CASE REPORT

Cardiobacterium hominis Endocarditis in a Healthy Adult - Rare but Not to Be Missed

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ABSTRACT

Cardiobacterium hominis is part of HACEK group and an atypical cause of infective endocarditis. It may cause similar clinical presentation to other cause of endocarditis. Establishing the diagnosis is challenging as it is a fastidious organism which rarely affects individual without previous cardiac lesion and requires advanced diagnostic tools for identification of species. A 23-year-old previously healthy man presented with intermittent fever for two months associated with palpitations and lethargy. He had undergone a dental procedure four months before the presenting symptoms. Physical examination revealed a pansystolic murmur best heard over the apex. Three aerobic blood culture bottles were positive and Gram stain consistently showed pleomorphic Gram-negative rods. The organism grew as tiny pin-point opaque colonies on sheep blood agar and chocolate agar after 48 hours of incubation but no growth was seen on MacConkey agar. Unsuccessful identification with VITEK 2 NH and VITEK 2 GN was later confirmed by polymerase chain reaction as *C. hominis*. He was treated with a six-week course of antibiotics.
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INTRODUCTION

Cardiobacterium hominis is a member of HACEK (*Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens* and *Kingella species*) group, which is fastidious Gram-negative microbiota that is found in the nose, mouth and throat (1-3). *Cardiobacterium hominis* endocarditis is rare and is usually found in individuals with previously diseased or damaged heart valves (3-4). However, it may occur in patients without evidence of previous heart disease (2). *Cardiobacterium hominis* endocarditis commonly follows indolent course of presentation and patients may present with weeks to months of constitutional symptoms (1-2). The identification of *C. hominis* is difficult as it is a slow grower bacterium that appears as very tiny colonies on routine culture media such as sheep blood agar. An enriched media is required to improve its growth. The availability of recent advanced automated blood culture systems such as BacT/ALERT® VIRTUO® (BioMérieux) has enhanced the recovery of *C. hominis*. Besides that, better diagnostic tools such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and PCR amplification of 16S ribosomal DNA has increased the success rate in identifying *C. hominis* (3-5). As growing *C. hominis* can be time-consuming, the susceptibility testing is also difficult to perform. *C. hominis* is generally sensitive to penicillin although beta-lactamase producing isolate has been reported in some literatures (2,4). The clinical outcome is generally good if the organism is identified early and treated appropriately.

CASE REPORT

A 23-year-old gentleman with no known medical illness presented with intermittent fever for two months. He had fever about three to four times per week which resolved spontaneously. He also experienced palpitation even at rest, but there was no chest pain or shortness of breath. There was no history of loss of weight or appetite, night sweats, chills or rigors, cough, lethargy, myalgia or arthralgia, heart failure symptoms such as orthopnoea or paroxysmal nocturnal dyspnoea and lower limb swelling. He had sought treatment at a nearest clinic and was found to have pansystolic murmur. He was then referred to a general hospital for further investigations.

There was no family history of heart problems. He had history of visiting dentist four months ago for a tooth extraction. There was no antibiotic prophylaxis given after the procedure. He denied any history of

intravenous drug use or involvement in any other high-risk behaviours.

On physical examination, he was alert, conscious and not septic looking. His vital signs were stable with heart rate of 86 beats per minute, respiratory rate of 16 breaths per minute and blood pressure of 120/70mmHg. Cardiovascular examination revealed a pansystolic murmur heard loudest over the apex and radiating to the back. Otherwise, other systemic examinations were unremarkable. His electrocardiography (ECG) showed sinus rhythm. An echocardiography was done and demonstrated vegetations (size of 1.19cm x 0.7cm and 0.95cm x 1cm) over the mitral valve leaflet and plate, as well as severe mitral regurgitation. The ejection fraction was 65%. The other remaining heart valves were functioning well with no pericardial effusion or clot/thrombus seen.

His full blood counts and renal profiles were normal. His inflammatory markers were raised with C-reactive protein at level of 59.6 mg/L (normal level < 5.0mg/L) and erythrocyte sedimentation rate at 40mm/hr (normal level < 20mm/hr). He was empirically started on intravenous (IV) ampicillin and intravenous gentamicin.

Three sets of blood cultures were collected prior to commencing the antibiotic therapy. The bottles were loaded in BacT/ALERT Virtuo automated instrument. Three aerobic blood cultures were positive after two days of incubation. There was no growth seen in blood culture from the anaerobic bottles. Gram stain from blood sample showed pleomorphic Gram-negative rod arranged in rosettes (Fig. 1A). The organism grew as tiny pin-point opaque colonies on 5% sheep blood agar and chocolate agar after 48 hours of incubation at 37 oC in 5% CO2 (Fig. 1B), no growth on MacConkey agar and it was positive for oxidase but negative for catalase test. Identification by using VITEK 2 Neisseria-Haemophilus (NH) and VITEK 2 Gram-negative bacilli (GN) identification card (BioMeárieux) failed to identify the bacteria. In view of difficult identification with the available methods in our laboratory, the isolate was sent to a reference laboratory. Polymerase chain reaction (PCR) was done and *Cardiobacterium hominis* was identified.

The patient was well throughout his stay and was continued on intravenous ampicillin and intravenous gentamicin. He was later transferred to another hospital in his hometown to complete the antibiotic therapy for six weeks.

DISCUSSION

Infective endocarditis (IE) is the infection involving the heart valves and endocardium. The three most common etiological agents are Staphylococcus aureus, streptococci and enterococci. Approximately 2-5% of cases of IE are caused by HACEK group organisms (*Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens* and *Kingella species*) (3-4). These organisms reside in the human oral cavity and upper respiratory tract (1,3).

C. hominis is part of the HACEK group and is an uncommon cause of IE. A history of cardiac abnormalities, prosthetic heart valve, previous rheumatic heart disease and dilated cardiomyopathy have been described as predisposing factor for *C. hominis* endocarditis (3-4). A preceding history of dental procedure as well as oral infection will increase the risk of developing infective endocarditis with these organisms (3-5). A traumatised mucosa surface in the oral cavity following a dental procedure especially in those involving manipulation of gingival tissue promotes the entry of such bacteria resulting in bacteraemia. The subsequent adhesion of circulating bacteria to the valvular surface with ability to survive on the surface will propagate as vegetation. As our patient had a prior history of tooth extraction, this factor was likely to be the source of infection in this case. A contaminated endoscopic instrument or injectable contrast material can also cause local infection especially when tissue is breached. However, bacteraemia from gastrointestinal endoscopy carries a rather low risk of getting infective endocarditis (2).

C. hominis is fairly an organism of low virulence (1). No evidence of infection was demonstrated after inoculation of as great as 109 microorganisms was

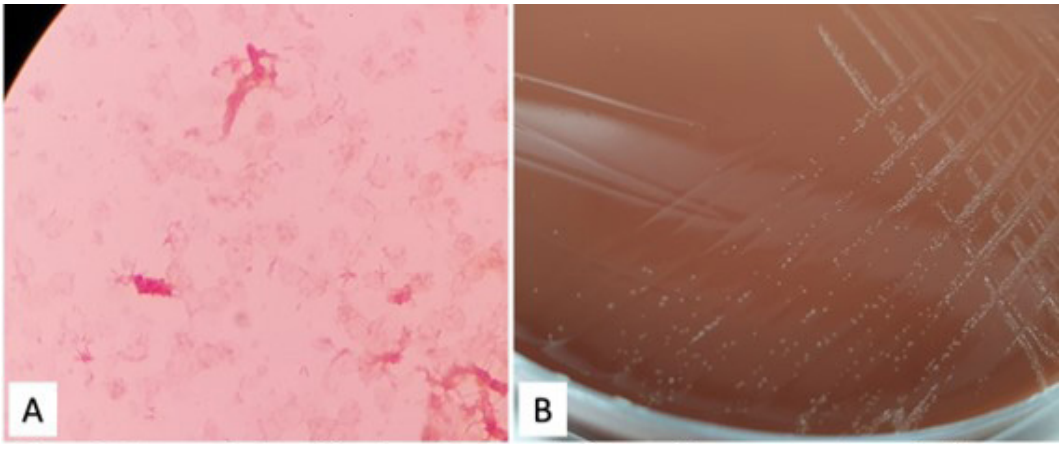

Figure 1: (A) Gram stain from blood sample showed pleomorphic Gram negative rod with rosettes arrangement and (B) organism appeared as tiny pin-point opaque colonies after 48 hours of incubation at 37°C in 5% CO_2

injected into mice, hamsters, guinea pigs, rabbits and pigeons (2). Nevertheless, almost all reported cases of *C. hominis* bacteraemia were complicated with infective endocarditis (1-2). *C. hominis* endocarditis follows a subacute course where infected patients will develop insidious onset of symptoms, ranging from weeks to months (4-5). Several constitutional symptoms being reported in the literatures include lethargy, chills, myalgias, arthralgias, loss of appetite and loss of weight. Although there were no associated constitutional symptoms except for palpitation seen in our patient, he had been feeling unwell for two months prior to seeking medical attention.

C. hominis has been characteristically described as pleomorphic Gram-negative rods that usually seen in pairs, short chains, rosettes or clusters. This bacteria usually grows in standard enriched media and optimal growth is achieved with the presence of 5% CO2. HACEK organisms classically grow slowly and need extended incubation periods. With the current improved culture media and automated culture systems such as BacT/ALERT Virtuo, incubation period of about three to seven days may be sufficient to obtain growth of these organisms (3,5). BacT/ALERT virtuo is an advanced, automated blood culture system that has improved automation and enhanced detection algorithm that help to shorten the time to detection. Diagnosis of *C. hominis* has also been made easier with current diagnostic tools such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and PCR amplification of 16S ribosomal DNA from sample.

Previously reported literature showed that majority of *C. hominis* were sensitive to penicillin. Nevertheless, beta-lactamase-producing *C. hominis* has been described in case reports (2,4). Currently, third-generation cephalosporin has been recommended as the first-line treatment for *C. hominis* endocarditis. Alternatively, combination of ampicillin and gentamicin can be given as treatment. In our case, the patient was treated with ampicillin and gentamicin as he was responding well to the medications.

Endovascular infection complicates 95% of all cases of *C. hominis* bacteraemia, with aortic valve being the most frequently affected. A review on English literatures from 1962 to 2005 on *C. hominis* endocarditis showed aortic valve was infected in 39% (24 out of 61) patients while mitral valve was involved in 31% (19 out of 61) patients (2). Embolism in peripheral and central nervous systems are also commonly seen in *C. hominis* endocarditis, especially when the aortic valve is involved (1,3,4). Large friable vegetation is also seen in *C. hominis* endocarditis (5). Valve replacement was required in more than half of native valve endocarditis involving aortic valve as compared to only few cases in mitral valve involvement (2). In our case, however, the mitral valve was affected and emboli was not seen.

The prognosis of *C. hominis* endocarditis is generally favourable, with cure rate of 93% in both native and prosthetic valve infections (1). A combination of early diagnosis and timely administration of antibiotic has resulted in good outcome in our patient and he responded well to the treatment without complications. A new baseline after completion of antibiotic therapy should be established by performing a transthoracic echocardiography. He should receive education on the possibility of recurrence and proper daily dental hygiene with regular dentist evaluation.

CONCLUSION

Cardiobacterium hominis is an unusual cause of endocarditis in which it may have similar clinical presentation to other causes of endocarditis. It commonly follows a protracted clinical course, with symptoms appear for weeks to months before a diagnosis is made. Even though it is common in adults with pre-existing valvular heart disease, it should be suspected in healthy individuals who had previous history of dental procedure involving manipulation of gingival tissue. Prolonged incubation of blood cultures has often been required in the past as it is slow grower bacteria . However, longer incubation period is no longer needed with the availability of latest automated blood culture system. With current advanced identification system like MALDI-TOF, the turnaround time for the detection of this bacteria will be shorter that will facilitate in prompt management of patients.

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