Journal of Microbiology, Immunology and Infection (2017) 50, 557–558

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Aggregatibacter aphrophilus culture-negative endocarditis diagnosed by 16S rRNA gene sequencing in excised mitral valve — A case report

Dear Editor,

We read with great interest the article by Cheng et al.,[1] published in the Journal of Microbiology, Immunology, and Infection, who reported a rare case of non-typhoidal *Salmonella* infective endocarditis (IE). The authors reviewed published IE studies including at least 500 cases between 1976 and 2014 and found that non-typhoidal *Salmonella* was the predominant gram-negative pathogen other than HACEK (acronym for *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella* species) that cause native valve endocarditis. Among the references reviewed in the article, fastidious HACEK was rarely reported in culture-proven gram-negative IE using traditional culture methods.[1] This reminds us the possibility that culture-negative IE caused by fastidious bacteria could be under-recognized and improvement of diagnostic accuracy is warranted. Herein, we reported a case IE due to *Aggregatibacter aphrophilus*, which was identified by 16S rRNA sequencing as the culprit pathogen in the excised valve tissue.

Case report

A 47 year-old male without previous medical history was admitted to a university hospital in Tainan with a 2-week history of intermittent fever, chills, and decreased urine output. A grade 4/6 systolic murmur over the apex radiating to axillary area and back was noted on cardiac auscultation. Fundoscopic examination revealed Roth's spots at left eye. Transesophageal echocardiography revealed a vegetation located at posterior leaflet of mitral valve. Six sets of blood cultures were sterile. He was empirically treated by ceftriaxone and vancomycin, followed by ciprofloxacin and teicoplanin, and then daptomycin and ertapenem due to recurrence of cutaneous drug eruptions. After defervescence, he underwent mitral valve repair with ring annuloplasty. Mitral valve endocarditis was confirmed pathologically. Gram stain and valvular tissue culture failed to identify any microbe. The diagnosis of *A. aphrophilus* infection was made by 16S rRNA polymerase chain reaction (PCR) and sequencing. The partial sequences of the amplified fragment were 99.0% identical to the 16S rRNA gene of *A. aphrophilus* ChDC A108 (accession number KF933760). He was discharged uneventfully 16 days later after cardiac surgery and recovered without sequels.

HACEK IE is difficult to diagnose since the growth of bacteria are fastidious. Therefore, the chance of identifying those pathogens in blood cultures or valvular tissues is probably low.[2] For IE patients without conclusive microbiological evidences, 16S rRNA PCR with sequencing is an alternative choice in addition to conventional culture methods. Previous studies show that this method has superior sensitivity compared to Gram stain or culture methods for pathogen identification in valve samples obtained from surgically treated IE patients.[3]

Despite the rarity, *A. aphrophilus*, one of the HACEK species, has been reported to be responsible for invasive infections, including brain abscess, liver abscess, osteoarticular infection, and infective endocarditis.[4,5] Antibiotic choices for *A. aphrophilus* include third-generation cephalosporins or fluoroquinolones.[5] Correct identification of causative pathogens could avoid unnecessary antibiotic exposure in IE patients. In this regard, sequencing of PCR-amplified 16S rRNA of valve tissue is recommended for culture-negative IE patients undergoing valve surgery.

http://dx.doi.org/10.1016/j.jmii.2016.10.002

Conflicts of interest

All the authors have nothing to disclose.

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Yu Liao
Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

Chwan-Yau Luo
Department of Surgery, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

Wen-Chien Ko
Po-Lin Chen*
Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

*Corresponding author.
E-mail address: cplin@mail.ncku.edu.tw (P.-L. Chen)

2 October 2016
Available online 29 June 2017