CASE REPORT

Aggregatibacter actinomycetemcomitans Endocarditis in a Patient with Chronic Periodontitis: A Case Report

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ABSTRACT

The HACEK organisms consist of the non-influenzae *Haemophilus* sp., *Aggregatibacter* sp., *Cardiobacterium* sp., *Eikenella corrodens* and *Kingella* sp. are responsible for a sizable percentage of infective endocarditis cases worldwide with the mortality rate of 18%. Amongst them, *Aggregatibacter actinomycetemcomitans* is the most common pathogen strongly associated with infective endocarditis. *A. actinomycetemcomitans* forms part of the oral microbiota and is also the etiological agent of periodontitis. Here, we present a case of a 37-year-old man with underlying obstructive uropathy, that sought treatment for postural hypotension and symptomatic anaemia with fever. Later, he had developed decompensated congestive cardiac failure with aortic regurgitation. A cardiac echocardiogram revealed the presence of vegetation on the aortic valve. Blood culture grew *A. actinomycetemcomitans*, and he was treated with furosemide and ceftriaxone. A further dental examination showed the patient is having chronic periodontitis, which could be the possible source of *A. actinomycetemcomitans* causing infective endocarditis. The patient was then transferred to the National Heart Centre for the first time for further management after completion of 4 weeks of intravenous antibiotics. As the pathogen is fastidious, rapid and newer technology like MALDI-TOF mass spectrometry provides rapid and accurate identification for appropriate patient clinical management.
Malaysian Journal of Medicine and Health Sciences (2023) 19(2):337-340. doi:10.47836/mjmhs19.2.47

Keywords: 16S rDNA, *Aggregatibacter*, Communicable disease, Malaysia, MALDI-MS

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INTRODUCTION

Infective endocarditis is a rare but severe medical condition for which the diagnostic guidelines are being continuously updated. *Aggregatibacter actinomycetemcomitans*, as one of the HACEK organisms, consists of the non-influenzae *Haemophilus* sp., *Cardiobacterium* sp., *Eikenella corrodens* and *Kingella* sp. is a common cause of culture negative endocarditis and occasionally associated with periodontitis and joint infections (1). The HACEK organisms are slow-growers that require prolonged incubation in CO_2 supplementation (1). This presents a diagnostic challenge to healthcare professionals. Therefore, a new and rapid method for identifying bacteria in a microbiology laboratory is important to guide the clinician for appropriate patient management.

CASE REPORT

A 37-year-old man with underlying ureteric colic and obstructive uropathy presented with giddiness and postural hypotension for one day associated with pallor and reduced effort tolerance for a week. Full blood count showed he was anaemic, and he was transfused with two pints of blood. On admission, he had a temperature spike, and he was treated empirically with cefuroxime after collecting blood culture. He was then discharged after three days of admission as his anaemic symptoms improved and he remained afebrile.

The aerobic blood culture bottle was positive after 48 hours of incubation; however, no organism was seen via Gram stain. Blood was sub-cultured on blood and chocolate agars, and the blood culture bottle was re-

incubated into the BACTEC system (BD company, United Kingdom). Small, whitish star-like colonies were observed on blood and chocolate agars after 48 hours of incubation at 37°C in CO_2 (Figure 1). Repeated Gram-stain from the aerobic blood bottle after re-incubation of 48 hours yielded Gram-negative coccobacilli, which appeared singly and in pairs (Figure 2). *A. actinomycetemcomitans* was identified using the matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry (Score value: 2.41) (BRUKER, United States) and confirmed by 16S rDNA sequencing (Accession no. LR899004). Anaerobic blood culture bottle was negative after 5 days of incubation. Blood culture result was informed to the managing team in the ward, and the patient was called for readmission for antibiotic treatment. He was started on intravenous ceftriaxone 2 grams once daily for *A. actinomycetemcomitans* bacteraemia.

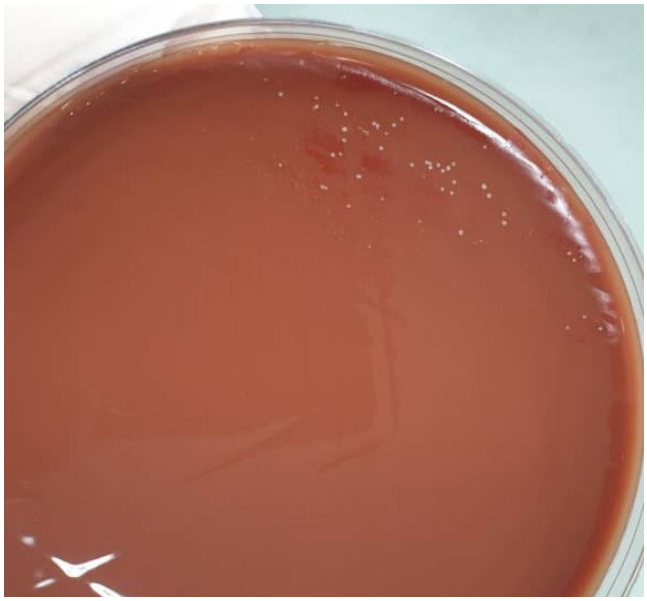

Figure 1: Culture of *A. actinomycetemcomitans* after incubation for 48 h which showed colonies which were small and star-lik in appearance

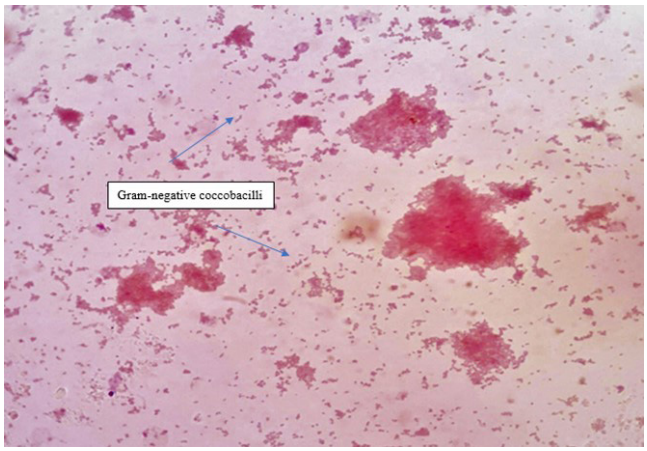

Figure 2: Gram stain of *A. actinomycetemcomitans* after incubation for 48 h which showed gram-negative coccobacilli that appeared singly and in pairs.

Upon further questioning during readmission, he had an episode of shortness of breath, generalized body weakness with orthopnoea, and bilateral lower limb oedema after being discharged from the ward. He denied chest pain or palpitation, and his bowel habit was normal. There was no haemoptysis, haematuria nor haematemesis, prolonged fever, respiratory tract infection or urinary tract infection. No history of drug abuse or recent traveling, and he denied having recent dental intervention or manipulation.

He was afebrile, alert, non-tachypnoeic, non-jaundiced but pale-looking with adequate hydration on clinical examination. Vital signs showed he was tachycardic (112 bpm), borderline hypotensive (104/64 mmHg) and pulse oximetry was 98% under room air. Corrigan pulse was detected, and a collapsing pulse was felt on palpation. No skin lesions nor lymphadenopathy were noted. On auscultation, an early systolic murmur was heard at the aortic region, and there was pan-systolic murmur at the mitral area radiating to the axilla. There were bi-basal crepitations with reduced air entry into bilateral lungs. Abdominal examination revealed no abnormality, no splenomegaly, and no bilateral pedal oedema were noted. Initial laboratory values showed a haemoglobin level of 7.6 g/L possibly secondary to chronic inflammation due to endocarditis; white blood cell count of 14,300 cells/mm^3 with a differential of 68.5 % neutrophils, 23.9 % lymphocytes, and 5.9 % monocytes with the C-reactive protein value of 81.5 mg/L which may indicate the presence of ongoing infection and inflammatory process. Cardiac echocardiogram showed ejection fraction of 39% with global left ventricular hypokinesia, severe aortic regurgitation, moderate tricuspid regurgitation, mild mitral regurgitation, mild left ventricular hypertrophy, and mild pericardial effusion over the anterior region with underlying bicuspid aortic valve.

A few days after readmission, he developed worsening breathlessness associated with diaphoresis, with oxygen saturation dropping to less than 90%. He was then intubated for airway protection in view of acute respiratory distress with severe respiratory acidosis, and he was started on intravenous infusion of noradrenaline for the hypotensive episodes. An internal jugular catheter was inserted, and chest radiography revealed cardiomegaly with haziness was noted over the bilateral lower zones. Electrocardiography revealed sinus tachycardia with ST depression over the inferior and lateral lead and reciprocal ST elevation over the anterior septal lead.

Repeated cardiac echocardiogram revealed vegetation on the aortic valve and dilated cardiomyopathy was observed. The diagnosis was then revised to Aggregatibacter endocarditis on the aortic valve with acute pulmonary oedema secondary to dilated cardiomyopathy with poor left ventricular function.

Blood culture was repeated in which three sets of blood cultures sent were negative after five days of incubation. He was referred to National Heart Centre for the first time for further management and was reviewed for dental clearance as requested by the Cardiology team upon the referral. Oral examination revealed chronic periodontitis with plaque-induced gingivitis. He responded well to the furosemide and ceftriaxone and was able to wean off the oxygen supply after three weeks of admission. He was then transferred to the National Heart Centre after completion of intravenous ceftriaxone for 28 days.

DISCUSSION

A. actinomycetemcomitans was first described as a human pathogen in 1912 when it was isolated from the pus culture of patients with actinomycosis of the jaw. This pathogen is a fastidious, gram-negative coccobacillary organism that colonizes the human upper respiratory tract, and it can be found in 25–30% of adults (1). Due to its fastidious nature, *A. actinomycetemcomitans* usually causes sub-acute or chronic endocarditis with prolonged symptomatic period (mean duration of 13 weeks) before diagnosis is confirmed by blood cultures after prolonged incubation for at least five days. Fever is present in most cases. Besides that, the other common clinical findings noted were anaemia, weight loss, peripheral stigmata of endocarditis, and microscopic haematuria (1). Even though the patient in this case presented with fever and symptomatic anaemia during his initial admission, endocarditis due to HACEK organism was not suspected and he was not further investigated to look for the source of endocarditis. The patient was further investigated and treated with appropriate antibiotic after blood culture positive for *A. actinomycetemcomitans*.

Blood culture remains the gold standard of diagnosis even though the fastidious growth requirement of the organism may delay the microbiological diagnosis (1). As for this patient, dental examination revealed chronic periodontitis with plaque-induced gingivitis which could be the possible source of *A. actinomycetemcomitans* endocarditis. *A. actinomycetemcomitans* is a significant cause of periodontitis in which the bacteria are found in the periodontal pockets of adults with refractory periodontitis and a majority of patients with localized aggressive periodontitis. Even though *A. actinomycetemcomitans* entry into the bloodstream has never been demonstrated, only a thin layer of crevicular epithelial cells separate the gingival tissues from the parenteral space of the host and, unintentional introductions may occur during tooth brushing or injuries, and maybe hastened by the presence of periodontitis (2).

Besides, the isolation of *A. actinomycetemcomitans* from other sterile body fluids as reported in cases of soft tissue infections, osteomyelitis, septic arthritis, spinal epidural abscess, pneumonia, empyema, pericarditis as well as urinary tract infections (1) suggests that the pathogen journeys from the oral cavity through the bloodstream to cause systemic infection. This is most likely the explanation for the origin of the *A. actinomycetemcomitans* endocarditis in our patient. Vertical and horizontal transmissions of *A. actinomycetemcomitans* are also possible as evidenced by the frequent detection of the organism from periodontal culture among family members of infected individuals as well as clonal spread of the organism within families (3).

The aortic valve is most commonly involved with the bicuspid aortic valve as the site of heart lesions (4). As a result of the endocarditis, the patient in this case developed decompensated congestive cardiac failure (ejection fraction of 39%) with aortic regurgitation that required surgical intervention. This is consistent with the findings of Paturel et al. (2004), where surgery was required in 82% of *A. actinomycetemcomitans*-associated endocarditis cases that resulted in severe complications such as heart failure, embolism, and peri-annular abscess formation (4).

Currently, the American Heart Association (AHA) and the European Society of Cardiology (ESC) guidelines for managing patients with endocarditis recommend the use of intravenous antibiotics for the duration of 4-weeks. Ampicillin is no longer the first-line treatment option as some HACEK group bacilli produce beta-lactamases. Thus, intravenous ceftriaxone monotherapy is recommended for endocarditis caused by HACEK organisms. Alternative drugs such as ampicillin/sulbactam or ciprofloxacin may be used only when the isolate is susceptible (5). This patient responded well to ceftriaxone, evidenced by the reduction in the vegetation size from 0.4 cm^2 to 0.21cm^2. Surgical intervention was required for him as he had decompensated heart failure complicated with severe valvular incompetence.

CONCLUSION

In conclusion, infective endocarditis due to the HACEK group should be suspected in a patient with underlying heart abnormality with evidence of chronic periodontitis. As the pathogen is fastidious, prolonged incubation may be needed, and newer technology like MALDI-TOF mass spectrometry or 16S rDNA is able to give accurate and rapid identification of the pathogen to guide clinicians for the proper management of the patient as well as to reduce the morbidity and mortality.

ACKNOWLEDGEMENT

This study was supported in part by funding from the University of Malaya Research University Grant-Tropical Infectious Diseases Programme (RU005-2020 and RU002-2019) and the UMCoE Top 100 Research Grant (UM.00000188/HGA.GV).

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