



Published in final edited form as:

Am J Med. 2011 July ; 124(7): e9–e10. doi:10.1016/j.amjmed.2011.02.026.

Establishing Diagnosis of *Haemophilus Parainfluenzae* as Etiology of Culture-negative Endocarditis Using DNA Sequence Analysis on Tissue Specimen

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To the Editor:

Dissemination of infected emboli into meningeal vessels can lead to meningitis as a result of endocarditis, but this presentation is very rare.¹ Herein we describe a case of endocarditis in a young patient who had oral piercing. *Haemophilus parainfluenzae* was identified as the cause of endocarditis using specimen-direct sequencing.

CASE SUMMARY

A 24-year-old healthy woman presented with headache, fever, and neck stiffness. Cerebrospinal fluid analysis revealed white cell count 15/mm³ (49% polymorphonuclear cells, 15% lymphocytes), glucose 64 mg/dL, and protein 72 mg/dL. Cerebrospinal fluid Gram stain and cultures were negative. The patient was treated for meningitis with intravenous ceftriaxone, vancomycin, and acyclovir. Although her symptoms improved, she continued to be intermittently febrile. A total of 14 serial blood cultures were all negative for growth. A transesophageal echocardiogram demonstrated vegetation on the anterior mitral valve with perforation of the mitral valve leaflets, confirming the diagnosis of endocarditis. A magnetic resonance imaging scan of the brain revealed 2 small inferior cerebellar infarctions. The patient underwent surgical repair of mitral valve leaflet. Culture and Gram stain of the intraoperative mitral valve tissue were negative.

Genomic DNA was extracted from the mitral valve tissue using an EZ1 tissue DNA kit (Qiagen, Valencia, Calif). Broad-range polymerase chain reaction (PCR) of the 5' 527

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Authorship: All authors had access to the data and a role in writing the manuscript.

Conflict of Interest: None.

nucleotide bases of the 16S bacterial rRNA gene was performed on this extract, using MicroSeq 500 PCR master (Applied Biosystems, Foster City, Calif). DNA sequencing and analysis were performed as described elsewhere;² sequence analysis revealed a 99.1% match to the reference organism, *H. parainfluenzae*. The patient completed a 6-week course of intravenous ceftriaxone 2 g intravenous daily and fully recovered.

DISCUSSION

Oral body piercing, an increasingly common practice, has significant potential for infectious complications including endocarditis.¹ To our knowledge, this report is the second case of *H. parainfluenzae* endocarditis associated with piercing,¹ and the sole case diagnosed by broad-range PCR of a culture-negative surgical specimen.

Isolated meningitis as the first manifestation of endocarditis is unusual.¹ Fewer than 80 cases of *H. parainfluenzae* endocarditis have been reported in the literature, and in a previous review, only one case of an embolic event in the meninges was reported.¹

Risk factors for development of endocarditis caused by this organism, which is indigenous to the mouth or nasopharynx of 5%–25% of healthy individuals, include dental work, nasopharyngeal infection, and tongue piercing.¹ As many as 85% of patients with *H. parainfluenzae* endocarditis develop occlusive disease; surgical intervention is often necessary and the case fatality rate is significant, reportedly between 10% and 35%.¹

Broad-range PCR and sequence analysis of the bacterial 16S rRNA gene is a powerful method to identify noncultivable bacteria directly from clinical specimens.³ Indeed, the presence of microbial DNA in heart valve tissue may soon be a major diagnostic criterion for endocarditis.³ Although the technical expertise required for this approach is not available in most clinical laboratories, the use of DNA-sequencing based procedures by regional reference centers is widespread.

CONCLUSIONS

The atypical presentation of aseptic meningitis in this case highlights the difficulties in diagnosing patients with endocarditis, and this delay may lead to destruction of cardiac structure. *H. parainfluenzae* may present as culture-negative endocarditis in the absence of molecular testing. Thus, when culture is negative, broad-range PCR on tissue specimens is a powerful tool to identify the infecting organism and enable directed therapy.

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