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CASE REPORT

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Cardiobacterium hominis endocarditis complicated by aortic root abscess: a case report

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Abstract

The present report describes a case of infective endocarditis complicated with aortic root abscess caused by *Cardiobacterium hominis* in a 56-year-old man. *C. hominis* is a microaerophilic, pleomorphic Gram-negative bacillus and member of the *Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *C. hominis*, *Eikenella corrodens* and *Kingella kingae* (HACEK) group, a group of bacteria known to be a rare cause of endocarditis. With prompt diagnosis and initiation of antimicrobial and surgical management, a successful outcome was achieved.

INTRODUCTION

Cardiobacterium hominis is a fastidious Gram-negative polymorphic bacillus that exists as normal flora of the oropharynx; it has been shown to be present in up to 68% of healthy individuals [1]. The organism is rarely identified as a cause of human infection; it was first identified in this context when it was isolated from four patients with infective endocarditis in 1962 [2]. In addition, it is a member of the *Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *C. hominis*, *Eikenella corrodens* and *Kingella kingae* (HACEK) group, a group of organisms that collectively are believed to be responsible for 1.4–3% of infective endocarditis cases [3].

Although *C. hominis* is of relatively low virulence, endovascular infection complicates 95% of all cases of bacteraemia, with the aortic valve most commonly affected [4]. The extension of infection into the peri-valvular tissue can manifest as abscesses, pseudoaneurysm and fistulae. These complications occur in 10–40% of cases of native valve endocarditis, necessitating urgent surgical management [5].

Infective endocarditis of the aortic valve is a serious, life-threatening condition, with a mortality of 30% at 1 year [6]. Often diagnosis and therefore treatment are delayed by subtle and non-specific presenting symptoms.

The major risk factors for native aortic valve endocarditis include: degenerative valve disease, diabetes, malignancy, intravenous drug use and congenital heart disease [7]. Furthermore, bicuspid aortic valve morphology is a documented independent risk factor for developing *C. hominis* infective endocarditis [8]. Neither intravenous drug use nor infections at another site in the body have been described as risk factors for *C. hominis* endocarditis [9].

CASE REPORT

A 56-year-old man with a past medical history that was significant only for seronegative rheumatoid arthritis and gout was admitted to the Acute Medical Unit (AMU) of the hospital. On admission he reported a history of fever, back pain, lethargy and polyarthralgia affecting the joints of the upper limbs bilaterally for the past 6 weeks.

Two months prior to admission, he had been admitted to a different hospital with acute right-sided quadrantopia, slurred speech and expressive dysphasia; in addition, he reported that in the 2 weeks prior to this event he had been experiencing severe lethargy and night sweats. Imaging revealed left posterior cerebral artery and middle cerebral artery infarcts. Blood tests revealed no pro-thrombotic predisposition, and in addition an echocardiogram was performed, which revealed no abnormality, while further investigations were

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Abbreviations: AMU, Acute Medical Unit; CRP, C-Reactive Protein; E-test, Epsilometer test; HACEK, *Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium. hominis*,*Eikenella corrodens* and *Kingella kingae*; MIC, Minimum Inhibitory Concentration; NVE, Native Valve Endocarditis; PCR, Polymerase Chain Reaction; PVE, Prosthetic Valve Endocarditis; TOE, Trans-Oesophageal Echocardiogram; TTE, Trans-Thoracic Echocardiogram.

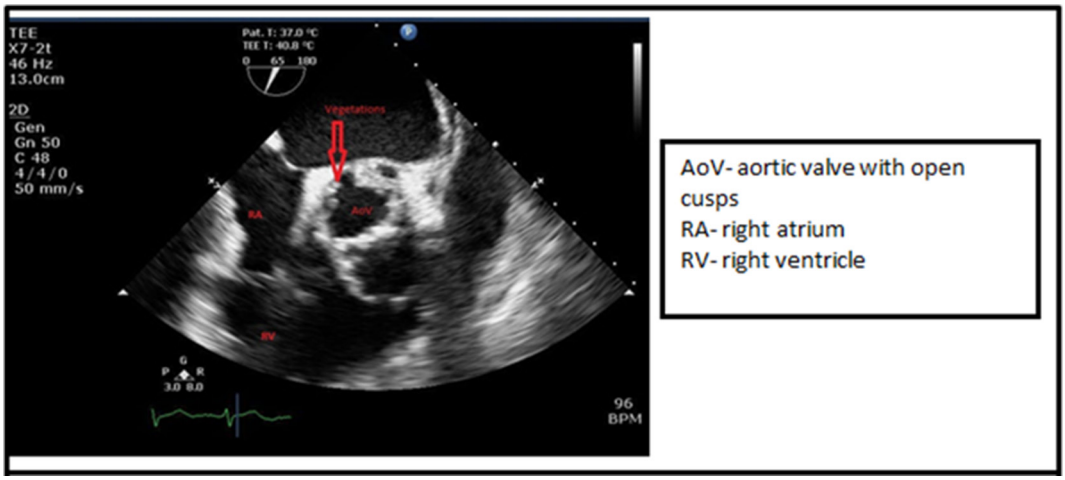

Fig. 1. TOE images demonstrating multiple vegetation attached to the aortic valve and aortic root with dilatation of sinus Valsalva anteriorly; likely to be an abscess cavity.

unremarkable. His C-reactive protein (CRP) was noted to be raised (65 mg l^{-1}) and this was attributed to a rheumatological cause. He was discharged with planned routine follow-up with his rheumatologist and community stroke team.

On examination at the AMU on the day of admission, he was febrile (38.1 °C). Cardiovascular examination revealed a soft S2, a grade III/IV aortic ejection murmur and a grade III/IV diastolic decrescendo murmur at the left lower sternal border. There were no peripheral stigmata of endocarditis present, there was no evidence of congestive heart failure and oral hygiene was unremarkable.

Laboratory investigations revealed a normocytic, normochromic anaemia with haemoglobin of 102 g l^{-1} and elevated inflammatory markers: the erythrocyte sedimentation rate was elevated at 110 mm h^{-1} and CRP was also raised at 76 mg l^{-1}, while the white cell count was measured at 5.2×10^{9} l^{-1} on admission and remained within the normal range throughout the admission.

In view of the presenting symptoms, clinical examination findings and laboratory investigations, an urgent bedside transthoracic echocardiogram (TTE) was performed, and this revealed appearances suggesting 'tiny mobile artefact on aortic cusps with moderate to severe aortic regurgitation and moderate aortic stenosis'. Four sets (aerobic+anaerobic) of blood cultures were taken within the initial 24 h period, and following the collection of these blood cultures intravenous ceftriaxone (2 g daily) and gentamicin (3 mg/kg/day) were initiated empirically, given the strong suspicion of infective endocarditis. On the third day post-admission a transoesophageal echocardiogram (TOE) was performed. The TOE demonstrated 'multiple vegetation attached to the aortic valve and aortic root with dilation of sinus Valsalva

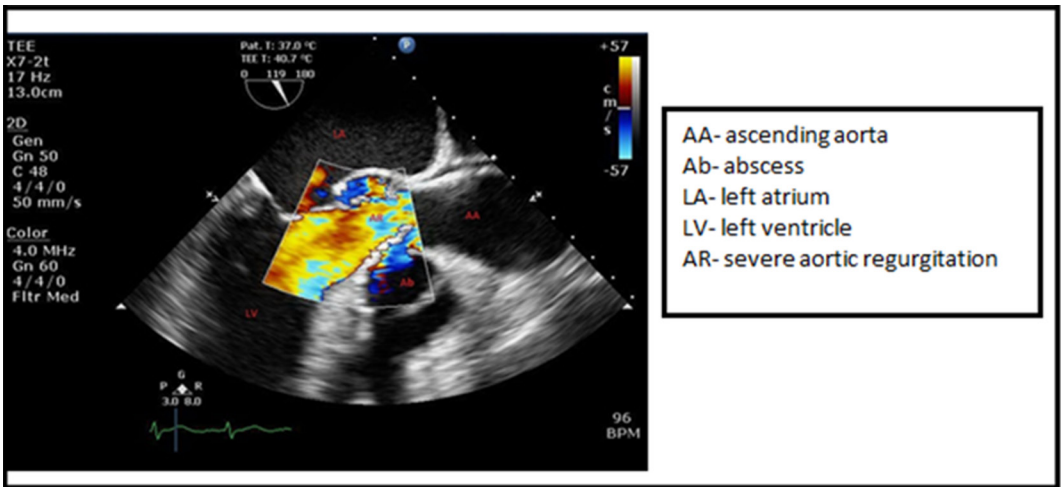

Fig. 2. Severe aortic regurgitation.

anterior, appearances suggestive of an aortic valve abscess', as demonstrated in Figs 1 and 2. The aortic valve morphology appeared to be bicuspid, with one anterior cusp; this morphology is believed to be an independent risk factor for HACEK endocarditis.

Between 65 and 85 h post-blood culture incubation the cultures became positive for slow growing Gram-negative coccobacilli. Three out of four cultures taken became positive. The isolates were identified as *C. hominis* by VITEK NH card. The bacteria were found to be sensitive to amoxicillin, ceftriaxone and gentamicin by the E-test method.

On the basis of the positive blood cultures and TOE findings, the patient was referred to a local cardiac centre for surgical intervention. He underwent successful tissue aortic valve replacement and pericardial patch closure of the aortic root. The aortic valve root debridement tissue culture was sterile, likely due to prior antibiotic effect. Ceftriaxone as a sole antibiotic agent was continued for 6 weeks post-surgery and no complications were reported in the 2 years to the present day, while disease recurrence was not observed.

DISCUSSION

The onset of *C. hominis* endocarditis is insidious, occurring most often following oral infection, dental procedure, or upper gastrointestinal endoscopy [10]. Many patients who develop *C. hominis* endocarditis have a preceding history of severe periodontitis or prior dental procedures without antimicrobial prophylaxis. *C. hominis* is considered to be part of the normal human oropharyngeal microbiota.

Numerous studies have demonstrated the possible association between poor oral hygiene and the development of infective endocarditis [11–13]. Oral commensal bacteria are important aetiological agents of infective endocarditis. It has been demonstrated that both a number of dental procedures and tooth brushing (in those with poor periodontal health) can cause transient bacteraemia of oral commensals [12, 13]. Transient bacteraemia itself will rarely effect otherwise healthy individuals, but in those who have a predisposed risk, such as those with heart valve disease or pacemaker implantation, etc., infective endocarditis may be established.

A randomized control trial conducted by Lockhart *et al.* in 2009 [13] investigated whether poor oral hygiene was a risk factor for developing bacteraemia after tooth brushing or single tooth extraction. The authors determined that infective endocarditis-related bacteraemia was associated with poor oral health and the presence of bleeding after tooth brushing. Bleeding after tooth brushing in particular was associated with an eightfold increase in the risk of developing infective endocarditis-related bacteraemia. The authors concluded that improving periodontal health may reduce a patient's risk of developing infective endocarditis.

A number of papers have attempted to classify the microbiome of the oral cavity and identify bacterial species whose relative prevalence is associated with poor oral health or oral infection [14–17]. On review of the published literature, information regarding the specific association between *C. hominis* and periodontal health proved to be scarce. A study by Colombo *et al.* in 2009 sought to identify micro-organisms that were significantly more prevalent in patients with periodontitis compared to those with good periodontal health [18]. *C. hominis* was among those oral bacteria that were significantly more prevalent in those with good periodontal health.

In order to further explore the potential risk factor presented by poor oral health for the development of infective endocarditis further enquiries were made into the patient's dental history and oral health. He reported that he had undergone no dental procedures in the 5 years prior to admission for endocarditis. He also reported no recent oral infections, or any previous significant oral infections. He stated that he maintained good oral health but did report occasional bleeding of the gums after brushing.

One further association that was noted on review of the literature regarding the significance of *C. hominis* in the oral microbiome. In a study in which the enrichment of certain genera of bacteria in subjects with higher alcohol consumption was noted [19], one of these genera was *Cardiobacterium*, suggesting that heavy drinking may influence the composition of the microbiome. This patient, however, gave no history of alcohol consumption that significantly exceeded the recommended maximum alcohol intake.

However, as previously discussed, the patient was found to have bicuspid aortic valve morphology on echocardiogram. Bicuspid aortic valves are frequent congenital malformations, with multifactorial inheritance patterns [20]. With the significant reduction in rheumatic fever cases in the developed world, it is likely that bicuspid aortic valves will become the most common predisposition for infective endocarditis [21]. It has additionally been demonstrated that aortic root abscesses are also more likely to occur in patients with bicuspid aortic valves [22].

Despite modern imaging techniques and the existence of clinical criteria, clear issues remain with the diagnosis of infective endocarditis using the Duke criteria. The criteria incorporate clinical signs and symptoms, imaging and the results of serological and culture investigations.

The criteria have been suggested to be of lesser value in key patient groups, such as those with prosthetic valve infections and intravenous drug users with right-sided heart infections [23].

The relatively low frequency of 'classic' clinical signs of infective endocarditis, particularly peripheral vascular and immunological phenomena, creates difficulties in clinical diagnosis. Revisions to the original guidelines have attempted to address these difficulties and it is likely that with the emergence of new diagnostic technologies the guidelines will undergo further modifications.

Previous case reports have suggested that blood cultures for *C. hominis* may require extended periods of incubation [24–26].

However, due to the advanced technology in microbiology, the more recent case reports have demonstrated growth of *C. hominis* in less than 5 days [27, 28], as described in the present case. In cases of culture-negative endocarditis, diagnosis has been made through a broad-range polymerase chain reaction (PCR) assay performed on valvular tissue [29].

The often complex diagnostic process demonstrates the importance of an investigative approach that combines facets of clinical judgement and the use of modern laboratory and imaging techniques to provide an integrative diagnosis.

In a study of patients diagnosed with HACEK endocarditis by Das *et al.* [30], *C. hominis* was deemed to be the causative organism in 27% of cases. The clinical course is usually insidious in onset, with a prolonged subacute course in most cases [31]. In the present case, the multiple vegetation and aortic root abscess identified on TOE likely reflected a prolonged chronicity of the illness; this is also in keeping with the timeline of symptomatic illness given by the patient.

Third-generation cephalosporin is the antibiotic of choice for infective endocarditis caused by infection with *C. hominis* [5] [32]. In our patient, the E-test methodology demonstrated susceptibility to ceftriaxone, and in addition sensitivity to ciprofloxacin (MIC) was demonstrated in order to provide an oral option; this has been utilized in a number of described cases where resistance to first-line therapy is present [33]. Current European Society for Cardiology endocarditis guidelines [32] recommend that the standard antibiotic treatment for HACEK organisms is as follows: ceftriaxone 2 g day^{-1} for 4 weeks in native valve endocarditis (NVE) and for 6 weeks in prosthetic valve endocarditis (PVE). If the organism is found not to produce beta-lactamase, (previously HACEK organisms were consistently sensitive to ampicillin, however, increasingly, beta-lactamase-producing strains are isolated), ampicillin (12 g day^{-1} intravenously, divided into four or six doses) plus gentamicin (3 mg/kg/day, divided into two or three doses) for 4–6 weeks is an option. Ciprofloxacin (400 mg 8–12 h^{-1} intravenously or 750 mg 12 h^{-1} orally) is a less well-validated alternative. The American Heart Association guidelines are in concurrence with European guidelines on the use of third-generation cephalosporin, and furthermore, the time frame for treatment is identical. Similarly, the guidelines acknowledge the paucity of data and reports regarding the use of fluoroquinolones as a sole agent in the management of HACEK endocarditis [34].

The presence of aortic root abscess in the present case report was an indication for urgent surgical management. It is likely, given the known insidious course of *C. hominis* endocarditis, that the left posterior cerebral artery and middle cerebral artery infarcts 2 months prior to this patient's admission during which endocarditis was diagnosed were secondary to emboli from an undetected endocarditis. The lack of any other definitive predisposition from blood tests, imaging findings (although only TTE was carried out) and further investigation would perhaps lead us to consider that this initial presentation was a missed opportunity for identifying a potential underlying endocarditis.

C. hominis is infrequently identified as a cause of endocarditis. Although it may clinically present in a similar fashion to other causes of endocarditis, it typically follows a prolonged subacute course. Even without known risk factors, and with a lack of immunological and vascular phenomena, endocarditis should be suspected in cases of fever without origin. The case illustrates the importance of prompt diagnosis and management of *C. hominis* endocarditis, which, when achieved, can result in good outcomes for the patient.

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Conflicts of interest
The authors declare that there are no conflicts of interest.

Ethical statement
Written consent has been obtained from the patient.

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