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Endocarditis Caused by *Rochalimaea quintana* in a Patient Infected with Human Immunodeficiency Virus

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***Rochalimaea quintana* and *Rochalimaea henselae* are closely related, fastidious, gram-negative rickettsiae. Thus far, the spectrum of human *Rochalimaea* sp. infections has not included endocarditis. We describe a 50-year-old human immunodeficiency virus-positive man who developed endocarditis caused by *R. quintana*. DNA relatedness studies, which compared our patient's blood culture isolate with known *Rochalimaea* species, identified the organism as *R. quintana*. Our report expands the spectrum of *Rochalimaea* sp. infections and identifies a new infectious cause of endocarditis.**

Rochalimaea quintana, a fastidious, gram-negative rickettsia, is the causative agent of trench fever, a disease characterized by fever, bone pain, splenomegaly, and rash (14). Recently, *R. quintana* has been isolated from the blood of a human immunodeficiency virus (HIV)-infected patient living in the United States (16) and from HIV-infected patients with cutaneous bacillary angiomatosis (4). A very closely related organism, *Rochalimaea henselae*, has been established as a cause of cutaneous bacillary angiomatosis, persistent bacteremia, and peliosis hepatis (4, 8, 11, 16). Most *R. henselae* infections have involved HIV-infected patients (3, 10, 12, 16). Therefore, at least two species of *Rochalimaea* cause contemporary human infections within the United States (7). According to our review of the literature and a MEDLINE search, the spectrum of human *Rochalimaea* sp. infections has not included endocarditis. Herein, we describe an HIV-infected patient who developed endocarditis caused by *R. quintana*.

A 50-year-old, homosexual, HIV-positive man presented with a swollen, erythematous left palm. He had no history of intravenous drug use, opportunistic infections, renal disease, or rheumatic or congenital heart disease. He complained of fatigue, weight loss, and night sweats, but denied fever. He owned three adult cats and was frequently scratched by the cats. In addition, the cats had abundant fleas. The patient had no known contact with lice. Two months prior to admission his CD4 lymphocyte count was 200 cells per mm^3. At the time of admission, he was taking dideoxyinosine, trimethoprim-sulfamethoxazole, and cimetidine.

Physical examination showed a normal temperature, a holosystolic murmur that had not been present on previous examinations, a palpable spleen, left palm erythema and swelling, and tenderness localized over the left fourth-digit tendon. Laboratory studies showed a hematocrit of 22.0%, a leukocyte count of 2.3×10^9/liter, a platelet count of 121×10^9/liter, serum urea nitrogen of 12.9 mmol/liter, and serum creatinine of 362 μmol/liter. Urinalysis revealed greater than 30 erythrocytes per high-power field and no casts.

After two sets of blood for culture were obtained, intravenous ceftriaxone, 2 g daily, was started for presumed cellulitis. An echocardiogram obtained on the fourth day after admission showed a small echogenic mass on the right coronary cusp of the aortic valve, an echogenic mass (0.5 by 0.2 cm) on the anterior leaflet of the mitral valve, moderate mitral regurgitation, and moderate aortic regurgitation. Testing of serum for antibodies to *Coxiella burnetii*, *Brucella* sp., and *Francisella tularensis* was negative.

Several days later, the patient's hand inflammation had resolved and his serum creatinine had decreased to 248 μmol/liter. He was discharged on hospital day 8 with the diagnosis of endocarditis and the plan to continue ceftriaxone for an additional 4 weeks.

The patient's blood cultures, which had been inoculated into BACTEC 26 bottles, showed growth index changes indicating the presence of microorganisms on days 28 and 42 after they were inoculated. Gram stains (with safranin and carbofuchsin used as counterstains) were performed but were negative. Nevertheless, the bottles with increased growth indices were subcultured onto enriched chocolate agar plates (BBL blood agar base with 5% defibrinated sheep blood agar heated for 10 min at 90°C by standard protocols) and were incubated in 3% CO_2 in a candle jar with increased humidity at 35°C. Pinpoint colonies were seen on day 4. On day 7, these colonies were approximately 1 mm in diameter, round, tan colored, and somewhat dome shaped. Gram staining showed tiny coccobacillary gram-negative rods that were best visualized with carbofuchsin counterstaining. The organism was oxidase and catalase negative.

Antimicrobial susceptibility testing by the disk diffusion method (1) was attempted. After standardizing the inoculum to a 0.5 McFarland standard, the organism was streaked onto chocolate agar plates. Individual plates were incubated in a moist candle jar at 35°C with one antimicrobial disk to each plate. After 18 h, no growth was noted. The plates were reexamined at 48 and 72 h; at 72 h, there was an approximately 50-mm visible zone of inhibition on plates with doxycycline, ceftriaxone, erythromycin, and tetracycline

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TABLE 1. DNA relatedness of strain B-92-002100 to *Rochalimaea* species

Source of unlabeled DNA	% Relatedness to labeled DNA from[a]:								
	Strain B-92-002100			*R. quintana*^{T}			*R. henselae*^{T}		
	55°C	D	70°C	55°C	D	70°C	55°C	D	70°C
Strain B-92-002100	100	0.0	100	100	0.5	100	59	10.5	32
R. quintana VR 358^T	97	0.0	97	100	0.0	100	60	10.0	32
R. quintana A				100	1.0	100			
R. quintana B				100	0.5	100			
R. henselae 87-66^T	76	9.0	47	67	11.0	28	100	0.0	100
R. henselae 90-615				68	11.0	28	100	0.5	98
R. henselae G6779				64	11.0	28	100	0.5	99
R. vinsonii VR 152^T	67	10.0	41						

[a] Wayne et al. (15) recommended that a genetic species be defined as strains that are 70% or more related with less than 5% divergence in related sequences. By this definition, strain B-92-002100 definitely is *R. quintana*. D, divergence, calculated to the nearest 0.5%.

disks. A 38-mm zone was seen on the plate with a ciprofloxacin disk. These results were considered nonstandardized because of the slow growth of the organism, and MIC testing by the agar dilution method was attempted. The MICs were ≤0.03 μg/ml for erythromycin and ceftriaxone and 0.5 μg/ml for ciprofloxacin. *Staphylococcus aureus* ATCC 29213 was used as a quality control strain.

The cellular fatty acid composition of the isolate, based on an average ± standard deviation of three determinations, was $C_{14:0}$, 0.19% ± 0.03%; $C_{16:0}$, 17.65% ± 1.66%; $C_{17:0}$, 0.52% ± 0.26%; $C_{18:0}$, 21.33% ± 4.68%; and $C_{18:1}$, 35.28% ± 4.39%. The composition of cellular fatty acids resembled those of both *R. quintana* and *R. henselae*, but was somewhat more consistent with *R. quintana*, having $C_{18:0}$ in amounts averaging less than 22% (16). The organism was unreactive with *R. henselae*-specific antibodies (9).

DNA relatedness studies were performed to compare the isolate from our patient (strain B-92-002100) with known *Rochalimaea* isolates. Extraction and purification of DNA and the hydroxyapatite hybridization method for determining DNA relatedness were performed as described previously (2). DNA hybridization results are given in Table 1. Labeled DNA from *Rochalimaea* sp. strain B-92-002100 was 97% related to *R. quintana* in reassociation reactions at both 55 and 70°C. There was no evidence of divergence within the related sequences. In the reciprocal reaction, using labeled *R. quintana* DNA, relatedness was 100% by using both optimal and stringent criteria, with 0.5% divergence within related sequences. Labeled DNA from strain B-92-002100 was 76% related (9% divergence) to *R. henselae* at 55°C and 47% related to *R. henselae*, its next closest relative, at 70°C. These DNA hybridization results thus identified isolate B-92-002100 as *R. quintana*.

Upon isolation of the organism from blood cultures, ceftriaxone was discontinued, and doxycycline, 100 mg twice daily, was begun. One week later, the patient was found to have a grade II diastolic murmur that had not been present on previous examinations, and the doxycycline was changed to erythromycin, 500 mg four times daily. Following the original positive blood cultures, nine subsequent sets did not show any growth, despite prolonged incubation. Nine months later, the patient continues to take erythromycin, and although his diastolic murmur has persisted, his renal insufficiency has improved (168 μmol/liter) and his anemia has resolved.

Trench fever was first encountered in Europe in World War I and subsequently occurred in Europe in World War II, in Mexico, and in North Africa (5). Prior to a recent report, in which investigators isolated *R. quintana* from blood cultures obtained from an HIV-infected man living in Oklahoma, *R. quintana* had not been isolated in North America (16). In addition, a different group of investigators performed 16S rRNA gene sequence analysis on a skin biopsy specimen taken from a patient in California (who had cutaneous bacillary angiomatosis) and found sequences homologous to those of *R. quintana* (8). More recently, *R. quintana* was isolated from three HIV-infected patients with cutaneous bacillary angiomatosis (4). In those five patients (4, 8, 16), as well as in our patient, the clinical manifestations were not typical of classic trench fever and in no instance was the vector established. Thus far, therefore, the human body louse remains the only known vector for *R. quintana* infections.

Our DNA relatedness studies clearly establish our patient's isolate as *R. quintana*. On the basis of the clinical findings for our patient, his echocardiographic results, and the isolation of *R. quintana* from blood cultures obtained from the patient, we conclude that *R. quintana* caused our patient's endocarditis. Alternatively, one could conclude that our patient had bacteremia caused by *R. quintana* and endocarditis caused by a second organism that did not grow in the cultures that were obtained. This latter scenario seems highly unlikely given the negative serology tests for *C. burnetii*, *Brucella* sp., and *F. tularensis* and, despite prolonged incubation, the failure to isolate an organism (other than *R. quintana*) from blood cultures.

Our report expands the spectrum of manifestations caused by *Rochalimaea* sp. infections, a spectrum that now includes cutaneous bacillary angiomatosis (3, 8), persistent bacteremia (10, 16), peliosis hepatis (6, 11), disseminated infection (12), intracranial mass lesions (13), trench fever (14), and endocarditis. In addition, we identified a new infectious cause of endocarditis. Our isolation of *R. quintana* illustrates the value of prolonged incubation of blood cultures in the attempt to isolate fastidious organisms. Moreover, we would like to emphasize the need for communication between clinicians and microbiologists to ensure that the necessary steps are taken in order to isolate fastidious organisms such as *R. quintana*. The vector for *R. quintana* in North America remains unknown at this time.

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