Two cases of endocarditis due to *Bartonella henselae*

James Fu, Sharmini Muttaiyah, Sushil Pandey, Mark Thomas

*Bartonella henselae*—the slow-growing, fastidious Gram-negative bacillus which causes cat scratch disease—is a recently recognised cause of endocarditis. To our knowledge, until now, there have not been any cases of endocarditis caused by this organism recognised in New Zealand. We describe two recent patients with endocarditis caused by *B. henselae*.

Case report 1

A 67-year-old woman (with a past history of a mitral valvotomy in 1968 for rheumatic mitral stenosis) presented to hospital with symptomatic atrial flutter. She was febrile (38°C), had multiple splinter haemorrhages on her finger nails, and several Osler’s nodes on the dorsal surface of her fingers (Figure 1) and had both a grade 1/4 early diastolic murmur and a grade 1/4 ejection systolic murmur. She had not received any medical treatment, and in particular had not received any antimicrobial medications in the preceding months.

Figure 1. Right middle finger of Case 1 showing multiple small splinter haemorrhages in nail-bed and an Osler’s node adjacent to the PIP joint

Initial investigations revealed a haemoglobin level of 9.9 g/dL, a total leukocyte count of $9.1 \times 10^9$/L, and an erythrocyte sedimentation rate (ESR) of 64 mm/hr. A
midstream specimen of urine contained $30 \times 10^6$ WBC/L and $>1000 \times 10^6$ RBC/L with hyaline and cellular casts, and her serum creatinine level was 255 $\mu$mol/L.

A transthoracic echocardiogram showed a $0.4 \times 1.0$ cm vegetation on the anterior mitral leaflet with moderate mitral regurgitation, and a $1.0 \times 0.6$ cm vegetation on the right cusp of the aortic valve without significant valve dysfunction. An ultrasound of the renal tract showed a subtle diffuse increase in renal echogenicity. Three blood cultures collected over 1 hour remained sterile after 10 days of incubation.

A diagnosis of culture-negative endocarditis was made and the patient was treated with ceftriaxone 2 gm 24 hrly alone for 9 days, then with benzyl penicillin 3 mU 4 hrly and gentamicin 120 mg 24 hrly.

On day 15 of medical treatment, a repeat echocardiogram showed worsening valvular dysfunction and she proceeded to replacement of her aortic and mitral valves with porcine bioprostheses. Both excised valves were cultured but remained sterile after seven days incubation. However microscopy of the mitral valve revealed small numbers of pleomorphic Gram variable organisms and PCR amplification of bacterial 16S ribosomal DNA from the aortic valve tissue produced an amplicon with a 100% match for the published sequence for \textit{B. henselae}.

A serum sample collected 30 days after presentation had titres of IgM and IgG antibodies to \textit{B. henselae} of >1:80 and 1:2048 respectively. Her postoperative antimicrobial treatment comprised another 10 days of intravenous penicillin 3 mU 4 hrly and gentamicin 120 mg 24 hrly followed by doxycycline 200 mg daily for a further 28 days.

Two months after discharge from hospital she presented with blurring of vision in the right eye and was found to have bilaterally swollen optic nerves. A cranial magnetic resonance (MRI) scan showed minor inflammation of both optic nerves.

A cerebrospinal fluid sample contained $<1 \times 10^6$ WBC/L. PCR amplification of blood and cerebrospinal fluid failed to detect any \textit{B. henselae} DNA, and two sets of blood cultures remained sterile after 10 days of incubation. No further antimicrobial therapy was given and her visual problems improved with corticosteroid therapy. She remained well after a further 10 weeks of follow-up.

**Case report 2**

A 23-year-old man with known rheumatic valvular heart disease presented to hospital in Tahiti with fever and was found to have moderate aortic and mitral valve regurgitation with vegetations present on both valves. There was evidence of embolic disease affecting his popliteal arteries bilaterally. Blood cultures were sterile and he was treated with amoxicillin plus clavulanic acid, an aminoglycoside and rifampicin.

Ten weeks after his initial presentation he was transferred to Auckland City Hospital and underwent aortic valve replacement and mitral valve repair. A serum sample collected 3 days after arrival at Auckland City Hospital had titres of IgM and IgG antibodies to \textit{B. henselae} of <1:20 and 1:16384 respectively. No organisms were seen in the mitral valve vegetations or in the aortic valve tissues, but PCR amplification of bacterial 16S ribosomal DNA from the aortic valve produced an amplicon with a 100% match for the published sequence for \textit{B. henselae}. 
He was treated for a further 2 weeks with an aminoglycoside and for 6 weeks with doxycycline 100 mg BD. He has remained well 9 weeks after completion of this treatment.

Discussion

The overwhelming majority of organisms that cause infective endocarditis are readily isolated from blood cultures incubated for 10 days. However in a small minority of patients with infective endocarditis no organism is isolated, commonly either because previous antimicrobial therapy has partially cured the infection, or because the infection is due to an unusually fastidious or slow-growing organism (Table 1).

Table 1. Aetiological agents in infective endocarditis

<table>
<thead>
<tr>
<th>Agents</th>
<th>Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococci</td>
<td>60–80</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>30–40</td>
</tr>
<tr>
<td>Enterococci</td>
<td>5–18</td>
</tr>
<tr>
<td>Other streptococci</td>
<td>15–25</td>
</tr>
<tr>
<td>Staphylococci</td>
<td>20–35</td>
</tr>
<tr>
<td>Coagulase-positive</td>
<td>10–27</td>
</tr>
<tr>
<td>Coagulase-negative</td>
<td>1–3</td>
</tr>
<tr>
<td>Gram-negative aerobic bacilli</td>
<td>1.5–13</td>
</tr>
<tr>
<td>Fungi</td>
<td>2–4</td>
</tr>
<tr>
<td>Miscellaneous bacteria</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Mixed infections</td>
<td>1–2</td>
</tr>
<tr>
<td>Culture-negative</td>
<td>&lt;5–24</td>
</tr>
</tbody>
</table>

*Bartonella (previously known as* *Rochalimaea*) *henselae* was first identified as a cause of endocarditis in 1993. Subsequent investigations have shown that *B. henselae* is responsible for approximately 6% cases of culture negative endocarditis and that it can be diagnosed either by detection of serum antibodies to *B. henselae* (sensitivity >90%) or by detection of *B. henselae* DNA in excised valve tissue (sensitivity approx 90%)—or less reliably by isolation of *B. henselae* from blood cultures incubated for 3 weeks (sensitivity approx 20%).

Other important infective causes of culture negative endocarditis include *C. burnetii* (approx 50%), *B. quintana* (approx 20%), and *Tropheryma whipplei, Mycoplasma* spp, *Chlamydia* spp, and *Legionella* spp (all very rare).

Patients with culture-negative endocarditis comprised 21/189 (11%) episodes of endocarditis reported from Green Lane Hospital between 1959 and 1976; 5/102 (5%) episodes reported from Auckland Hospital between 1979 and 1986; but none of 78 episodes reported from Middlemore Hospital between 1976 and 1986. Each of these case series were collated before the identification of *B. henselae* as a cause of endocarditis and before the introduction of modified diagnostic criteria which would be expected to increase the rate of diagnosis of culture negative endocarditis.
Two cases of endocarditis due to *B. henselae* have been reported from Australia, one in a 50-year-old Queensland man and the other in a 44-year-old man transferred from New Caledonia.8,9 *B. henselae* DNA has been detected in 11% of 114 cat fleas collected from cats presenting to veterinary clinics in three New Zealand towns.10 *B. henselae* is likely to have been the unrecognised cause of occasional cases of endocarditis in New Zealand in the past.

The optimum antibiotic regimen for *B. henselae* endocarditis remains unclear. *In vitro*, *B. henselae* are highly susceptible to beta-lactam agents, aminoglycosides, macrolides, tetracyclines, and rifampin.

A review of 101 cases of *Bartonella* endocarditis found that the outcome was improved in patients who received at least 2 weeks of treatment with an aminoglycoside.11 The current recommendation of the American Heart Association is for 2 weeks of gentamicin 3 mg/kg daily plus 6 weeks of doxycycline 100 mg BD.12 Valvular surgery is commonly required in patients with *Bartonella* endocarditis.

We hope that these two cases will stimulate clinicians to consider the diagnosis of endocarditis due to *B. henselae* in patients whose blood cultures remain sterile. Failure to identify the cause of endocarditis in such patients is likely to result in inappropriate treatment with a reduced likelihood of cure.

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**References:**


