# A pediatric case of *Cardiobacterium hominis* endocarditis

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# Abstract

Gram negative endocarditis is relatively rare in pediatrics but when they occur they are most frequently caused by one of the HACEK (Haemophilus species, Actinobacillus actinomycetemcomitans, C. hominis, Eikenella corrodens and Kingella kingae) group of microorganisms. Within the HACEK group of microorganisms there have been approximately 100 cases of Cardiobacterium hominis endocarditis reported in the literature, but only 2 previous cases of endocarditis and one case of pericarditis have been reported in children. In this report, we present a case of a 12-year-old boy with a right ventricle to pulmonary artery conduit for Tetralogy of Fallot with pulmonary atresia who presented at an annual cardiology examination with a 3 week history of fatigue and was found to have a vegetation on routine echocardiogram. Subsequent blood cultures grew Cardiobacterium hominis and the patient was treated successfully with 6 weeks of appropriate antibiotic therapy. We present this case and a review of the literature of the HACEK group of microorganisms in pediatrics.

# **Case Report**

A 12 year old boy, who was status post repair (shortly after birth) of Tetralogy of Fallot with pulmonary atresia and subsequent replacements of right ventricle to pulmonary artery conduit 4 years prior to current evaluation, was seen in an outside Pediatric cardiology clinic for his annual follow-up appointment. The appointment had been scheduled one month earlier on the patient's request, due to the onset of generalized fatigue and decreased endurance of 2-3 weeks duration. The patient denied symptoms of fever, chest pain, dizziness or syncope.

The patient had a history of poor dentition, poorly controlled asthma, sleep apnea, and allergic symptoms, which led to an adenoidectomy two years prior to current presentation. The most recent right ventricle to pulmonary artery conduit replacement occurred 4 years prior to presentation which was complicated by Staphylococcus aureus mediastinitis. In clinic, by report, the physical examination revealed a well looking boy with thin habitus, in no acute distress with a heart rate of 102 beats/min, respiratory rate of 16 breaths/min and a blood pressure of 94/70 mmHg. Respiratory examination was significant for mild end expiratory wheezes. Cardiovascular examination demonstrated a regular rate and rhythm with a normal S1 and split fixed S2. A 3/6 graded harsh, early peaking, mid pitch systolic ejection murmur and a soft 2/4 graded diastolic murmur were heard best at the left sternal border. Of note, there were no peripheral stigmata of endocarditis (splinter haemorrhages, Osler nodes or Janeway lesions) and the remainder of the physical examination was unremarkable. A routine echocardiogram showed a bright and thickened conduit valve with a suggestion of mass attached to the leaflet. This was not present on the previous echocardiogram (approximately 2 years prior).

Blood work at the clinic appointment was significant for a mildly elevated ESR of 25 mm/hour, CRP of 11.5 mg/L and a WBC of 5.92 cell/cm<sup>3</sup> with 16% of monocytes. Repeat blood work 2 days later showed slight improved CRP of 7.6 mg/L, unchanged ESR and CBC, normal electrolytes, LFT, CXR, and sinus films. A throat culture was positive for Streptococcus and ASO titre was elevated. The patient was started on amoxicillin for Streptococcal pharyngitis. At this time, the patient spiked a fever of 38.3°C. The blood cultures taken both at presentation and two days later became positive for a slow growing gram negative rod.

Based on the positive blood cultures and the findings on the ECHO, the patient was referred for admission at University of Michigan C.S. Mott Children's Hospital with the diagnosis of subacute bacterial endocarditis four days after the initial clinic visit. Upon admission the patient was continued on amoxicillin for the Streptococcal pharyngitis and empirical treatment for bacterial endocarditis with intravenous (i.v.) vancomycin and i.v. piperacillin/tazobactam was initiated. Infectious Diseases was consulted three days after admission and the antibiotics were narrowed to i.v. ceftriaxone 1700 mg q 12 hours since blood cultures had become negative after the first few doses of amoxicillin. At this time, oropharyngeal flora was suspected and organisms such as Kingella and Haemophilus species are not particularly virulent and are susceptible to ceftriaxone.

Aerobic and anaerobic blood cultures obtained on admission and on the subsequent day remained negative. A trans-thoracic echocardiogram on the second day after admission demonstrated evidence of a new



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oscillating mass on a pulmonary valve leaflet concerning for a possible vegetation. The local laboratory was initially unable to identify the gram negative rod isolated from their clinic and the organism was sent to the University of Michigan microbiology laboratory where it was identified as *Cardiobacterium hominis* (*C. hominis*) that was susceptible to amoxicillin/ clavulanate, meropenem, ceftriaxone and levofloxacin and resistant to ampicillin. The combined susceptibilities from the two laboratories are shown in Table 1.

Throughout the duration of admission, the patient remained afebrile and well-appearing and was discharged home on the fifth hospital day in stable condition on i.v. ceftriaxone therapy through a right upper extremity peripherally inserted central catheter line to complete a 6 week course of antibiotics. Two weeks into the course of treatment, the patient developed an intense pruritic rash near his peripherally inserted central catheter (PICC) site and along the PICC line track concerning for allergy. Ceftriaxone was discontinued and ampicillin/ sulbactam was started. However, the patient developed another lacy rash and ampicillin/sulbactam was then switched to levofloxacin 10 mg/kg/day orally for the remaining two weeks of antibiotic therapy.

### Discussion

C. hominis is a fastidious gram negative





bacillus which is part of the normal oropharyngeal flora.<sup>1</sup> It is a member of the HACEK (Haemophilus parainfluenzae, Haemophilus aphrophilus, and Haemophilus paraphrophilus, Actinobacillus actinomycetemcomitans, C. hominis, Eikenella corrodens, and Kingella kingae) group of microorganisms and is differentiated from them by a positive oxidase reaction and the production of indole.<sup>2</sup> HACEK organisms account for between 3-10% of the cases of native valve endocarditis but are the most common gram negative cause of endocarditis in children.<sup>3,4</sup>

The presentation of endocarditis with one of the HACEK microorganisms is often insidious in onset. Patients often experience malaise with or without low grade fevers which can last weeks to months before seeking medical attention or a diagnosis is confirmed.<sup>5</sup> According to the Duke clinical criteria for the diagnosis of infective endocarditis, blood cultures should be incubated for at least two weeks. This allows time for slow growing bacteria like C. hominis and other HACEK microorganisms.6 Eighty-three percent of cases have also presented with constitutional symptoms such as fatigue.7 The patient presented here was afebrile prior to admission but had some intermittent fevers during the early phase of the admission. The patient therefore met modified Duke Criteria for definite infective endocarditis (echocardiographic findings, fever, predisposition, and positive blood cultures).

C. hominis is a slow growing, pleomorphic, gram negative bacillus. It is microaerophilic growing best with increased CO<sub>2</sub> and 100% humidity and incubation may take up to 14 days although most cultures will become positive within 5 days.8 While C. hominis can be distinguished from other HACEK organisms by its characteristic fermentations pattern, glucose, maltose, mannitol, sorbitol, mannose and sucrose, the production of indole is a significant feature of the organism. In this case 3 days incubation was required for the gram negative bacilli to grow and it took 3 weeks for the organism to be identified as C. hominis. There have also been reports of cases where C. hominis could not be isolated from a standard

blood culture. Mueller et al. describe a case of culture-negative endocarditis where *C. hominis* was diagnosed using broad-range polymerase chain reaction amplification of the 16 ribosomal RNA gene from arterial embolic tissue. They proposed the use of this technique to be beneficial as a supplement to the rapid, specific and sensitive identification of fastidious microorganisms.<sup>9</sup>

Initial isolates of C. hominis were penicillin and ampicillin sensitive. However, beta-lactamase producing strains of C. hominis have been identified and since antimicrobial susceptibility testing may be difficult to perform on HACEK microorganisms,6 the American Heart association now recommends that all HACEK microorganisms should be considered ampicillin resistant and third generation cephalosporins should be the treatment of choice.<sup>10</sup> For patients who cannot tolerate beta lactams, trimethoprim/sulfamethoxazole, fluroquinolones and aztreonam are appropriate alternatives.6 This is the second case demonstrating beta-lactamase-producing C. hominis in a Pediatric patient. The first Pediatric case of beta-lactamase-producing C. hominis was described in a 7-year-old girl with a history of Tetralogy of Fallot who was treated with aztreonam.7 The initial plan in the case presented here was to treat the patient for a 6-week course with Ceftriaxone. However, due to reactions concerning for an allergic response to

ceftriaxone and ampicillin/sulbactam, levofloxacin was used to complete the 6-week course.

Underlying heart disease is the major risk factor for developing endocarditis with approximately 76% of cases occurring in patients with surgically repaired structural cardiac abnormalities.<sup>6,7</sup> Because HACEK microorganisms are part of the normal oral flora, recent dental procedures are a risk factor for developing endocarditis with this group of microorganisms - especially for patients with underlying heart disease. Wormser et al. noted that 12 of 27 patients with endocarditis caused by one of the HACEK microorganisms had recent dental work or an oral infection prior to presentation.<sup>11</sup> Additionally children with congenital heart disease harbor HACEK microorganisms to a greater extent and have more gingival inflammation than healthy children.<sup>12</sup> In this case, the patient did not undergo a dental procedure but was noted to have poor dentition and developed pharyngitis with Group A Streptococcus which may have facilitated C. hominis entry.

### Conclusions

The HACEK group of microorganisms can cause endocarditis in children, most commonly

#### Table 1. Antibiotic susceptibilities of C. hominis.

Antibiotic	MIC value (ug/mL)	Interpretation
Ertapenem	2	Susceptible
Meropenem	≤0.5	Susceptible
Meropenem 2	≤0.25	Susceptible
Trimethoprim/sulfamethoxazole	≤0.5	Susceptible
Levofloxacin	≤2	Susceptible
Moxifloxacin	≤0.06	Susceptible
Amoxicillin/clavulanate	≤0.5/0.25	Susceptible
Ampicillin	4	Resistant
Beta-lactamase	-	Positive

#### Table 2. A summary of pediatric case reports of C. hominis.

Case	Age	Sex	Cardiac anomaly	Treatment	Complication	Surgery	Outcome
1	17	М	Aortic valve	Ceftriaxone 6 weeks/gent and flucloxacillin 2 weeks	None	Valve replacement	Good
2	5	М	Tetralogy of Fallot with pulmonary atresia	Ceftriaxone	None	Valve replacement	Good
3	10	М	Tetralogy of Fallot with pulmonary atresia	Ceftriaxone amp-sulbactam and levofloxacin	None	None	Good
Pericarditis	10	F	None	Ceftriaxone	None	Partial pericardictomy	Good

with *K. kingae* and *H. parainfluenzae. C. hominis* is a rare cause of endocarditis in children and to our knowledge this is the third pediatric case reported. Additionally, there has been one reported case of *C. hominis* pericarditis in an otherwise healthy child (Table 2).

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