Bartonella quintana Aortitis in a Man with AIDS, Diagnosed by Needle Biopsy and 16S rRNA Gene Amplification

Sulggi A. Lee,a Sara K. Plett,b Anne F. Luetkemeyer,a Gina M. Borgo,a Michael A. Ohliger,b Miles B. Conrad,b Brad T. Cookson,d,e Dhruba J. Sengupta,a Jane E. Koehlerb

Department of Medicine, Division of HIV/AIDS, University of California, San Francisco, San Francisco, California, USAa; Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, California, USAa; Microbial Pathogenesis and Host Defense Program and Department of Medicine, Division of Infectious Diseases, University of California, San Francisco, San Francisco, California, USAa; Department of Laboratory Medicine, University of Washington, Seattle, Washington, USAb; Department of Microbiology, University of Washington, Seattle, Washington, USAa

A 48-year-old heterosexual African male with type II diabetes presented to an emergency room (ER) with several months of abdominal pain, back pain, polydipsia, loss of 30 pounds of body weight, and subjective fevers. He was febrile (38.6°C) and tachycardic, with a glucose level of 298 mg/dl. He was given intravenous fluids and metformin and discharged from the ER. Subsequently, his HIV-1 test returned a positive result; his CD4+ T cell count was 68 cells/mm3 (7%), and his HIV-1 RNA level was 537,519 copies/ml. He was empirically started on antiretroviral therapy and prophylactic trimethoprim-sulfamethoxazole. Four weeks later, the patient described persistent abdominal and back pain, fever, and chills. The mid-thoracic back pain was sharp, constant, and relieved by leaning forward.

The patient worked as a taxi driver, lived alone in an apartment, and had no pets. He grew up in Ethiopia and moved to the United States in 1991. He reported being heterosexual and denied contact with commercial sex workers or having surgeries or tattoos. He reported no alcohol, tobacco, or illicit drug use. He had last traveled to Ethiopia in 2006, stayed in rural areas with goats, sheep, cows, dogs, and cats, and consumed only store-bought milk and meat.

On examination, the patient had no thrush or lymphadenopathy. His abdomen was soft and mildly tender in response to palpation throughout, without rebound. There was no tenderness in response to palpation along the spine. He had no cutaneous lesions. His laboratory results were notable for a white blood cell count of 2.9 × 10³/µl, with 38% polymorphonuclear cells, 36% lymphocytes, 8% monocytes, 15% eosinophils, and a hemoglobin level of 8.9 g/dl. His liver function test results were normal.

Single-phase phase-contrast-enhanced CT results demonstrated aortitis with periaortic tissue thickening. DNA amplification of biopsy tissue revealed Bartonella quintana, and Bartonella serologies were subsequently noted to be positive. The patient improved with prolonged doxycycline and rifabutin treatment. This case illustrates how molecular techniques are increasingly important in diagnosing Bartonella infections.
AFB smear result and negative culture results for bacteria, fungi, and AFB. The patient was started on empirical *M. tuberculosis* (rifabutin, isoniazid, pyrazinamide, and ethambutol) and *M. avium-M. intracellulare* (clarithromycin) therapy because of the histopathological tissue AFB stain result (even though the bacilli had an atypical appearance), the severe immunosuppression of the patient due to AIDS, the severity of the illness and location of the lesion, and the patient’s long-term potential exposure in a country where *M. tuberculosis* is endemic.

The patient’s pain significantly improved over the next 2 weeks on therapy. Because no microorganisms were isolated from the biopsy tissue and because of the high-risk location of the lesion and the potential long-term therapy required, the formalin-fixed, paraffin-embedded pathology specimen was sent to the University of Washington Molecular Diagnostics Laboratory (UW-MDL) for identification of the rod-like organisms using PCR DNA amplification. PCR tests were negative for *M. tuberculosis* and *M. avium-M. intracellulare*, but PCR using broad-range, bacterial 16S rRNA gene primers unequivocally identified *Bartonella quintana* (forward primer 27F sequence, 5'-AGAGTTTGATCCTGCTCAG-3'; reverse primer 357ml sequence, 5'-CTGCTGCCAGCCCGTA GGAG-3'). The amplified product included 263 nucleotides of the 16S rRNA gene (GenBank accession number KR866081). Basic Local Alignment Search Tool (BLAST) analysis revealed a 100% match to three different strains of *B. quintana* (RM-11, Toulouse, and Fuller) in the database. The closest match with any other known *Bartonella* spp. was 98% nucleotide identity with *B. henselae* and *B. grahamii*. Notably, the last case of *B. quintana* identification by PCR at UW-MDL had occurred more than 1 year earlier, making laboratory contamination unlikely. PCR using broad-range fungal primers detected *Malassezia restricta*, a common skin commensal which, according to UW-MDL researchers,

FIG 1 (A) Computed tomography (CT) angiography of the aorta demonstrating circumferential soft tissue thickening of the aorta inferior to the origin of the superior mesenteric artery (arrow), with abnormal periaortic soft tissue indistinguishable from the aortic wall. Heterogeneous enhancement of the soft tissue suggests active inflammation and calcifications present in periaortic tissue. (B) A left paraspinal approach CT-guided percutaneous biopsy specimen demonstrates direct sampling of the inflamed aortic tissue. (C) Follow-up CT angiogram, obtained approximately 7 months after presentation, demonstrating near-complete resolution of circumferential mural thickening and enhancement consistent with treatment response.

FIG 2 On histopathological examination, the core biopsy tissue was sparsely cellular, showing mostly acellular fibrous tissue with occasional spindle cells. Initially, the AFB tissue staining was interpreted as showing occasional rod-like structures (red arrow). Ultimately, these rod-like structures were considered to lack the characteristic beading typically seen with mycobacterial organisms, and therefore the rod-like structures were considered to represent artifacts.
is a common cause of contamination in tissue blocks. Fungal blood and biopsy culture results were negative.

Doxycycline (100 mg administered orally [p.o.] twice a day [b.i.d.]) therapy was started after the B. quintana PCR results were obtained. The patient reported no direct risk factors for B. quintana infection, including prior homelessness or infestation with body lice, and no pruritic rash. He did occasionally provide rides to homeless passengers in his taxi cab, but never saw any lice in his cab or on his body. Subsequent serological tests for Bartonella were performed, and an indirect fluorescence antibody (IFA) test for Bartonella (ARUP Laboratories) demonstrated a B. quintana IgG of 1:1,024 (negative, <1:64) and IgM of <1:16 (negative, <1:16) and a B. henselae IgG of >1:1,024 and IgM of <1:16 (Table 1). After PCR results were obtained, we attempted unsuccessfully to culture blood for Bartonella. Unfortunately, the sole blood specimen available that was drawn before the patient received antibiotics was only 1 ml, the specimen had been refrigerated for 3 weeks, and the blood was in a heparin tube (instead of the ideal EDTA tube), all of which are suboptimal for isolation.

The result of Warthin-Starry silver staining of the core biopsy tissue sample was negative, and histopathological examination revealed no specific characteristics of Bartonella infection.

A repeat CTA procedure performed 3 weeks after hospital discharge demonstrated no change, but the ESR had decreased to 29 and the CRP level to 1.0 and his eosinophilia had resolved. The patient charge demonstrated no change, but the ESR had decreased to 29 and the CRP level to 1.0 and his eosinophilia had resolved. The patient charge demonstrated no change, but the ESR had decreased to 29 and the CRP level to 1.0 and his eosinophilia had resolved. The patient charge demonstrated no change, but the ESR had decreased to 29 and the CRP level to 1.0 and his eosinophilia had resolved.

We report a case of B. quintana aortitis in a man with AIDS. No other B. quintana aortitis cases in AIDS patients were identified in a review of the literature. Most causes of aortitis are autoimmune (e.g., giant cell arteritis, Takayasu’s arteritis, rheumatoid arthritis, HLA-B27 spondyloarthopathies, and antineutrophil cytoplasmic antibody [ANCA]-associated arthropathies) or idiopathic (2). Among the infectious causes, bacterial organisms such as Salmonella, Staphylococcus, and Streptococcus spp. are the most common (3). Luetic aortitis caused by Treponema pallidum is rare and usually involves the ascending aorta (4). Mycobacterial aortitis is uncommon in the developing world and usually involves erosion of the aortic wall by a continuous lesion (5). There has been one case report of an immunocompromised elderly woman in whom serology confirmed the presence of B. henselae infrarenal abdominal aortic aneurysm and endocarditis (6). Another case report describes detection of B. quintana by 16S rRNA gene amplification in biopsied aortic tissue from a non-HIV-infected man who underwent abdominal aortic aneurysmal repair (7), but he had no risk factors for body lice exposure, exhibited no signs of infection, and had negative Bartonella serologies and Warthin-Starry stain results.

Three Bartonella species are the most common causes of human infection: B. quintana, B. henselae, and B. bacilliformis (8). Immunocompromised, HIV-infected patients develop B. quintana and B. henselae infections, with symptoms that include relapsing bacteremia, fever of unknown origin, endocarditis, and bacillary angiomatosis (BA). Although those two species have equal predilections to cause cutaneous BA in HIV-infected patients, B. quintana has a unique tropism for bone and heart valves, whereas B. henselae is more likely to infect liver, spleen, and lymph nodes (9). The origin of the aortic lesion in this patient is uncertain; without TEE, concomitant endocarditis was not completely eliminated. Another possible origin is extension of a contiguous vascular BA lesion into the aortic wall. One case report described B. quintana in a patient with AIDS manifesting as a single, large intra-abdominal BA lesion which eroded into the mesenteric vasculature (10). CD4+ T cell counts were in the very low range at which BA occurs (9) for both the latter patient (10 cells/mm3) and our patient (68 cells/mm3).

Bartonella infections can be diagnosed (8) by histopathological examination of tissue with Warthin-Starry silver stain, by special Bartonella blood culture analysis (9) (unavailable in most hospital laboratories), by serological assays, and increasingly, by PCR amplification of DNA extracted from biopsy tissue, using specific or

**TABLE 1** Bartonella quintana and Bartonella henselae serologies by indirect fluorescence assay, CD4+ T cell counts, and Bartonella treatment

<table>
<thead>
<tr>
<th>Date of sample collection</th>
<th>Bartonella quintana</th>
<th>Bartonella henselae</th>
<th>CD4 count (in cells/mm3) (%)</th>
<th>Bartonella treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgM titer</td>
<td>IgG titer</td>
<td>IgM titer</td>
<td>IgG titer</td>
</tr>
<tr>
<td>13 May 2013</td>
<td>&lt;1:16</td>
<td>1:512</td>
<td>&lt;1:16</td>
<td>&gt;1:1,024</td>
</tr>
<tr>
<td>13 June 2013</td>
<td>&lt;1:16</td>
<td>1:512</td>
<td>&lt;1:16</td>
<td>&gt;1:1,024</td>
</tr>
<tr>
<td>13 July 2013</td>
<td>&lt;1:16</td>
<td>Indet</td>
<td>&lt;1:16</td>
<td>&gt;1:1,024</td>
</tr>
<tr>
<td>15 August 2013</td>
<td>&lt;1:16</td>
<td>1:128</td>
<td>&lt;1:16</td>
<td>1:512</td>
</tr>
<tr>
<td>12 September 2013</td>
<td>&lt;1:16</td>
<td>1:64</td>
<td>&lt;1:16</td>
<td>1:1,024</td>
</tr>
<tr>
<td>31 October 2013</td>
<td>&lt;1:16</td>
<td>1:64</td>
<td>&lt;1:16</td>
<td>1:512</td>
</tr>
<tr>
<td>11 July 2014</td>
<td>&lt;1:16</td>
<td>1:64</td>
<td>&lt;1:16</td>
<td>1:128</td>
</tr>
</tbody>
</table>

**Note:** Bold font indicates positive indirect fluorescence assay (IFA) test results.

**Note:** Treatment drugs: C, clarithromycin; R, rifabutin; I, isoniazid; P, pyrazinamide; E, ethambutol; D, doxycycline.

**Note:** Indet, indeterminate; i.e., a high degree of nonspecific fluorescence was observed.
broad-range primers (as in this case). IFA is currently the most accessible method of diagnosis, but there are a number of caveats with existing IFA tests. First, the Bartonella IgM test result is almost always negative even in acute cases in immunocompetent patients. Second, AIDS patients with profound immunocompromise often do not develop anti-Bartonella antibodies (11). Third, as seen in this case, there often is IFA cross-reactivity between B. quintana and B. henselae (11). Our patient had B. quintana, but his B. henselae titers were consistently higher than his B. quintana titers (Table 1). Bartonella titers of >1:800 have been shown to have a high positive predictive value for endocarditis (12); presumably, such titers would be predictive of other endovascular infections. Had Bartonella been considered a causative agent at clinical presentation (which it was not, based on patient history), serological testing might have obviated an invasive procedure for diagnosis.

There are no prospective studies of Bartonella treatment in immunocompromised hosts. Because of the high incidence of relapse after short courses of antibiotics, erythromycin or doxycycline treatment is recommended for a minimum duration of 3 to 6 months for severe infections (1). Of note, the initial clinical response to antimycobacterial treatment was most likely due to the administration of rifabutin and clarithromycin; both drugs are active against Bartonella species (8). Following IFA titers has been useful to ensure decrease with treatment; a subsequent severalfold titers of H.11022/H11022 could herald relapse (1).

**Nucleotide sequence accession number.** The amplified product including 263 nucleotides of the 16S rRNA gene of B. quintana was deposited in GenBank under accession number KR866081.

**ACKNOWLEDGMENTS**

We declare that we have no conflicts of interest. We have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Potential conflicts of interest that the editors considered relevant to the content of the manuscript have been disclosed.

J.E.K. received funding support from NIH grants R01AI52813 and R01AI103299 and a California HIV Research Program Award.


**REFERENCES**


