

When Blood Cultures Remain Negative: Diagnosing *Cardiobacterium hominis* Prosthetic Valve Endocarditis after a Bentall Procedure with Plasma Microbial Cell Free DNA Sequencing

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Introduction

HACEK organisms, including *Cardiobacterium hominis*, are fastidious Gram-negative bacteria that inhabit the oral and upper respiratory tract flora and can cause subacute, culture-negative endocarditis. Despite advances in blood culture methodologies, echocardiography and diagnostic criteria, identifying these infections can be difficult, particularly in patients previously exposed to antibiotics. We report a case of *C. hominis* prosthetic valve endocarditis presenting atypically as recurrent migratory cellulitis following Bentall surgery¹.

Case Description

A 51-year-old man with a history of bioprosthetic Bentall procedure with ascending aorta and hemiarch replacement two years earlier presented with recurrent migratory cellulitis over the preceding four months. Each episode was associated with fevers up to 104°F and transient improvement following antibiotic therapy:

- **Four months before admission:** Left foot and calf cellulitis treated with 7 days of cephalexin.

- **Three months before admission:** Right lower extremity cellulitis treated with antibiotics.
- **One month before admission:** Left arm cellulitis treated with cephalexin and bactrim.
- **Eight days before admission:** Painful violaceous lesion on the right palm followed by progressive swelling and pain of the left wrist despite clindamycin therapy.

On admission, the patient reported severe left-hand pain with erythema over the thenar and snuffbox region. He was afebrile, hemodynamically stable and had no audible cardiac murmur. Laboratory evaluation revealed WBC 7.95 K/ μ L, hemoglobin 12.1 g/dL, platelets 188 K/ μ L, CRP 33 mg/L and ESR 49 mm/hr. Three sets of blood cultures obtained over five days remained negative.

MRI of the left wrist demonstrated myositis with a suspected microabscess and surrounding soft tissue inflammation. Transthoracic echocardiography was unremarkable. However, the presence of a painful violaceous palmar lesion concerning for an Osler node raised suspicion for prosthetic valve infective endocarditis. Serologic testing for *Bartonella*, *Brucella*, *Coxiella burnetii*, *Legionella* and HIV was negative.

Transesophageal echocardiography revealed multiple vegetations on the bioprosthetic aortic valve, including a large mobile vegetation measuring 1.4×1.3 cm and paravalvular thickening concerning for early abscess formation. Given persistently negative blood cultures, plasma microbial cell-free DNA sequencing (Karius test) was performed and identified *Cardiobacterium hominis*, confirming prosthetic valve infective endocarditis. The patient was treated with ceftriaxone 2 g intravenously daily for six weeks, as surgical intervention was deferred.

Discussion

Blood culture-negative endocarditis (BCNE) may result from prior antimicrobial therapy leading to sterilized blood cultures, infection with fastidious organisms or infection caused by intracellular pathogens that cannot be detected using conventional culture techniques. True BCNE is most associated with organisms such as *Bartonella* spp. and *Coxiella burnetii*, which are typically identified through serologic testing or *Tropheryma whippelii*, which may require molecular diagnostics such as polymerase chain reaction (PCR) of valvular tissue for detection. In addition, fungal pathogens, including *Aspergillus* spp. and *Histoplasma capsulatum*, should be considered in selected patients, as these organisms are not routinely recovered from standard blood cultures².

Cardiobacterium hominis, a fastidious Gram-negative bacillus within the HACEK group

Haemophilus spp., *Aggregatibacter*, *Cardiobacterium*, *Eikenella* and *Kingella*, is an uncommon but well-recognized cause of infective endocarditis³. Although advances in automated blood culture systems have improved microbial detection, diagnosis remains challenging, particularly in patients exposed to antibiotic therapy^{2,3}. As a constituent of the normal oropharyngeal flora, *C. hominis* is considered a low-virulence pathogen and typically causes a subacute form of infective endocarditis. Patients often experience vague constitutional symptoms for weeks to months before diagnosis, with a reported mean symptom duration of approximately 145 days, substantially longer than that observed in staphylococcal or streptococcal endocarditis⁴.

This case highlights an atypical presentation of *C. hominis* prosthetic valve endocarditis manifesting as recurrent migratory cellulitis and soft tissue inflammation rather than classic cardiac symptoms. Repeated antibiotic exposure likely contributed to persistently negative blood cultures and delayed diagnosis. The patient's recurrent episodes of cellulitis were likely embolic manifestation of infective endocarditis, culminating in the development of a painful palmar lesion suggestive of an Osler node, which prompted further investigation. Notably, transthoracic echocardiography was unrevealing, whereas transesophageal echocardiography identified multiple prosthetic valve vegetations and possible early perivalvular extension. Furthermore, this case demonstrates the diagnostic value of plasma microbial cell-free DNA sequencing (Karius Spectrum) in identifying fastidious pathogens when conventional microbiologic testing is nondiagnostic. Most HACEK endocarditis cases respond well to medical therapy with 4 to 6 weeks of intravenous ceftriaxone, although surgical intervention may be required in selected patients⁵.

Conclusion

Clinicians should maintain a high index of suspicion for BCNE in patients with recurrent unexplained inflammatory or infectious syndromes and a history of prosthetic valve implantation. Non-culture-based diagnostic modalities can be invaluable in identifying fastidious pathogens and guiding targeted therapy.

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