

Case Report: *Bartonella quintana* Endocarditis Outside of the Europe–African Gradient: Comprehensive Review of Cases within North America

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Abstract. Clinical syndromes associated with *Bartonella quintana* infection can be insidious and difficult to diagnose for multiple reasons. Clinically, *B. quintana* can manifest as asymptomatic bacteremia or with subtle subacute constitutional symptoms. Second, it is a fastidious organism that is difficult to identify using traditional culture methods. Last, the body louse vector of *B. quintana* transmission is likely not uncommon in most patients affected, who are homeless and of low socioeconomic status. Therefore, barriers in seeking medical care and financial constraints for medications are important considerations. The mainstay of literature surrounding *B. quintana* endocarditis is from Europe and the developing nations. Herein, we describe a case of native valve endocarditis secondary to *B. quintana* in a homeless male with preexisting valvular disease and undertake a comprehensive literature review of documented *B. quintana* endocarditis in North America.

CASE PRESENTATION

A 49-year-old immunocompetent male with longstanding schizophrenia, homelessness, and alcohol abuse was hospitalized for nonspecific fatigue and found to be febrile, tachycardic, and tachypneic with radiographic right lung consolidation suspicious for pneumonia. He was treated with 7 days of levofloxacin with resolution of his symptoms. His past medical history was significant for emphysema, paroxysmal atrial fibrillation, and mitral valve prolapse with asymptomatic severe mitral regurgitation. A transthoracic echocardiogram (TTE) performed during this hospitalization confirmed prolapse of thickened mitral leaflets with severe mitral regurgitation of unknown etiology. He was discharged as he did not have indications for valvular surgery. As he was homeless and did not regularly seek medical care, the duration of his mitral valve prolapse was unknown.

Three months later, he was readmitted to hospital with fever and hypoxic respiratory failure. Pneumonia was suspected based on repeat chest radiograph, and treatment ensued with a 4-day course of piperacillin/tazobactam and vancomycin followed by a 6-day course of amoxicillin/clavulanic acid with clinical improvement. A microbiological diagnosis was elusive.

Two months following his second hospitalization, he decompensated again with respiratory failure requiring mechanical ventilation. His respiratory status was thought to be secondary to congestive heart failure exacerbated by alcohol withdrawal superimposed on preexisting mitral regurgitation. Repeat TTE did not demonstrate progression of valve leaflet thickening nor worsening regurgitation. Medical therapy was augmented successfully to keep him free from congestive heart failure symptomatology post-extubation. During his convalescence, the patient developed acute left upper visual field deficit corresponding with a small left superior cerebellar hemispheric infarct. Previous small infarcts in the left parietal and temporal lobe were also noted. Given the concern of embolization, he underwent urgent mitral valve replacement.

Intraoperatively, multiple friable calcified lesions were noted throughout the anterior leaflet along with multiple ruptured cords. The etiology of his endocarditis was not thought to be infectious given his abacteremia; therefore, the infectious disease service was not involved and the patient discharged from hospital without antimicrobials.

His discharge was short lived as was readmitted to hospital 3 weeks postoperatively with fevers and fatigue. By this time, a unique strain of *Bartonella quintana* was identified based on polymerase chain reaction and sequencing a segment of the *ribC* gene on the native mitral valve using a previously described protocol.¹ Multi-locus sequence typing was performed to determine the *B. quintana* sequence type (ST) as previously described by Arvand et al.² who used a collection of 16 isolates spanning 70 years and three continents. Of the nine loci used for ST designation, only five were reported as variable, and therefore sequenced for the characterization of the Calgary strain (18-36-16718_Calgary2018). The loci and respective number of alleles are shown in Table 1. The GenBank accession numbers for these sequences are as follows: MH909241 (*atpF*), MH909242 (*ftsZ*), MH909243 (*groEL*), MH909244 (*nlpD*), MH909246 (*rpoB*), and MH909245 (*ribC*). This strain yielded a unique ST when compared with the STs of the other human strains described previously.

Serologically, he was found to have an immunofluorescent assay IgG titer of 1:4,096 to *B. quintana*. After assessment by the infectious diseases service, a 6-week course of ceftriaxone 2 g daily and doxycycline 100 mg twice daily in conjunction with a 2-week synergistic course of gentamicin 3 mg/kg/day was initiated. On completion of intravenous ceftriaxone, the patient completed an additional 6 months of doxycycline therapy and has sustained cure during community follow-up assessments.

A literature search was completed using MEDLINE publications from 1946 to the present and the PubMed database using the keywords “*Bartonella quintana*” and “endocarditis.” All published cases of *B. quintana* endocarditis from North America were included whereas redundant cases were excluded.³ To our knowledge, this is the 13th case of *B. quintana* endocarditis in North America, fourth in Canada, and the first in Western Canada.^{4,5}

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TABLE 1

Comparison of allelic profiles and STs between the Alberta strain and previously published human isolates of *Bartonella quintana* (adapted from Arvand et al.)²

Strains	Geographic origin	<i>atpF</i>	<i>ftsZ</i>	<i>groEL</i>	<i>nlpD</i>	<i>rpoB</i>	ST
SH-Perm	Russia	1	1	1	1	1	1
Oklahoma	Oklahoma City, OK	1	1	1	1	1	1
Jouhanneau	Paris, France	1	1	1	1	1	1
UR.BQ.MBA 263	Marseille, France	1	1	1	1	1	1
UR.BQ.MNHP 295	Marseille, France	1	1	1	1	1	1
JK-31	CA	1	1	1	1	2	2
HROEH (DNA)	Rostock, Germany	1	1	1	1	2	2
UR.BQ.TIE 326	Toulouse, France	1	1	1	1	2	2
UR.BQ.MTF 357	Marseille, France	1	1	1	1	2	2
Toulouse	Toulouse, France	1	1	1	2	2	3
Munich	Munich, Germany	1	1	2	1	2	4
Fuller	Yugoslavia	1	1	2	2	3	5
UR.BQ.MTF 335	Marseille, France	1	2	3	1	2	6
Adelaide 1300/002	Adelaide, Australia	2	2	3	1	2	7
18-36-16718_Calgary2018	Calgary, Canada	1	2	1	1	2	Not assigned

ST = sequence type.

DISCUSSION

Bartonella quintana is a gram-negative rod-shaped facultative bacterium associated with multiple syndromes. However, because it can present as an asymptomatic chronic infection, it has been implicated in multiple outbreaks and represents the most common vector-borne infection in the homeless population.⁶ Transmission of the pathogen is by contamination of skin abrasions with the feces of an infected body louse (*Pediculus humanus corporis*).^{7,8}

Syndromes. Historically, *B. quintana* was associated with trench fever, a relapsing 5-day fever characterized by severe headache, orbital pain, and myalgias. Named in reference to the soldiers of World War 1, trench fever was estimated to be responsible for up to one third of all illnesses in the British Army during the Great War.⁹⁻¹¹

Bacillary angiomatosis was recognized as a manifestation of *Bartonella* infection in the immunocompromised host during the early 1990's.^{12,13} Abnormal vascular invasion by *Bartonella* leads to solitary or multiple papulonodular lesions. Although bacillary angiomatosis can affect visceral organs and lymph nodes, *B. quintana* has a greater tropism for cutaneous and bone involvement compared with other species of *Bartonella*.¹⁴

Asymptomatic chronic *B. quintana* bacteremia upward of 18 months have been reported in the homeless population.¹⁵⁻¹⁷ Evasion of host immunity by *B. quintana* and chronicity of bacteremia likely increases the development of infective endocarditis.

Bartonella quintana, the most common cause of infective endocarditis within the *Bartonella* species, is a recognized cause of blood culture-negative endocarditis (BCNE), defined as endocarditis in which a microbiological etiology remains unidentified despite three different blood samples and incubation in a blood culture system for at least 5 days. However, geographic variability of incidence rates in BCNE between 12% and 60% likely reflects differences in diagnostic algorithms and isolation procedures within various microbiology laboratories.^{18,19} Although most of the literature regarding *B. quintana* endocarditis are concentrated in Europe and Africa, a re-emergence in North America over the last 5 years has been noted²⁰ (Table 2). Endocarditis from *B. quintana* typically manifests with subacute constitutional

symptoms and can occur in individuals without known valvular disease.²¹

Diagnosis. Given the fastidious nature of *Bartonella*, the traditional methodology of isolating by culturing blood and tissue has an unsurprising sensitivity rate of less than 30%.²¹ Although histopathology and silver staining can be helpful, these techniques are nonspecific for *Bartonella* disease.²² Consequently, serology testing and more recently, molecular tools are mainstays used to confirm a clinical suspicion of *Bartonella* infection. Although indirect immunofluorescence is specific to *Bartonella*, it is not species specific. Thus, the role of 16s rRNA gene sequencing has been instrumental in identifying new syndromes associated with *B. quintana* infections. Sensitivity and specificity of a microbiological diagnosis in BCNE has increased greatly with molecular testing on resected valvular tissue.²³

Echocardiographic features of *B. quintana* endocarditis are variable, but appear to have tropism for affecting left-sided heart valves. Unlike other species of *Bartonella*, *B. quintana* can affect those without known valvular disease and often requires valvular surgery for cure, as outlined in Table 2.

Treatment. Treatment for *Bartonella*-associated infections are based on in vitro antibiotic susceptibility studies and observational data rather than robust systematic reviews. Localized *B. quintana* infections can be treated with a 3-6-month course of erythromycin or doxycycline.²⁴⁻²⁶ For systemic *B. quintana* infections, including trench fever, bacteremia, and endocarditis, consensus recommendations suggest that a 2-week 3-mg/kg/day aminoglycoside course with a 4-6-week course of doxycycline 200 mg/day is necessary.^{17,27,28} Ceftriaxone is also usually used in concert with doxycycline for at least 6 weeks in endocarditis.²⁹ Valvular surgery is almost always required in the cases of *B. quintana* endocarditis.³⁰

Prevention of *B. quintana* involves attention to personal hygiene with regular bathing and washing of clothes in water at temperatures higher than 50°C.³¹ Thus, in patients experiencing homelessness, providing laundry and bathing facilities along with insecticide application to shared bedding units within homeless shelters are important. Examination of clothing and collection of serologic tests for louse-borne diseases in homeless shelters have been successfully implemented to prevent spread.³²

TABLE 2
Literature review of documented *Bartonella quintana* infective endocarditis within North America

Reference	Age/ gender	HIV status	Location	Risk factors	Clinical presentation	Valves involved	Previous valvular disease	Antibiotic therapy	Surgery	Outcome
Spach et al. ³³	50M	+	Seattle	U	Constitutional symptoms with embolic phenomenon	Aortic, mitral	No	Ceftriaxone x 28 days, DOX x 7 days, ERY x 270 days	No	Cure
Spach et al. ³⁴	39M	-	Seattle	Homeless, alcohol abuse	Constitutional symptoms and exertional dyspnea	Aortic	No	Preop: Nafcillin/GENT x 2 days AMP/GEN x 9 days, AMP x 10 days Post op: VAN x 10 days, ERY x 42 days, Azithromycin x 90 days	Yes	Cure
Raoult et al. ⁴ Case records of Massachusetts General Hospital ³⁵	81F 38M	- -	Halifax Boston	U Homeless	U Swelling of fingers and toes	Aortic Aortic, mitral	Yes No	DOX AMP/GENT x 42 days, ERY IV x 42 days, ERY PO x 60 days	No No†	Death Cure
Patel et al. ³⁶	31M	+	Rochester	Incarceration	Right common femoral artery embolus	Aortic	Yes	VAN/GEN x 10 days, DOX x 90 days	Yes	Cure
Rahimian et al. ³⁷	51M	-	New York	Previous alcohol abuse	Exertional dyspnea and weight loss	Aortic	No	U	Yes	U
Raybould et al. ³⁸	55M	-	Washington	Homeless, alcohol abuse, self-reported louse infection months before presentation	Exertional dyspnea, peripheral edema, weight loss	Aortic, mitral	No	RIF/DOX x 180 days	Not	Cure
Keynan et al. ⁵	63F	U	Subarctic Manitoba	Alcohol abuse, animal skinning	Decompensated congestive heart failure	Aortic, mitral	No	U	Yes	U
Ghidey et al. ³⁹	52M	U	Washington	Homeless, alcohol abuse	U	Aortic, mitral	U	RIF or GENT/DOX x 14 days, DOX 28 days	Yes	U
Ghidey et al. ³⁹	55M	U	Washington	Homeless, alcohol abuse	U	Aortic, mitral	U	RIF or GENT/DOX x 14 days, DOX 28 days	Yes	U
Ghidey et al. ³⁹	57M	U	Washington	Homeless, alcohol abuse	U	Aortic	U	RIF or GENT/DOX x 14 days, DOX 28 days	Yes	U
Babiker et al. ⁴⁰	48M	-	Rural Pennsylvania	Previous incarceration, bioprosthetic aortic valve	Exertional dyspnea, constitutional symptoms	Aortic	Yes	DOX/RIF x unknown period	No	Cure

U = unknown; AMP = ampicillin; DOX = doxycycline; ERY = erythromycin; GENT = gentamicin; RIF = rifampin; VAN = vancomycin.

* Patient left against medical advice and was selective about tests.

† Patient recommended to have surgery but refused.

Our case highlights important considerations in *B. quintana* endocarditis. *Bartonella quintana* endocarditis ought to be considered in homeless individuals with valvular disease and multiple hospitalizations for heart failure symptomatology. It is conceivable that our patient had chronic bacteremia with transient improvement and sterilization of blood cultures owing to short courses of antibiotics. Serology and molecular testing were valuable in confirming a microbiological diagnosis in our patient.

CONCLUSION

The case described herein represents the 13th documented case of *B. quintana* endocarditis in North America and the first in Western Canada. As most literature regarding *B. quintana* endocarditis is in Europe and developing countries, this review represents the most up-to-date and comprehensive summary of cases within North America. The challenges outlined in obtaining a microbiological diagnosis in persons not connected with medical care likely underestimate the true prevalence of this condition. With increased recognition of *Bartonella* infection syndromes, combined with improvement of serologic testing and molecular diagnostics, it is likely that the identification of *Bartonella* disease will be more prevalent going forward. *Bartonella* endocarditis can manifest as an occult infectious process and should be considered in homeless individuals even in the absence of a known cardiac valvulopathy. Outbreaks of asymptomatic chronic *Bartonella* bacteremia within the homeless population coupled with challenges in financial and medication compliance makes infection prevention and control and public health measures important considerations.

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