Prosthetic Joint Infection Due to *Cardiobacterium hominis*: Report of First Known Case and Review of *C. hominis* Septic Arthritis Literature

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Abstract: Introduction. The *Cardiobacterium* species is a pleomorphic Gram-negative bacterium discovered in 1964 and is part of the HACEK (*Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*) group of organisms known to cause endocarditis. It has low virulence and can also cause dacryocystitis, septicemia and abdominal abscess. We report a patient with *C. hominis* prosthetic joint infection in the absence of definitive endocarditis. **Case Report**. A 57-year-old man presented to his orthopedic surgeon 17 months after left total knee arthroplasty with a 4–5-day history of left knee pain following yard work. He had an aortic valve replacement in 2003, mitral valve repair in 2006 and bovine aortic valve replacement in 2019 (12 months previously). Aspirate of knee joint fluid was grossly cloudy. Two of two preoperative blood cultures revealed *Cardiobacterium* species after 4 days' incubation. He was initially treated with intravenous vancomycin plus piperacillin/tazobactam followed by 6 weeks of parenteral ceftriaxone followed by five months of oral cefdinir. Patient is infection-free 6 months after completion of antimicrobial therapy. **Discussion.** *Cardiobacterium hominis* is a slow-growing, fastidious, capnophilic, Gram-negative bacillus commonly found in normal oral and upper respiratory flora. Google Scholar™ and PubMed®searches were conducted and this is the first reported case of prosthetic joint infection due to *Cardiobacterium hominis*. We found three previously reported cases of *C. hominis* pyogenic arthritis: one patient with native knee pyogenic arthritis, one patient with cervical spondylodiscitis and one patient with lumbar spondylodiscitis and epidural abscess. Two of these three patients had TEE-documented infective endocarditis and one had a bioprosthetic aortic valve without evident vegetation on TEE. Our patient had a bioprosthetic aortic valve without TEE evidence of endocarditis. *C. hominis* should be added to the list of organisms that can cause bacteremically spread prosthetic joint infection.

Keywords: *Cardiobacterium hominis*; Prosthetic Joint Infection; *HACEK* Group; Bacteremia

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Introduction

Cardiobacterium hominis is a fastidious Gram-negative bacterium primarily known for causing infective endocarditis [1–4]. It was first described in 1964 when it was classified as CDC group IID. It has been included as the "C" in the *HACEK* group of fastidious Gram-negative bacteria that are part of the normal human oropharyngeal or urogenital microbiota. The acronym *HACEK* was originally coined to describe a group of fastidious Gram-negative bacteria that are often responsible for patients with smoldering subacute bacterial endocarditis [1,2]. The "*H*" represents *Haemophilus*; the "*A*" represents *Aggregatibacter*, previously *Actinobacillus*; the "*C*" represents *Cardiobacterium*; the "*E*" represents *Eikenella*; and the "*K*" represents *Kingella.* Each of these microorganisms can also cause pyogenic arthritis [5–11]. A recently published review of native joint septic arthritis found members of the *HACEK* group to be the primary pathogen in 27 of 436 (6.2%) infected native joints [12]. We describe the first reported patient with an infected prosthetic knee joint due to *C. hominis* and review the literature for other patients with pyogenic arthritis due to *C. hominis.*

Case Presentation

A 57-year-old man with degenerative joint disease and a left total knee arthroplasty 17 months previously presents to his orthopedic surgeon with a 4–5-day history of the gradual onset of severe left knee pain and redness after performing 5–6 h of yard work the prior day. He went from normal activity one week previously to requiring a walker or wheelchair when he came for the orthopedic visit. He denies injury, tattooing, piercing, dental work, injection drug use or any other risk factor for bacteremia. His past medical history is pertinent for aortic valve replacement in 2003, mitral valve repair in 2006, left total knee arthroplasty in 2018 (17 months prior to this admission) and bovine aortic valve replacement in 2019 (12 months prior to this admission). Examination revealed a swollen, tender and mildly erythematous left knee with palpable joint effusion and a decreased range of motion. The left knee was aspirated and analysis revealed no crystals, negative Gram-stain smear, but a total white blood cell count of 10,771/μL with 95% neutrophils and 5% mononuclear cells. Pain was initially relieved by the aspiration but worsened over the next two days and patient was admitted to hospital; re-aspiration of the knee revealed a white blood cell count of 22,237/μL with 93% neutrophils and 7% mononuclear cells. The remainder of the physical examination was negative, including the absence of heart murmur and absence of any peripheral manifestations of endocarditis. On the second hospital day, the patient underwent operative drainage and debridement of the knee. Surgeons found 30 mL of bloody/purulent material in the knee joint. Patient had extensive irrigation and debridement and polyethylene insert exchange with primary closure. All knee hardware was well-seated and showed no evidence of instability or deep infection. Both blood cultures obtained 20 min apart on the day of admission revealed *Cardiobacterium hominis* on day 3 of incubation. Identification and susceptibility testing was confirmed by the reference laboratory, ARUP Labs (Associated Regional and University Pathologists, Inc.) in Salt Lake City, UT, USA. Both pre-operative knee aspirates and intra-operative fluid cultures remained sterile. Postoperative transesophageal echocardiography showed a normally seated and functioning bioprosthetic aortic valve and a normal native mitral valve with no evidence of vegetation on any structure. The *C. hominis* isolate was susceptible to ampicillin, ceftriaxone, ciprofloxacin, levofloxacin and meropenem. The patient was treated with 6.5 months

total antimicrobial therapy: 6 weeks of parenteral ceftriaxone followed by 5 months of oral cefdanir. He remains well 6 months after completion of antimicrobial therapy.

Review of the Literature

Google Scholar™ and PubMed®searches were conducted using each combination of *Cardiobacterium hominis*/HACEK with septic arthritis, pyogenic arthritis and prosthetic joint infection. References from the search were reviewed and the reference list of each article was also reviewed for similar cases. We found only three case reports of *Cardiobacterium hominis* septic arthritis [13–15]. The patients are summarized in Table 1.

Table 1: *Cardiobacterium hominis* Septic Arthritis—Review of the Literature.

Reference	First Author	Gender	Age (Years)	Infected Joint	Positive Cultures for *Cardiobacterium hominis*	Cardiac Valve Type/Status	Surgery	Antibiotic Rx	Outcome
DMID	Apisarnthanarak [13]	Male	82	Native left knee	2 of 2 blood cultures: day 3 of incubation	Bio-prosthetic MV endocarditis documented: perforation and vegetation on TEE	Multiple knee aspirates	IV Ceftriaxone x 42 days then lifetime suppressive oral cefixime	Survived
MMID	Ducoulombier [14]	Male	64	C4-C5 spondylodiscitis	2 of 3 blood cultures: day 5 of incubation	Vertebral osteomyelitis; Bio-prosthetic AV present without vegetation on TEE	None	IV Amoxicillin x 42 days + IV gentamicin x 7 days	Survived
JIM	Yadava [15]	Male	75	L4-L5 spondylodiscitis	2 of 2 blood cultures; CT-guided culture of L4-L5 disc space	Native MV endocarditis documented; Vertebral osteomyelitis; epidural abscess	None	IV Ceftriaxone x 28 days	Expired after 28 days of IV therapy
Current Report	Otchere	Male	57	Prosthetic left knee	2 of 2 blood cultures: day 3 of incubation	Bio-prosthetic AV present without vegetation on TEE	Surgical drainage of knee with poly-exchange	IV Ceftriaxone x 42 days	Survived
Total	**All**	**4 Male/ 0 Female**	**Mean: 69.5 Years**	**1 Native Knee/ 1 Prosthetic Knee/ 1 C-spine/1 L-spine**	**4 of 4 with + blood cultures; 1 of 4 with + joint culture**	**2 Bio-prosthetic AV; 1 Bio-prosthetic MV; 1 Native MV. 2 of 4 with endocarditis as noted**	**2 of 4 (both knees) requiring aspiration and/or surgery**	**Ceftriaxone in 3 patients; Amoxicillin in 1 patient**	**3 of 4 survived treatment course**

Abbreviations: IV = Intravenous; AV = Aortic valve; MV = Mitral valve; L = Lumbar; C = Cervical; TEE = Transesophageal echocardiogram.

The first patient was an 82-year-old woman with a history of a remotely placed bioprosthetic mitral valve who presented with severe left native knee pain [13]. Left knee aspirate revealed 65,000 WBC/μL, a negative joint fluid culture and two positive blood cultures for *C. hominis*. Transesophageal echocardiogram revealed perforation of the bioprosthetic mitral valve and non-critical mitral regurgitation. The patient was deemed unfit for operative valve replacement and was treated with 6 weeks of parenteral ceftriaxone and lifetime suppressive therapy with oral cefixime.

The second patient was a 64-year-old man with remote (20 years previously) bioprosthetic aortic valve replacement and a 3-month history of gradually worsening upper neck pain. MRI of the spine revealed C4–C5 changes compatible with spondylodiscitis [14]. Two of three sets of blood cultures yielded *Cardiobacterium hominis*. Transesophageal echocardiogram revealed a normally functioning bioprosthetic aortic valve. He completed 6 weeks of parenteral amoxillin and improved dramatically.

The third patient was a 75-year-old man with a 2-week history of dull aching lower back pain. He had a past history of bioprosthetic aortic valve 4 years previously [15]. Physical exam showed fever and tenderness to percussion of lower vertebral area. TEE revealed native mitral valve endocarditis. He was treated with IV ceftriaxone but died at another facility of unknown illness 4 weeks into the treatment course.

Discussion

This is the first reported case of *C. hominis* prosthetic knee infection, the second reported case of *C. hominis* septic arthritis of the knee joint and the fourth reported case of *C. hominis* joint infection when axial joints are included in the review [13–15]. In all four patients including ours, the definitive microbiological diagnosis was made by the isolation of *C. hominis* from multiple blood cultures. In only one patient, the patient with lumbar discitis, was a positive culture for *C. hominis* obtained from the joint itself [15]. This demonstrates the critical need for obtaining blood cultures in any patient with suspected pyogenic arthritis as blood cultures may be the only source for the isolation of the definitive microbiologic pathogen. In infections caused by fastidious bacteria such as *Cardiobacterium*, it may be very difficult to obtain a positive culture from the joint aspirate or surgical tissue specimen.

In two of the previously reported cases of pyogenic arthritis due to *C. hominis,* infective endocarditis was also diagnosed [13,15]. In our patient there was a high suspicion for endocarditis but TEE revealed no definitive evidence of endocarditis. Since our patient required 6 weeks of parenteral antibiotics because of the infected prosthetic joint, we believed that this 6-week course of therapy would be more than a sufficient length of treatment even if the bioprosthetic aortic valve were occultly infected.

From a surgical standpoint in our patient, an incision, debridement and polyethylene exchange were chosen over a one-step complete hardware replacement or a two-step hardware replacement with an antibiotic spacer because both the femoral and tibial components were well-seated and easily debrided. The length of antimicrobial therapy follows the Clinical Practice Guidelines of the Infectious Disease Society of America for patients with well-seated and apparently uninfected tibial and femoral components [16]. The 6-month follow-up of the patient revealed that he was doing well with no evidence of relapse of infection.

Conclusions

C. hominis should be added to the list of organisms that can cause bacteremically spread prosthetic joint infection. Blood cultures may be the only positive diagnostic test and these may require 3–5 days of incubation to positivity rather than the usual 1–2 days of incubation required for other organisms such as staphylococci, streptococci and aerobic Gram-negative bacilli. Since two of the three previously described patients had coexistent infective endocarditis, a thorough search should also be made to identify any coexistent cardiovascular pathology [13,15]. There is no universally accepted length of oral suppressive therapy for Gram-negative peri-prosthetic joint infections. Microorganism characteristics and susceptibility patterns will play a key role in antimicrobial selection by the infectious disease physician [17].

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