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Case report

Endocarditis caused by *Bartonella Quintana*, a rare case in the United States

Mahsa Mohammadian[a], Saira Butt[b,*]

[a] Shiraz University of Medical Sciences, Shiraz, Iran
[b] Division of Infectious Diseases, Indiana University School of Medicine, Indianapolis, IN, USA

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ABSTRACT

Bartonella quintana is a relatively rare cause of endocarditis in the United States (USA). Historically it was linked with trench fever, but cardiac involvement seems to be more prevalent recently. There are some known risk factors associated with *Bartonella quintana* endocarditis such as human immunodeficiency virus (HIV) infection, alcoholism, homelessness and poor hygiene. We report a case of 37-year-old African man, with culture negative endocarditis, emboli and rising *B. quintana* and *B. henselae* IgG titers. *B. quintana* DNA was subsequently detected from the mitral valve sample with 16S rRNA gene and ribC primer sets. Eventually, blood culture for *B. quintana* was positive after 21 days. Patient was successfully treated with doxycycline and gentamicin. There have been a few cases of *B. quintana* endocarditis in the USA and most of them were associated with HIV infection, homelessness or alcoholism. The case reported here highlights the importance of high clinical suspicious for *Bartonella species* in blood culture negative endocarditis in the USA in appropriate setting and will help to increase awareness among physicians for early diagnosis and treatment.

Introduction

Bartonella quintana is a small, fastidious, gram-negative rod that has facultative intraerythrocytic lifestyle. After transmission by the human body louse, bacterial entry across the skin occurs and adherence to and infection of erythrocytes and endothelial cells ensue. It may result in bacteremia that can persist for prolonged periods, even for years. It accounts for 75% of endocarditis caused by *Bartonella species* [1]. Besides human body louse which is the main vector, *B. quintana* has been found in cat fleas, monkey fleas and cat dental pulp, suggesting potential methods of transmission [2]. Blood transfusion was discussed as another potential route of infection due to undetected organism in erythrocytes and in one study it was reported in 3.2% of asymptomatic blood donors from Brazil [3].

More than a million soldiers were infected with *B. quintana* during World War I. The disease was known as ''trench fever''. Some cardiac involvement was also reported at that time. Since 1990s, urban trench fever was detected mostly among patients with HIV infection or those who were homeless or had history of chronic alcoholism. The first case of endocarditis caused by *B. quintana* was reported in 1993 [2]. Most patients have nonspecific symptoms such as fever, fatigue and weight loss. In a case series comprising 348 blood culture negative endocarditis cases from France, *Bartonella species* accounted for 28% of the cases. Almost all the patients had fever as a presenting symptom, whereas about 50 to 70% had symptoms of heart failure such as exertional dyspnea and about 50% had insidious weight loss. Physical examination findings typically included cardiac murmur, and the aortic valve either in isolation or with another valve was the most frequently affected valve, including in the pediatric age group. Splenomegaly was present in 42% of the patients [4].

In this case report, we present a male with absence of previously mentioned risk factors or exposures besides his immigration from an African country, who developed *B. quintana* endocarditis, which is exceedingly rare in the United States. Our purpose of this report is to increase clinical suspicion for *Bartonella species* in blood culture negative endocarditis in the USA.

Case report

A 37-year-old African man was transferred to our hospital from an outside facility with an aortic valve vegetation, multiple embolic strokes and possible brain mycotic aneurysm, with concern for fungal endocarditis. He was initially admitted to an

* Corresponding author at: Indiana University School of Medicine, 550 N University Blvd, Indianapolis, IN, 46202-5114, USA.
E-mail address: sairbutt@iu.edu (S. Butt).

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outside hospital with chief complaints of progressive shortness of breath and chest pain for 2 weeks with occasional non-drenching night sweats, fatigue, unintentional ten pounds weight loss in the last 6 months and intermittent sharp chest pain radiating to the neck. His past medical history was significant for latent tuberculosis infection and treatment with 9 months of isoniazid was completed 3 months prior to the presentation. The patient's immunization was up to date and he denied tobacco or alcohol consumption, any recent travel, any prior history of sexually transmitted infections, past or recent history of lice infestation, injection drug abuse, incarceration and homelessness as well. Originally from Democratic Republic of Congo and migrated to Indiana, USA a year prior to the presentation, the patient was married and lived with his wife and 3 children. He worked as school teacher in Congo but at the time was working at a donut shop. In Congo, he had a cow at his home and used to drink raw cow's milk. The patient was not taking any medications. On admission, physical examination demonstrated normal vital signs, cachexia, a 4/6 systolic murmur at the apex with radiation to the axilla, palpable thrill, diastolic 3/6 murmur at the apex, Janeway lesions on bilateral feet and soles and L4-L5 lumbar vertebral tenderness to palpation.

Initial laboratory investigations demonstrated WBC count of 5×10^9 cells per liter (with normal differentiation), hemoglobin of 8.9 g/dL, hematocrit of 27%, and 3 sets of negative blood cultures. Transesophageal echocardiogram (TEE) revealed trileaflet aortic valve with a mobile vegetation, severe aortic and mitral regurgitation, mitral valve stenosis and thickening. CT scan of the chest and abdomen showed bilateral pleural effusions, right lung apex nodular opacities, emphysematous changes, no cavitary lesion, cardiomegaly with prominently dilated left atrium, hepatosplenomegaly with periportal lymphadenopathy, and wedge-shaped hypodense lesions within the peripheral spleen. Left pleural fluid tap was cloudy and analysis showed WBC count 1086 cells/micro L (40% lymphocytes, 11% PMN, 27% monocytes, 22% mesothelial cells), negative acid-fast bacteria stain, pH 7.48, protein 1.7 g/dL, glucose 125 mg/dL, LDH 75 units/L and negative culture. Later during the hospital course, patient complained of headache and brain MRI was done. Findings were small acute infarct in the left posterior cerebellar hemisphere with some parenchymal enhancement concerning for an infectious etiology. Also, a probable subacute infarct in the right posterior corona radiata was reported and the vessels adjacent to the posterior sylvian fissure were suspicious for a possible mycotic aneurysm.

Upon admission to our facility, we initiated empiric antimicrobial therapy for presumptive diagnosis of culture negative endocarditis. He was placed empirically on intravenous (IV) ceftriaxone 2 g daily, oral (PO) doxycycline 100 mg daily, PO rifampin 600 mg daily and IV gentamicin 5 mg/kg daily to cover fastidious organisms, *Coxiella, Rickettsia, Mycoplasma, Brucella and Bartonella*. *Bartonella species* was part of our differential diagnosis as the patient was originally from Democratic Republic of Congo. *Bartonella* species (mostly *henselae* and *quintana*) are among the most common causes of blood culture negative endocarditis in Africa, being responsible for 9.5%–28.4% of all cases [5]. Pertinent laboratory results were as follows: negative mycobacterial and fungal blood cultures, negative *Brucella* and *Coxiella* serologies, negative HIV antibody, Rheumatoid factor 83 U/mL, Anti smooth antibody 1:640, negative coombs test, *Rickettsia typhi* IgM not detected and IgG >1:256, *B. henselae* IgM and IgG were indeterminate at first and the repeat sample in a week demonstrated *B. henselae* IgG $\geq$ 1:1024 by immunofluorescnece (IFA), *B. henselae* IgM < 1:20, *B. quintana* IgG $\geq$1:1024), *B. quintana* IgM <1:20. Based on these positive serologies, ceftriaxone and

Table 1
Literature review of endocarditis cases caused by bartonella quintana globally (excluding United States).

Author	Context/setting	HIV status	Findings	Risk Factors
Drancourt et al. [9]	In France: 3 men with infective endocarditis (IE) were investigated for *bartonella* spp. infection by using serology & molecular studies.	Negative in all 3 patients (pts).	Positive blood culture (BC) in one pt, positive serologies in all 3 pts, positive molecular studies on valvular vegetations and lymph nodes biopsy in all 3 pts for *B. quintana.*	All were alcoholic and homeless.
Raoult et al. [10]	22 pts with BC negative IE from France, England, Canada, and South Africa, were investigated.	N/A	5 pts were infected with *B. quintana*, 4 pts with *B. henselae,* & 13 pts with an undetermined *bartonella species.*	9 pts were homeless, 11 pts were alcoholic, 4 pts owned cats & 13 pts had preexisting valvular heart disease.
Benslimani et al. [11]	108 pts with suspicion of IE were investigated in Algeria. 62 cases had BC negative IE. Samples were tested by serologic or molecular methods or both.	N/A	Among 18 cases of zoonotic and arthropod borne bacteria, 14 cases were infected by *B. quintana,* 2 cases by *Brucella melitensis*, 2 cases by *Coxiella burnetii*	34 pts were from rural areas, 61 pts lived in urban areas, 1 pt was in prison, and no information could be obtained for 12 pts. 61.5% had poor socioeconomic level.
Fournier et al. [12]	48 cases, mostly African-European, with chronic BC negative, were investigated. Almost all had fever & vegetation on echocardiograph. All were established to be infected by *bartonella species* through culture or PCR.	No association between HIV and *bartonella* infection was found.	38 pts (79%) were infected by *B. quintana* & another 10 pts (21%) by *B. henselae*. Pts who received an aminoglycoside for more than 14 days were more likely to fully recover and survive.	Pts with *B. quintana* IE were mostly male (84.2%), with less likely to have previous valvular disease but more likely to be homeless, alcoholic and have body lice.
Saison et al. [13]	Case report of a 40-year-old woman in France with subacute IE, who had good socioeconomic condition. She had a history of arthralgia and palpitation for a few months, with large aortic vegetation, regurgitation and valve abscess. Splenic and renal infarction were detected later.	Negative	IgG titers for *B. quintana* and *B. henselae* were elevated & PCR on excised valve tissue confirmed *B. quintana* as the cause. Doxycycline and gentamicin were effective.	No body lice, no poor sanitary condition, no chronic alcoholic intoxication was found.
Tasher et al. [5]	5 pts between 7–16 years old, from Ethiopia with heart defects and IE were investigated. All were afebrile with minimal symptoms, 3 had heart failure.	Negative in all 5 pts.	All had vegetation on echocardiogram, high *Bartonella* IgG titers. *B. quintana* DNA was detected in excised vegetations in 4 pts. 2 pts had embolic events.	Poor & crowded living conditions were present in all pts.
Boudebouch et al. [14]	A recent survey on 19 pts in Morocco, with BC negative IE was done. Serologic and/or molecular methods were used.	N/A	4 pts were infected by zoonotic agents including *B. quintana*, *Staphylococcus aureus*, *Streptococcus equi*, and *Streptococcus oralis*. 70.6% of pts had vegetation, 35.9% had valvular abscess.	17.6% of pts had alcohol dependence, 5.9 % had drug abuse history. 36.8% of pts lived in poverty with poor hygiene, including the pt who had *B. quintana* endocarditis.

rifampin were discontinued. Patient underwent aortic valve and mitral valve replacements. Subsequently, *B. quintana* DNA was detected from mitral valve by PCR amplification targeting the riboflavin synthase gene (ribC) and 16S rRNA gene. Cultures on chocolate agar turned positive for *B. quintana* after 21 days and *B. quintana* endocarditis diagnosis was confirmed. Post valve replacements, doxycycline was continued for total of six weeks and gentamicin was given for the first two weeks.

Discussion

We report *B. quintana* endocarditis in an African HIV negative male in absence of alcoholism and homelessness, which are the major risk factors for endocarditis with this organism. Endocarditis caused by *Bartonella species* is likely underestimated in the USA. It should be part of the differential diagnosis in patients with negative blood cultures especially with African-European origin. In Table 1, we present a literature review of endocarditis cases caused by *B. quintana* globally (excluding the USA).

In USA, trench fever or other complications of infection by *B. quintana* have been reported especially in population with known risk factors. Yet, endocarditis caused by the same organism is extremely rare especially in a patient with no HIV infection. In 1993, the first case of endocarditis was reported in Seattle by Spach et al. Patient was a 50-year-old man with HIV infection, who developed endocarditis and DNA studies revealed *B. quintana* as a new pathogen [6]. The second reported case was a man with newly diagnosed AIDS, who presented with months of back pain and fever. CT scan demonstrated aortitis with periaortic tissue thickening. DNA amplification of biopsy tissue revealed *B. quintana*, and serologies were noted to be positive [7]. The first report of *B. quintana* endocarditis in HIV negative patient in the USA was in 2016 in Washington D.C. In this study done by Ghidey et al. three patients had the diagnosis over a period of 1 year, who were all homeless with history of alcoholism, and negative for HIV infection. Positive IgG and negative IgM titers were detected in all and final diagnosis was made based on PCR on DNA extracted from excised valves [8].

In conclusion, we present a rare case of *B. quintana* endocarditis in an immunocompetent patient in the USA. We suggest checking serial immunofluorescence serologic assays as standard screening test which should be confirmed by PCR on valve specimen. We also advice to keep blood cultures in the laboratory for at least 21 days. Treatment with gentamicin and doxycycline is found to be effective alongside valve replacement surgery.

Conflict of interest

The authors declare no potential conflicts of interest.

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Consent

Consent was obtained from the patient.

Authors' contribution

Mahsa Mohammadian: Writing the original draft, literature review and editing.

Saira Butt: Reviewing and editing the article and the physician in charge of the patient care at the hospital.

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