Pulmonary Valve Prosthesis Endocarditis Caused By *Coxiella burnetii*

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Abstract

Background *Coxiella burnetii* is a gram-negative bacterium assigned to the family of *Rickettsiaceae*. Less than 1% of Q-fever infection leads to infective endocarditis (IE). Cases of reported pulmonary valve (PV) prosthesis endocarditis are scarce.

Case Description A patient with a PV prosthesis endocarditis caused by *Coxiella burnetii* was seeking asylum in Germany. Prosthesis replacement was performed. All obtained blood cultures showed no growth as well as microbiological cultures of the prosthetic valve tissue. A polymerase chain reaction analysis on the explanted prosthesis detected DNA of *Coxiella* spp.

Conclusion Diagnosing IE caused by *Coxiella burnetii* requires an interdisciplinary effort from both clinicians and microbiologists.

Keywords
- endocarditis
- pulmonary valve
- infection

Introduction

Coxiella burnetii is a polymorphous, gram-negative bacterium assigned to the family of *Rickettsiaceae*. Human pathogenic infection, so-called Q-fever, is caused by the inhalation of contaminated dust, direct contact to infected animals, or during the processing of contaminated samples. Sporadic outbreaks of acute Q-fever occur regularly in rural areas with high prevalence of farming, but larger outbreaks affecting wider areas have been reported.[1] Estimation of Q-fever infectivity is high, and doses of 10 organisms may cause illness. However, only a small fraction (~1%) of all acute Q-fever infections leads to chronic infection, with infective endocarditis (IE) being the most important long-term sequel.[2] Fifty percent of patients with IE need surgical intervention in combination with antibiotic treatment. Cases of reported pulmonary valve (PV) prosthesis endocarditis are rare, with only 0.5 to 2% of described IE cases involving the native PV. However, prosthesis endocarditis can be diagnosed in 20% of all IE patients.[3]

Case Report

In August 2016, a 33-year-old male presented with a temperature of 40°C, hepatosplenomegaly, scleral icterus, mild pruritus, fatigue, and diarrhea. In 2014, the patient had undergone biological PV replacement (Medtronic Freestyle) in Albania. The underlying disease for primary PV replacement was not identified. Cannabis and cocaine consumption until 2014 was reported. Past medical history revealed bilateral pulmonary embolisms in 2014 with a background of antithrombin III deficiency and inadequate oral anticoagulation. Upon admission, the patient was taking rivaroxaban. There was no sign of any neurologic deficit; heart and lung auscultation were normal. The liver and spleen were distinctly palpable. He was seeking asylum in Germany and living in a refugee hostel.

Our findings included a C-reactive protein level of 85.4 mg/L, leucocyte count of 5.68/nL, bilirubin level of 2.20 mg/dL, creatinine level of 0.99 mg/dL, and an international normalized ratio of 1.26. Transesophageal echocardiography (TEE) showed

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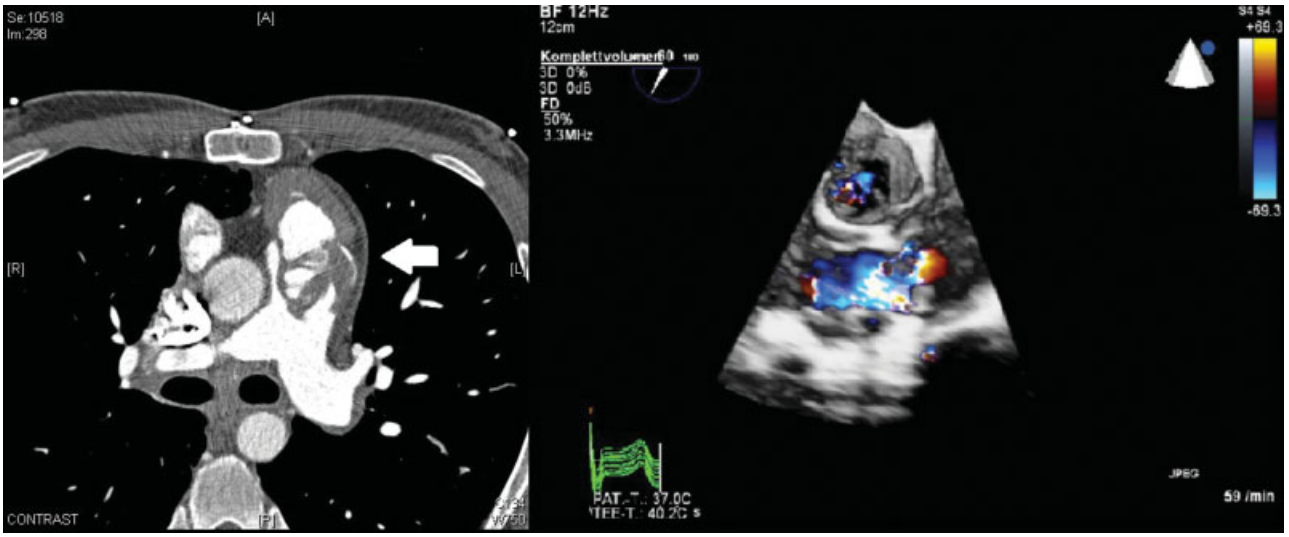

Fig. 1 Left: thrombotic vegetation of pulmonary valve (PV) prosthesis in preoperative CT scan (marked by *arrow*). Right: intraoperative transesophageal echocardiography illustrating the PV prosthesis stenosis and moderate regurgitation due to intracardiac vegetation.

major PV stenosis and moderate PV regurgitation with prolapse of one valve leaflet (►**Fig. 1**). The peak pressure gradient and the mean pressure gradient were measured at 50 and 25 mm Hg, respectively. Paravalvular leakage with avulsion was identified, and undulating vegetations were detected on the prosthetic leaflets. The remaining three organic valves showed no signs of IE. However, second-degree tricuspid regurgitation with annulus dilatation was seen with signs of right ventricular hypertrophy and reduced pump function. Tricuspid annular plane systolic excursion was 1.3 cm. Left ventricular function was satisfactory with an ejection fraction of 68.9%. Computed tomography (CT) scan revealed multiple peripheral pulmonary embolisms, signs of portal hypertension, and hepatosplenomegaly. Taking into consideration one major criterion (positive TEE with an intracardiac mass) and three minor criteria (pulmonary embolism, predisposing heart condition, and fever) of the modified Duke criteria for IE, the empirical antibiotic regimen was switched from ampicillin/sulbactam to ampicillin, vancomycin, and gentamicin.[4] Dental examination showed a chronic apical periodontitis of molar 36 after endodontic treatment 3 months prior to admission. The molar was then extracted.

Operative Technique

After resternotomy, we performed cardiopulmonary bypass through the ascending aorta and cannulation of the venae cavae. The core temperature was cooled to 34°C. The surgery was performed on a beating heart.

The right outflow tract was opened above the implanted freestyle PV prosthesis. The prosthesis was completely destroyed by thrombotic and inflammatory tissue, obstructing the valve. After removal of the infected prosthesis, a new 27-mm PV prosthesis (Carpentier-Edwards Perimount Magna Ease) was implanted. The right outflow tract was reconstructed with a Hemashield graft patch (Maquet).

Intraoperative TEE showed no signs of endocarditis of the tricuspid valve. After replacement of the PV prosthesis, only minimal first-degree tricuspid regurgitation remained.

Microbiological Results

All six preoperatively obtained pairs of peripheral blood cultures showed no growth after a standard incubation period of 5 days in the BD BACTEC FX (Becton Dickinson, Franklin Lakes, New Jersey, United States) at 36°C. Urine cultures were negative, and all analyzed stool samples revealed no enteropathogenic microorganisms or parasites. A hepatotropic viral infection could also be ruled out. Standard microbiological cultures of the heart valve tissue on BD Columbia Agar with 5% Sheep Blood (Becton Dickinson, Sparks, Maryland, United States), bioMérieux PVX Chocolate Agar (bioMérieux, Genève, Switzerland), and BD Schaedler KV agar with 5% Sheep Blood (Becton Dickinson) showed no growth. As a result, we performed a 16s in-house polymerase chain reaction (PCR) analysis on the tissue of the PV prosthesis. DNA of *Coxiella spp.* was detected and identified as *Coxiella burnetii* in the subsequent sequencing. Q-fever IgM titers for phase II were 1:256, whereas those for phase I were 1:512. Titers for both phase I and II immunoglobulin G were >1:64.000.

Postoperative Course

Postoperative recovery went without further complications, and antibiotic treatment was adjusted to doxycycline and ciprofloxacin as recommended in the European Society of Cardiology guideline on the management of IE.[4] The patient was discharged to the local refugee hostel after 2 weeks. Antibiotic treatment with doxycycline 100 mg twice daily and ciprofloxacin 500 mg three times a day was recommended for a total of 6 months. Unfortunately, no further follow-up was possible after discharge. It was impossible to ascertain if the patient had received the prescribed 6 months of antibiotic therapy.

Discussion

Patients who are immunocompromised, pregnant, and/or have undergone prosthetic cardiac valve replacement are

most prone to developing a chronic cardiac *Coxiella burnetii* infection. Fournier et al identified *Coxiella burnetii* in 37% of blood culture negative endocarditis (BCNE) cases in their study. They confirmed that analyzing cell cultures and PCR results from valvular biopsies were significantly more sensitive than blood cultures or PCR analysis of blood samples. Comparing diagnostic tests, immunofluorescence assays were the most efficient followed by PCR. However, even with comprehensive diagnostic strategies in 37% of 740 cases of BCNE, they could not identify any pathogenic microorganism.[5]

Typical risk factors for PV endocarditis are male gender, intravenous drug abuse, central venous catheter infection, alcohol consumption, and congenital heart disease.[3] After initial treatment, patients should be monitored for 5 years for potential relapse. Unfortunately, we have no follow-up information of our patient; we have been unable to contact the patient after returning to the refugee hostel.

The increased influx of refugees to member countries of the European Union, especially toward the end of 2015 and the beginning of 2016, has led to a rising number of complicated infectious disease cases in Germany. These are due to (1) rarely reported infectious disease pathogens and (2) cases where patients were diagnosed at a later, chronic stage of the infectious disease.[6] Many refugees come from rural areas, implicating a higher risk of zoonotic infections such as Q-fever. Of most identified pathogenic agents in BCNE, zoonotic bacteria are the most frequent. *Coxiella brunetii* is one of the main identified etiological agents followed by *Bartonella* species.[5]

The need to take a precise patient history to establish a correct diagnosis is hampered by language barriers and a lack of translators in the destination countries. In summary, these difficulties increase the risk of misdiagnosing and inadequate treatment of refugees with a chronic infectious disease such as Q-fever.

Conclusion

Diagnosing IE caused by *Coxiella burnetii* requires an interdisciplinary effort from both clinicians and microbiologists: on one side, diligent history taking is necessary including possible zoonotic exposition and, on the other side, molecular amplifying techniques and blood-based antibody analysis are necessary to detect *Coxiella burnetii*, as the pathogen does not typically grow in blood cultures.[5]

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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