Antiphospholipid Antibody Syndrome With Valvular Vegetations in Acute Q Fever

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Background. Coxiella burnetii endocarditis is considered to be a late complication of Q fever in patients with preexisting valvular heart disease (VHD). We observed a large transient aortic vegetation in a patient with acute Q fever and high levels of IgG antiphospholipid antibodies (IgG aCL). Therefore, we sought to determine how commonly acute Q fever could cause valvular vegetations associated with antiphospholipid antibody syndrome, which would be a new clinical entity.

Methods. We performed a consecutive case series between January 2007 and April 2014 at the French National Referral Center for Q fever. Age, sex, history of VHD, immunosuppression, and IgG aCL assessed by enzyme-linked immunoabsorbent assay were tested as potential predictors.

Results. Of the 759 patients with acute Q fever and available echocardiographic results, 9 (1.2%) were considered to have acute Q fever endocarditis, none of whom had a previously known VHD. After multiple adjustment, very high IgG aCL levels (>100 immunoglobulin G G–type phospholipid units; relative risk [RR], 24.9 [95% confidence interval [CI], 4.5–140.2]; P = .002) and immunosuppression (RR, 10.1 [95% CI, 3.0–32.4]; P = .002) were independently associated with acute Q fever endocarditis.

Conclusions. Antiphospholipid syndrome with valvular vegetations in acute Q fever is a new clinical entity. This would suggest the value of systematically testing for C. burnetii in antiphospholipid-associated cardiac valve disease, and performing early echocardiography and antiphospholipid antibody dosages in patients with acute Q fever.

Keywords. Q fever; Coxiella burnetii; antiphospholipid antibodies; valvular heart disease.
As a consequence, the objectives of this study were to test whether the primary infection with *C. burnetii* could cause cardiac valvular vegetations, to define acute Q fever endocarditis, and to determine whether the occurrence of these vegetations is correlated to IgG aCL levels. We also investigated the outcome of patients with acute Q fever endocarditis.

**PATIENTS AND METHODS**

Since 1985, the French National Referral Center for Q fever has tested for *C. burnetii* in >200,000 samples from all over the country [19]. Clinical and echocardiographic data were prospectively obtained for all positive samples and collected in a computerized database between January 2007 and April 2014. All patients subsequently diagnosed with acute Q fever who had available echocardiographic results were included. Exclusion criteria were age <18 years, absence of patient consent, persistent Q fever infections (chronic endocarditis >3 months after acute Q fever, vascular infection, osteoarticular infection, persistent lymphadenitis, other rare forms of persistent infections), preexisting autoimmune disease, histology on an excised valve excluding endocarditis, pregnancy, and lack of available echocardiographic results. The main outcome measure was the occurrence of a vegetation (acute Q fever endocarditis). Data regarding history of endocarditis, recent surgery, or oral/dental procedures were also collected. The study was approved by the local ethics committee (Comité de Protection des Personnes Sud Méditerranée 1) under registration number 1355 and by the French National Drugs and Health Products Agency. All patients gave written informed consent.

Acute Q fever was defined as previously published [20]. IgG aCL levels, tested retrospectively before and prospectively after January 2012, were quantified from the same tube as previously reported at diagnosis [15]. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were systematically advised following a previously published protocol [15, 20]. Patients without at least 1 echocardiogram available were excluded. Echocardiography was performed according to standardized criteria [21, 22] by local cardiologists who were not blinded in any way. A significant VHD was defined as a bicuspid aortic valve or other congenital heart disease, a prosthetic valve, a grade ≥2 valve stenosis or regurgitation [21, 22], a mitral valve prolapse, and a remodeling or thickening valve [23]. Antibiotic prophylaxis with doxycycline and hydroxychloroquine for 12 months was recommended only for patients with a significant VHD [20]. This prophylaxis was not advocated in any patient without significant VHD, even if IgG aCL levels were very high [15].

Acute Q fever endocarditis was defined as the presence of a valvular vegetation by echocardiography (TTE or TEE) within 3 months of the onset of symptoms in a patient with acute Q fever according to the definition detailed above. Chronic Q fever endocarditis was defined based on recently updated criteria [18], with the exclusion of acute Q fever endocarditis. For patients fulfilling chronic Q fever endocarditis criteria [18], doxycycline and hydroxychloroquine were advised for 18–24 months [12].

The Wilson score method for binomial proportions was used to estimate the confidence interval (CI) for the incidence of acute Q fever endocarditis among eligible patients. Each group (acute Q fever without VHD, acute Q fever with VHD but without vegetation, chronic Q fever endocarditis) was compared to acute Q fever endocarditis (reference group), using 2-sided Fisher exact test for qualitative variables, and Kruskal–Wallis rank test with Dunn correction for multiple comparisons for quantitative variables. Receiver operating characteristic (ROC) analysis was used to determine the IgG aCL threshold value with the maximal sensitivity and specificity for acute Q fever endocarditis. We used a rare-events logistic regression model [24] to assess potential predictors of acute Q fever endocarditis using the ReLogit package for Stata [25]. King and Zeng [24] demonstrated that conventional logistic regression underestimates the probability of rare events (such as those <5% of the data). Therefore, they developed corrections for the biases occurring in logistic regression when explaining such rare outcomes. All variables of interest were first tested in a univariate rare-events logistic regression model; variables that had a liberal P value <.20 were considered eligible to enter the multivariate model. Finally, only variables with a P value <.05 were maintained in the final multivariate model. Relative risks and their 95% CIs from the multivariate rare-events logistic regression model were estimated by stochastic simulation using 3000 replications and the ReLogitQ package for Stata [24].

**RESULTS**

**Screened Patients**

Over the course of the 7-year study (January 2007–April 2014), 1440 patients with a diagnosis of active *C. burnetii* infection were included in the National French Referral Center for Q Fever database (Figure 1) [18]. Final diagnoses were categorized as acute Q fever (1094 cases), chronic endocarditis (227 cases), vascular infection (73 cases), lymphadenitis (31 cases), osteoarticular infections (11 cases), Q fever during pregnancy (30 cases), or other forms of infection (156 cases; 1 patient could have several forms of infection). Seven hundred fifty-nine patients with acute Q fever had echocardiographic data available including 195 cases with a VHD (26%).

**Patients With Acute Q Fever Endocarditis**

Of the 759 assessable patients, 9 were ultimately considered to have acute Q fever endocarditis (Table 1). The frequency of acute Q fever endocarditis was estimated at 1.18 per 100 acute Q fever patients (95% CI, .62–2.24). Seven of these 9 patients were male, and the mean age (± SD) was 53 ± 11 years. Five patients were immunocompromised, 2 suffered from alcohol addiction, and 2 had no notable medical history. Two patients had
a known ischemic heart disease without VHD. No patient had recent surgery or oral/dental procedures. Symptoms included fever in all cases and cardiac and respiratory failure in 1 case each. Pneumonia was noted in 4 cases. In 6 cases, hepatitis was noted, including hepatic failure in 1 patient for whom liver biopsy identified a typical granulomatous hepatitis [26]. Eight patients had negative blood cultures. One patient (patient 5) had positive blood cultures for coagulase-negative Staphylococcus species diagnosing a dual-pathogen endocarditis. Serological titers were consistent with acute Q fever in all cases, with the presence of immunoglobulin M (IgM) or seroconversion. Polymerase chain reaction was positive for C. burnetii in blood in 1 case. IgG aCL levels were highly elevated in all 9 cases; the median level was 126 GPLU (range, 66–1828 GPLU), while normal values were <22 GPLU [15]. IgG and IgM anti-β-2-GP-I were negative in all 4 patients tested. The activated partial thromboplastin time ratio was increased (>1.3) in 7 of 9 patients (range, 1.6–2.4). The only 2 patients tested were positive for lupus anticoagulant. Workup for other causes of elevated IgG aCL was not performed systematically as sera were tested retrospectively in most cases (2007–2011).

Vegetations were localized to the aortic valve in all 9 cases (Supplementary Video 1). The median delay between the onset of symptoms and vegetation diagnosis was 31 days (range, 7–66 days). TTE found the vegetation in 6 cases. In 2 cases, the vegetation was found only by TEE after TTE, and in 1 case, it was not possible to determine which mode of echocardiography made the diagnosis. The size of vegetations ranged from 5 mm to 10 mm. An aortic regurgitation was discovered in 4 cases, and in 1 case, a mitral regurgitation was found. In the other 5 cases, no valve dysfunction was noted. Valve thickening was present in 5 patients involving the aortic valve (2 cases), the mitral valve (2 cases), or both (1 case). One echocardiogram with vegetation (patient 5, Supplementary Video 1) and 1 without vegetation (an acute Q fever patient followed in our cardiology unit) were read by 2 other cardiologists (see Acknowledgments) who were blinded to the purpose of the study. Both cardiologists confirmed the vegetation in the included patient and the absence of such abnormality in the negative control patient.

Increased IgG aCL Level With No Previously Known VHD in Acute Q Fever Endocarditis

Of the 759 patients with acute Q fever and available echocardiographic results, we compared the characteristics of the 9 patients with acute Q fever endocarditis vs each of the 3 other groups: acute Q fever patients with VHD but without vegetation (186 cases), acute Q fever patients without VHD (564 patients), and patients with chronic Q fever endocarditis (227 cases) (Table 2). Sex ratio and age were not significantly different between the acute Q fever endocarditis patients and the other groups. Strikingly, none of the patients with acute Q fever endocarditis had a known history of VHD before acute Q fever, which was significantly different compared with patients with

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Figure 1. Study flow diagram. *One patient could have several forms of persistent infection.*
Table 1. Characteristics of Patients With Acute Q Fever Endocarditis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Year of Dx</th>
<th>Age/Sex/Region</th>
<th>Medical History</th>
<th>Q Fever Diagnostic, Serology*</th>
<th>IgG aCL (GPLU)</th>
<th>Echocardiography Delay From First Symptoms to Vegetation</th>
<th>Treatment Regimen, Duration</th>
<th>Q Fever Outcome: Later Fulfill Persistent Endocarditis Criteria/Last Serology (Delay From Diagnosis in mo)/Infection Status Considered at Positive IgG aCL (≥22 GPLU)</th>
<th>Outcome</th>
<th>Disappearance of Vegetation, No. of Positive Echocardiograms, Diagnosis to Last Positive Echocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2010)</td>
<td>58/M/Rhône-Alpes</td>
<td>Diabetes, coronaryopathy</td>
<td>Febrile hepatitis, flulike syndrome, confusion 0/200/100 0/400/200 (positive PCR for C. burnetii on blood)</td>
<td>1828</td>
<td>7 mm aortic vegetation, aortic regurgitation, mitral thickening (TEE, normal TTE), 66 d</td>
<td>Doxycycline and hydroxychloroquine, 18 mo</td>
<td>Yes (A0B2C2) 100/0/0 200/0/0 21 mo, cured</td>
<td>No, 28 GPLU at 21 mo</td>
<td>Yes, 5, 14 mo</td>
<td></td>
</tr>
<tr>
<td>2 (2011)</td>
<td>64/M/Pays de la Loire</td>
<td>Ischemic heart disease, diabetes,</td>
<td>Febrile, flulike syndrome, cardiac failure 200/100/0 400/200/0</td>
<td>66</td>
<td>Aortic vegetation without valve dysfunction, aortic valve thickening, mitral calcification (TEE), 10 d</td>
<td>Doxycycline and hydroxychloroquine, unknown duration</td>
<td>No, 50/0/0 100/0/0 12 mo, cured/died from mesenteric infarction 15 mo later</td>
<td>Yes, 2.6 mo</td>
<td>No, 3, 6 mo</td>
<td></td>
</tr>
<tr>
<td>3 (2011)</td>
<td>65/F/Rhône-Alpes</td>
<td>Primary polycythemia on hydroxyurea</td>
<td>Febrile hepatitis and pneumonia, 25/100/0 50/200/0</td>
<td>119</td>
<td>7 mm aortic vegetation without other valve anomaly (TEE), 10 d</td>
<td>Doxycycline, 18 m and hydroxychloroquine, 12 mo</td>
<td>Yes (A0B1C2) 400/0/0 800/0/0 26 mo, cured</td>
<td>No, 36 GPLU at 26 mo</td>
<td>Yes, 5, 12 d</td>
<td></td>
</tr>
<tr>
<td>4 (2011)</td>
<td>37/M/Portou-Charentes</td>
<td>No particular medical history, cooked raw goats 1 mo before</td>
<td>Febrile hepatitis, flulike syndrome 800/50/0 1600/100/0</td>
<td>103</td>
<td>Aortic vegetation at TEE (TEE: valve thickening) 61 d</td>
<td>Doxycycline and hydroxychloroquine, 11 mo then doxycycline alone, low compliance</td>
<td>Yes (A0B1C3) 50/0/0 23 mo, cured</td>
<td>Yes, 9 mo</td>
<td>Yes, 1, 0 d</td>
<td></td>
</tr>
<tr>
<td>5 (2012)</td>
<td>58/F/Provence-Alpes-Côte d’Azur</td>
<td>Alcoholism, diabetes, high blood pressure</td>
<td>Febrile pneumonia and respiratory failure 200/25/0 0 400/50/0</td>
<td>324</td>
<td>7 mm aortic vegetation without other valve anomaly (TEE) 14 d</td>
<td>Teicoplanin, ciprofloxacin, rifampin</td>
<td>Lost to follow-up at 1 w, only the first of 4 echocardiographs found the vegetation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (2012)</td>
<td>62/M/Rhône-Alpes</td>
<td>Alcoholism</td>
<td>Febrile jaundice and hepatic failure 200/100/0 0 400/200/0</td>
<td>833</td>
<td>5 mm aortic vegetation, mild aortic regurgitation and mitral regurgitation (TEE) 28 d</td>
<td>Doxycycline and hydroxychloroquine then doxycycline and fluoroquinolones</td>
<td>Yes (A0B0C3) 100/0/0 200/0/0 2 mo, cured</td>
<td>Yes, 25 d</td>
<td>No available data</td>
<td></td>
</tr>
<tr>
<td>7* (2012)</td>
<td>45/M/Portou-Charente</td>
<td>No particular medical history</td>
<td>Febrile hepatitis 100/100/0 200/200/0</td>
<td>742</td>
<td>10 mm aortic vegetation, grade II aortic regurgitation, mild left ventricular dilatation 68 mm (diastolic) (TEE) 7 d</td>
<td>Doxycycline and hydroxychloroquine, 12 mo</td>
<td>No 0/0/0 0/0/0 27 mo, cured</td>
<td>Yes, 6 mo</td>
<td>Yes, 5, 18 mo</td>
<td></td>
</tr>
<tr>
<td>8 (2013)</td>
<td>42/M/Portou-Charente</td>
<td>No particular medical history</td>
<td>Febrile hepatitis 25/200/0 1600 50/400/3200</td>
<td>126</td>
<td>Aortic vegetation, mild aortic regurgitation, mitral thickening (TEE and/or TEE*), 43 d</td>
<td>Doxycycline and hydroxychloroquine, ongoing</td>
<td>Yes (A0B2C2) 800/50/0 200/0/0 15 mo (under treatment)</td>
<td>Yes, 4 mo</td>
<td>No, 3, 11 mo</td>
<td></td>
</tr>
<tr>
<td>9 (2014)</td>
<td>46/M/Pays de la loire</td>
<td>Crohn disease treated by azathioprine</td>
<td>Febrile 200/100/0 200/200/0</td>
<td>168</td>
<td>8 mm aortic vegetation with aortic valve thickening (TEE), 31 d</td>
<td>Doxycycline and hydroxychloroquine, ongoing</td>
<td>Yes (A0B0C3) 800/50/50 800/50/50 6 mo (under treatment)</td>
<td>No, 50 GPLU at 62 d</td>
<td>No, 4, 2 mo</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: aCL, anticardiolipin antibodies; Dx, diagnosis; GPLU, immunoglobulin G-type phospholipid units; IgG, immunoglobulin G; PCR, polymerase chain reaction; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

* Serological titers as follows: phase I IgG, immunoglobulin M (IgM), immunoglobulin A (IgA), and phase II IgG, IgM, and IgA.

† Hydroxychloroquine was stopped by the patient due to photosensitivity. He later took doxycycline alone for a prolonged but unknown duration.

# Granulomatous hepatitis at histology.

% Index patient.

& TTE and TEE were performed at the same time with no precision on which exam led to diagnosis of vegetation. Vegetation of this patient is shown in Supplementary Video 1.
Table 2. Comparison of Patients With Acute Q Fever Endocarditis and Other Q Fever Patients Diagnosed Between January 2007 and April 2014 at the French National Referral Center for Q Fever (N = 986)

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Acute Q Fever Endocarditis (n = 9)</th>
<th>Acute Q Fever Without Vegetations (n = 750)</th>
<th>Acute Q Fever With VHD (n = 186)</th>
<th>Acute Q Fever Without VHD (n = 564)</th>
<th>Q Fever Chronic Endocarditis (n = 227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>7 (78%)</td>
<td>524 (70%)</td>
<td>130 (70%)</td>
<td>394 (70%)</td>
<td>162 (72%)</td>
</tr>
<tr>
<td>Age, y, mean ± SD</td>
<td>53 ± 11</td>
<td>50 ± 17</td>
<td>57 ± 18</td>
<td>47 ± 16</td>
<td>59 ± 16</td>
</tr>
<tr>
<td>VHD known before acute Q fever</td>
<td>0 (0%)</td>
<td>156 (21%)</td>
<td>156 (84%)****</td>
<td>0 (0%)</td>
<td>179 (80%)****</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>5 (56%)</td>
<td>86 (11%)**</td>
<td>31 (17%)**</td>
<td>55 (10%)**</td>
<td>32 (14%)*</td>
</tr>
<tr>
<td>Phase I IgG median [IQR]</td>
<td>200 (25–200)</td>
<td>400 (100–1600)</td>
<td>200 (50–800)</td>
<td>3200 (800–12 800)****</td>
<td></td>
</tr>
<tr>
<td>IgG aCL median [IQR]</td>
<td>126 (110–742) [66–1828] [range]</td>
<td>14 (4–88) [0–13 000] [8]</td>
<td>18 (4–99) [0–835]***</td>
<td>5 (0–17) [0–138]****</td>
<td></td>
</tr>
<tr>
<td>IgG aCL &gt;100 GPLU</td>
<td>8 (89%)</td>
<td>60 (18%)****</td>
<td>14 (16%)****</td>
<td>46 (19%)****</td>
<td>7 (8%)****</td>
</tr>
</tbody>
</table>

Abbreviations: aCL, anticardiolipin antibodies; GPLU, immunoglobulin G-type phospholipid units; IgG, immunoglobulin G; IQR, interquartile range; SD, standard deviation; VHD, valvular heart disease.

* A total of 334 patients without echocardiography results were excluded.

** One patient with exceptionally high IgG aCL levels (13 000 GPLU) was diagnosed after severe hepatitis. This individual presented with bilateral proximal pulmonary embolism and had a calcification and no vegetation at echocardiography. Sera with insufficient amount could not be tested for anticardiolipin antibodies.

* P < .05, ** P < .005, *** P < .0005, **** P < .00005 vs acute Q fever endocarditis patients.

Predictions of Acute Q Fever Endocarditis

Among the predictors tested in the rare events logistic regression model, which included age, sex, immunosuppression, phase I IgG antibodies, and very high IgG aCL levels (≥100 GPLU), only very high IgG aCL levels (RR 24.9 [95% CI 1.45–190.2]; P = .02) were independently associated with acute Q fever endocarditis (Table 3). Absence of history of VHD was not included in the model because, as all patients with acute Q fever endocarditis had such a characteristic, this variable was a perfect predictor.

Patient Outcomes

Median duration of follow-up was 16 months (range 3–36 months). One patient died of septic shock, 2 patients died of noncardiac causes, 1 patient died of suicide, and 2 patients died of unknown causes. Of the 9 patients with acute Q fever endocarditis, 8 had IgG aCL levels >100 GPLU vs 60 of 330 in other patients with acute Q fever (P < .00005). Among the predictors tested in the rare events logistic regression model, which included age, sex, immunosuppression, phase I IgG antibodies, and very high IgG aCL levels (>100 GPLU), only very high IgG aCL levels (RR 24.9 [95% CI 1.45–190.2]; P = .02) were independently associated with acute Q fever endocarditis (Table 3). Absence of history of VHD was not included in the model because, as all patients with acute Q fever endocarditis had such a characteristic, this variable was a perfect predictor.

ROC analysis found that the IgG aCL threshold value with the maximal sensitivity and specificity was 742 GPLU (95% CI 685–895; P < .0005). The IgG aCL threshold value was found to be 100 GPLU (100% sensitivity and 96% specificity; 95% CI 95–97; P < .00005). This IgG aCL level was highly indicative of acute Q fever endocarditis among patients with VHD (area under the ROC curve, 0.92 [95% CI 0.85–0.98; P < .0001]). The IgG aCL threshold value was also true when these individuals were compared to acute Q fever patients with VHD (area under the ROC curve, 0.92 [95% CI 0.85–0.98; P < .0005]) and compared to patients with chronic endocarditis (area under the ROC curve, 0.91 [95% CI 0.81–1.0; P < .0001]).
1–5 examinations for these individuals. For 2 patients, only the first echocardiogram found the vegetation (which was defined as a transient vegetation), whereas for the other 7 patients, at least 2 echocardiograms found vegetations that persisted for 12 days to 18 months. In 3 patients, the vegetation had not disappeared completely as of the last echocardiogram performed at 6, 7, and 11 months after initial diagnosis.

**DISCUSSION**

The co-occurrence of a vegetation on a cardiac valve and primary infection by *C. burnetii*, quoted here as acute Q fever endocarditis, is an emerging clinical entity appearing in several patients in different areas, at different times and identified by several echocardiographers. Association of vegetation and IgG aCL was previously reported in systemic lupus erythematosus and primary antiphospholipid syndrome [27]. We confirmed this association in Q fever patients without preexisting autoimmune disease. The pathogenic role of IgG aCL was further supported by the fact that none of the patients with acute Q fever endocarditis had a previous history of VHD [8]. Additionally, according to the Antiphospholipid Antibodies Task Force, IgG aCL should be not only considered diagnostic markers but also risk factors for clinical events [28].

Acute Q fever endocarditis differs radically from chronic Q fever endocarditis, which is characterized by a long-lasting disease prior to diagnosis [12] after unnoticed or undiagnosed primary infection [12], and is associated with age [20], history of VHD [8] (specifically bicuspid aortic valve and prosthetic valves [23]), and high serological phase I IgG levels [19]. As a result, almost all (8/9) patients with acute Q fever endocarditis did not fulfill the usual chronic Q fever endocarditis criteria [17, 18] at diagnosis of vegetation. Moreover, IgG aCL levels are usually negative in chronic Q fever endocarditis (Figure 2) [15].

As a putative pathophysiological scenario, primary infection with *C. burnetii* could cause explosive secretion of several autoantibodies [3, 4]. The pathogenic role of these autoantibodies is increasingly recognized, as recently found for autoimmune liver disease [3]. IgG aCL may be very frequent and highly elevated in this context [2, 4, 15]. These antibodies are known to have a particular tropism for endocardial endothelium, and their attachment to the heart valves may cause injury and noninfectious sterile vegetations [27]. In addition, the onset of autoimmune

![Figure 2](cid:2016:62 (1 March) Million et al)
valvular lesions could promote the binding of circulating infected monocytes/macrophages. Finally, persistence and replication of Coxiella burnetii in macrophages in the depth of the heart valves [14] defines chronic Q fever endocarditis with an insidious and silent evolution that can lead to the destruction of the valve within a period ranging from months to years [29].

The limitations of our work include the fact that all referring physicians were unblinded and may have been biased toward overcalling endocarditis. Conversely, the frequency of acute Q fever endocarditis (1% of acute Q fever patients) was probably underestimated because it was undiagnosed. Indeed, no cases were found in our series before 2009 when we identified the role of IgG aCL in VHD in Q fever [15]. As all acute Q fever endocarditis patients were French (ie, 97% of eligible patients), studies in other countries are needed. Notably, IgG aCL–associated thrombotic complications of Q fever have been reported in Spain and Australia [30, 31].

In conclusion, acute endocarditis caused by Q fever should be recognized as an early and potentially harmful autoimmune complication of Coxiella burnetii primary infection. Echocardiography is critical early in the disease to detect acute Q fever endocarditis, and not only underlying VHD. This is particularly true in patients with immunosuppression or with very high levels of IgG aCL (>100 GPLU), and vegetation in this context should never be neglected. Conversely, systematic C. burnetii testing should be evaluated in patients with antiphospholipid-associated cardiac valve disease [32] in endemic areas. Early diagnosis and treatment of acute Q fever endocarditis will prevent progression to chronic Q fever endocarditis [8, 20]. As hydroxychloroquine alone has a favorable effect on the pathogenic role and persistence of antiphospholipid antibodies [33, 34], prompt treatment would also be critical in the prevention of arterial emboli, previously associated with antiphospholipid antibodies in bacterial endocarditis of other causes [35] and in patients with acute Q fever [30, 31, 36].

Supplementary Data
Supplementary materials are available at (http://cid.oxfordjournals.org). Consisting of data provided by the author to benefit the reader, the posted materials are not copy edited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes
Acknowledgments. We thank Jean-François Avierinos and Erwan Saulaun for kindly reading the full video loop of patient 5 and of 1 patient with acute Q fever without vegetation, blinded to the purpose of the study. We thank the entire Q fever team (Carole Eldin, Clea Melenotte, Anastasia Papadioti, Jad Kerbaj, Cecile Nabet, Morgane Mailhe) for excellent editing and proofreading. We thank the entire Q fever team (Carole Eldin, Clea Melenotte, Anastasia Papadioti, Jad Kerbaj, Cecile Nabet, Morgane Mailhe) for kind reading the full video loop of patient 5 and of 1 patient with acute Q fever without vegetation, blinded to the purpose of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Financial support. This was work was supported by the French National Referral Center for Q fever.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Acute Q Fever Endocarditis • CID 2016:62 (1 March) • 543