and IgG 1:128, and of phase II IgM 1:1024 and IgG 1: 4096 (all tests microimmunofluorescence tests). A polymerase chain reaction was not performed. The antibiotic therapy was changed from the combination ampicillin plus flucloxacillin plus gentamicin (in accordance with the European Society of Cardiology ESC guideline on infectious endocarditis of unknown origin [1]) to doxycycline 100 mg b.i.d. plus hydrochloroquine 200 mg t.i.d. The initial antibiotic regimen resulted in a clinical improvement with a reduction in fever and the resolution of headache and chest pain. However, subfebrile temperature and weakness persisted until the start of doxycycline / hydrochloroquine. Leukocyte count normalized within 2 and CRP within 9 days, respectively.

Given the high titre of *C. burnetii*, we extended the anamnestic exploration, but the patient could not remember any contact with sheep, goats, or a history of tick bite. It is noteworthy that he is employed as a cemetery gardener and he recalled that a herd of wild boar had recently uprooted his cemetery. The wild boar had properly ploughed the ground and he was engaged in replanting the flowers and shrubs for several days. Headache and chest pain started two weeks after this intensive contact with potentially contaminated soil, so that we consider the wild boar as vector of *C. burnetii* as possible. The patient remained asymptomatic following the change of the antibiotic regimen and was discharged four weeks after admission. Long-term hydrochloroquine therapy afforded both ophthalmological control and the exclusion of glucose-6-phosphat-dehydrogenase deficiency. The antibiotic treatment was continued in accordance with guideline recommendations for 12 months following infection. A recent telephone contact four years later confirmed complete restitution.



**Fig. 1** Transesophageal echocardiography. Left: transgastric view, Right: right ventricular inflow-outflow view. AL anterior leaflet of the tricuspid valve, RA right atrium, AoV aortic valve, PV pulmonary valve. Arrows indicate on hypermobile, partially hypodense structure at the anterior leaflet of the tricuspid valve

## Discussion

**Diagnosis** In 2015, the European Society of Cardiology defined a single positive blood culture, a phase I IgG titre of  $\geq 1:800$ , or a polymerase chain reaction (PCR) from tissue as a major criterion for *C. burnetii* endocarditis [1]. Nevertheless, the diagnosis of Q fever in the absence of endocarditis and of chronic Q fever remains a matter of controversy. The Dutch consensus guideline which was developed in the aftermath of the *C. burnetii* epidemic 2007-2011 in the Limburg province states that a positive tissue or serum PCR alone and even in the absence of acute Q fever proves chronic Q fever [2], let alone that a combination of phase I IgG antibodies  $\geq 1:800$  and major echocardiographic findings prove chronic Q fever. In contrast, the French working group led by Prof. Raoult accepts a diagnosis of acute Q fever only if positive PCR findings in blood are accompanied by a clear focus in imaging (echocardiography, positron emission tomography PET, CT, MRI), and they demand a phase I IgG titre of  $\geq 1:6,400$  [3]. Both the mandatory imaging and the four-step higher phase I IgG titre exceed the aforementioned Dutch definition. Consequently, the Dutch guideline criteria exhibit a higher sensitivity and lower specificity compared to those of the French working group. We adhere to the Dutch and ESC argument that sensitivity is of greater importance in clinical practice, given that missing the diagnosis and inadequate treatment would result in high mortality and morbidity [4]. A reference for this mortality is the mentioned French National Reference Center for Q fever, which in 2434 patients with *C. burnetii* infection demonstrated that hepatitis (38.3%) and endocarditis (21.9%) were the most frequent clinical forms, the latter of which resulted in a mortality rate of 2.4 per 100 person-years [5]. Individual risk factors for the progression of *C. burnetii* endocarditis include pre-existent valvular pathologies (e.g. bicuspid aortic valve or mitral prolapse) and anticardiolipin antibodies [6]. Both of these have been excluded in our patient. It is also important to note that our patient had symptoms of acute Q fever and endocarditis, so that the above mentioned criteria and especially the phase I titres are not applicable.

**Infected valve** The largest study on blood culture-negative infective endocarditis was published by the French National Reference Center for Rickettsial Diseases, included 348 patients between 1983 and 2001 and identified 48% *C. burnetii* infections by serology, culture of valve specimens, microscopic examination, or direct PCR amplification. The infected valves were the aortic valve in 56%, the mitral valve in 46% and the tricuspid valve in only one case [7]. Q fever endocarditis of the tricuspid valve is a generally rare manifestation, with four reported cases in adults [8–11] and one in a child [12]. Right-sided

endocarditis in children following pulmonary artery and pulmonary valve replacement appears to be a more evident problem with at least 5 documented infections in children with congenital heart disease [13–15]. Thus, the case described here should serve to increase awareness of this particular localization. The therapy is independent of the suspicious cardiac valve, and consists of a combination of doxycycline plus hydrochloroquine, as proposed by Raoult et al. [16] and adopted by the ESC recommendation [1].

**Transmission** *C. burnetii* is a bacterium with extreme tenacity and contagiousness. It has two distinct forms, the large-cell-variant (LCV) and the small-cell-variant (SCV). The latter is dormant and non-replicative, yet resistant against dryness, heat, UV-radiation, and numerous disinfection agents. SCV is the transmitted and LCV the metabolic active variant in host cells.

The main mode of infection is the inhalation of contaminated aerosols [17]. It is postulated that transmission by ticks may also be a significant factor, given that dry tick faeces may contain up to  $10^{12}$  Coxiellae per gram faeces and remain infectious in sticky wool for up to two years [18]. However, the role of ticks as vectors of *C. burnetii* remains a matter of contention. The most prevalent tick species in Germany is *Ixodes ricinus*, with an infection rate of only 1.9% even in an endemic area in Thuringia [19]. Another prevalent tick in Germany is the so-called sheep tick *Dermacentor (D.) marginatus* which is suspicious as a vector due to its host adaptation, yet there was no DNA proof in 666 ticks [20] and only one such example in 1066 *Dermacentor* spp. ticks [21].

Consequently, Q fever remains a rare condition in urban settings. The official bulletin for Berlin indicates that there were two to four cases per year in the respective time frame (2014-18). With the exception of our patient there was only one further patient reported in the first half of 2018, and it is likely that the latter patient was infected in a Netherlands sheep farm [22]. Therefore, our patient could not have been infected in association with a local Q fever outbreak. In this concern one should be aware that up to 8% of wild boars in Berlin have a positive serology for *C. burnetii* [23]. The anamnesis of our patient, who was in close temporal and spatial exposure to wild boar, makes this infection chain plausible. Although there is no irrefutable proof, we believe that this case should serve to increase awareness of the potential for Q fever infection even in urban areas and even by wild boar. The lack of evidence in epidemiological and transmission data on ticks in Germany led to the establishment of the “Q fever - German Interdisciplinary Program for Research” [24, 25].

The special characteristics in our reported case of *C. burnetii* endocarditis are the infection in a metropolitan area distant from sheep contact and the right-heart manifestation. Our findings suggest, but do not prove, a potential transmission route via wild boar (*Sus scrofa*).

#### Abbreviations

C	Coxiella
CRP	C-reactive protein
CT	Computed tomography
D	Dermacentor
ESC	European Society of Cardiology
LCV	Large-cell-variant
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction
PET	Positron emission tomography
SCV	Small-cell-variant
TEE	Transesophageal echocardiography

#### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-024-09629-x>.

Supplementary Material 1.

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#### Authors' contributions

DH and BH wrote the manuscript. DH and AB assessed the patient, BH revised the manuscript. All authors read and approved the manuscript.

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#### Availability of data and materials

Data is provided both within the manuscript and (eVideo) supplementary files.

#### Declarations

#### Ethics approval and consent to participate

The article was published with written consent of the patient.

#### Consent for publication

The patient gave his written informed consent for the publication of this case report including the echocardiographic images.

#### Competing interests

The authors declare no competing interests.

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