증 례

A Case of Subacute Infective Endocarditis Caused by *Arcanobacterium haemolyticum* in a Patient with Mitral Valve Prolapse

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승모판탈출증 환자에서 발생한 *Arcanobacterium haemolyticum*에 의한 아급성 심내막염 1예

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Recently, we experienced a case of subacute infective endocarditis caused by *A. haemolyticum* on mitral valve prolapse complicated with systemic emboli, which was successfully treated with antibiotics and valve replacement surgery. To our knowledge, this is the first report to address infective endocarditis caused by *A. haemolyticum* in a immunocompetent patient who had mitral valve prolapse and survived with successful treatment. Greater awareness of this uncommon organism is needed to make an accurate diagnosis and perform a better clinical management in the early stage of the disease. Recommendation for the treatment of septic *A. haemolyticum* infections has not been established. Therefore, the treatment should be based on clinical experiences and *in vitro* susceptibility profiles of the individual strain. The site of infection as well as antimicrobial susceptibility profiles should be considered for appropriate antibiotics choice and decision to perform a surgical intervention.

Key Words : *Arcanobacterium haemolyticum*, Endocarditis, Mitral valve prolapse, Surgery

INTRODUCTION

Arcanobacterium haemolyticum has been implicated mainly in non-streptococcal pharyngitis and wound infections. Rarely, it has been reported to cause systemic or deep-seated infections, such as endocarditis, osteomyelitis, meningitis, and sepsis in patients with predisposing conditions, often in combination with other pathogens (1-4). Recently, we experienced a case of subacute infective endocarditis caused by *A. haemolyticum* on mitral valve prolapse complicated with systemic emboli, which was successfully treated with antibiotics and valve replacement surgery. To our knowledge, this is the first report to address infective endocarditis caused by *A. haemolyticum* in a immunocompetent patient who had mitral valve prolapse and survived with successful treatment.

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CASE REPORT

A 36-year-old woman was admitted to our hospital in July 2005 for intermittent fever with chill, general weakness, weight loss (14 kg for 4 months), multiple arthralgia and recurrent migrating soft tissue swelling on both feet, ankle joints and hands for 4 months.

Four months earlier, she had been diagnosed with mitral valve prolapse and mitral regurgitation on echocardiogram. She had no recent history of dental extraction or periodontal manipulation. On presentation, she appeared chronically ill-looking and had body temperature of 36.3℃, blood pressure of 100/70 mmHg, pulse rate of 98 beats/min, and respiratory rate of 20/min. A physical examination revealed slightly anemic conjunctivae, systolic murmur, and soft tissue swelling in left foot dorsum and right sole, which were accompanied with erythema and tenderness. Initial laboratory findings were; a white blood cell count of 12,200/uL with 78% of segment neutrophils, a hemoglobin of 11.2 g/dL and a platelet count of 200,000/uL. The results of electrolytes and liver function tests were normal except for hypoalbuminemia (3.0 g/dL). C-reactive protein level was 6.33 mg/dL (normal range, <0.3 mg/dL). Although there was no interval change in mitral valve prolapse with mitral regurgitation and no definite vegetation on transthoracic echocardiogram, we could not exclude the possibility of infective endocarditis. We performed blood cultures and started empirical antibiotics with ceftriaxone and gentamicin. Five days later, two sets of blood cultures showed gram-positive bacilli, which formed small colonies (diameter on 0.5 mm) with a narrow zone of hemolysis. It was catalase and urease negative, reverse CAMP test positive, nonmotile and did not ferment mannitol or xylose. It was identified as *A. haemolyticum* by the API Coryne strip (BioMérieux, France). In vitro antimicrobial susceptibility testing interpreted by clinical and laboratory standards institute (CLSI) breakpoint for *Staphylococcus aureus* (5), showed that the isolate was susceptible to penicillin, oxacillin, cephalothin, clindamycin, erythromycin, ciprofloxacin, teicoplanin and vancomycin, but resistant to gentamicin and arbekacin. Fever subsided after administration of antibiotics. Follow-up blood culture on the 5th day revealed no microorganism. However, on the 10th hospital day, she complained of sudden left flank pain and painful swelling of left index finger (Figure 1). On the 12th hospital day, visual acuity of her right eye decreased and improved 2 days later. Although the Arcano-

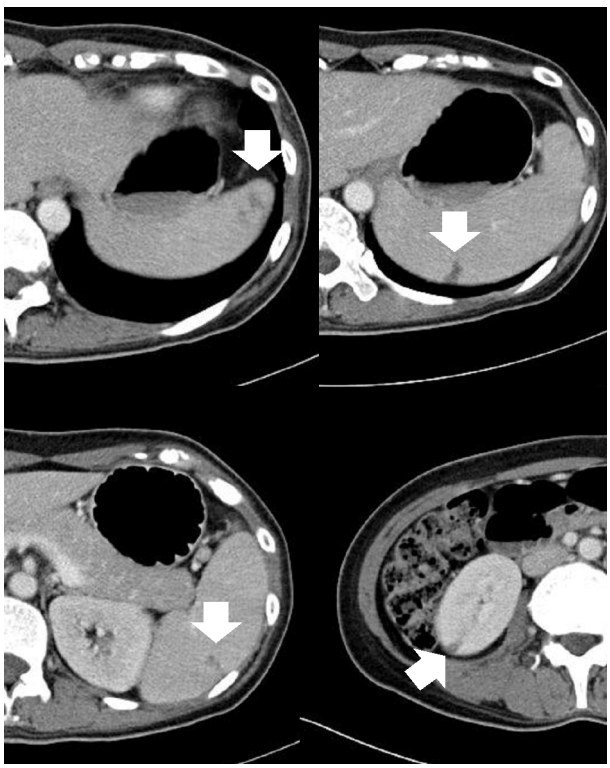

Figure 2. The abdomen CT scan showed borderline hepatosplenomegaly and multiple small low density foci (arrow) in spleen and kidney.

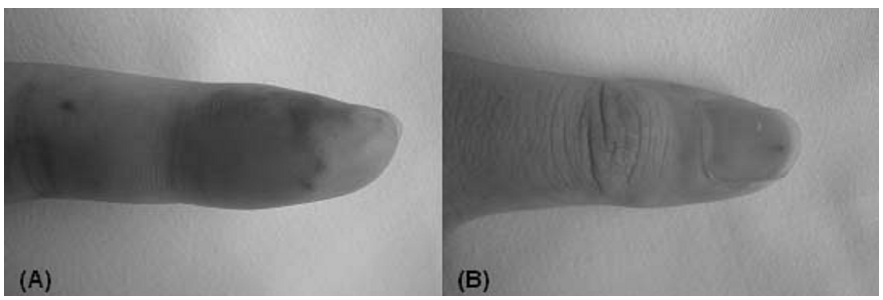

Figure 1. Oslers node A) on the pad of index finger and splinter hemorrhage B) in nail bed.

bacterium from this case was susceptible to the antibiotics used and negative conversion of blood culture had been achieved, clarithromycin was added. Because there was a report that treatment failure attributed to tolerance and failure of antibiotics to penetrate the intracellular location of the pathogen (6, 7). Abdomen CT scan showed borderline hepatosplenomegaly and multiple small low density foci in spleen and kidney (Figure 2). Brain MRI revealed small multifocal enhancing nodules in both periventricular and subcortical white matter on gadolinium enhanced T1WI, suggesting septic emboli. Transesophageal echocardiogram showed multiple small echogenic masses on the chordae tendinae and severe mitral regurgitation (MR). Though there was no sign of congestive heart failure, we made consultation to the chest surgeons for surgical correction in consideration of severe MR and the risk of recurrent embolism. On the 37^{th} hospital day, mitral valve replacement surgery and valvuloplasty of tricuspid valve was done. Ten months after surgery, she is doing well with coumadinization and has no sequelae associated with microemboli.

DISCUSSION

A. haemolyticum is facultatively anaerobic, catalase-negative, gram-positive rod with variable morphology depending on the growth media and conditions. *A. haemolyticum*, formerly known as *Corynebacterium hemolyticum*, was first isolated from nasopharynx and skin of American soldiers in the south pacific in 1946 (8). It was elevated to the genus *Arcanobacterium* on the basis of genetic analysis in 1982 (9). It has been known as an important cause of pharyngitis in adolescents and young adults, frequently causing an exanthema which usually resolve within a few days with or without therapy. Serious infections such as brain abscesses, meningitis, septicemia, endocarditis and osteomyelitis occur less frequently but are fatal if not treated promptly. In Korea, five cases of wound infection and peritonsillar abscess and one case of sepsis in diabetes patient has been reported (10, 11). Also, outbreak of pharyngitis with skin rash in middle school children in a regional area was confirmed to be arcanobacterial infection. Although it is an etiological agent of distinct human infections, the organism is frequently overlooked, probably because laboratories of microbiology tends to report diphtheroid organisms of Corynebacterium species as contaminants or normal flora, resulting in missed or delayed diagnosis. A correct identification and susceptibility testing of antibiotics for such isolates are essential for the proper management of infected individuals, especially with deep seated infection.

Recommendation for the treatment of septic *A. haemolyticum* infections has not been established because there are practically insufficient amount of cases to conduct prospective clinical trials. Therefore, the treatment should be based on clinical experiences and in vitro susceptibility profiles of the individual strain. As mentioned above, when treatment failure to antibiotics susceptible in vitro testing was suspected, macrolides or clindamycin in combination with rifampin or gentamicin should be considered (12, 13). Moreover, for patients with endocarditis or osteomyelitis, where the site of infection may prevent adequate drug penetration, the surgical removal of infected tissue should also be considered to eliminate the infection focus as in our patient. Also evaluation for organisms reported to produce co-infection, such as Epstein-Barr virus (EBV) and *Mycoplasma pneumoniae*, should be done. Our patient showed no evidence of infection by EBV, *M. pneumoniae* and had a negative result for autoimmune studies. The causes of death in previously reported endocarditis caused by *A. haemolyticum*, were cardiac arrest resulting from progression of congestive heart failure and fatal neurologic complication associated with septic embolism (2, 3).

In conclusion, greater awareness of this uncommon organism is needed to make an accurate diagnosis and perform a better clinical management in the early stage of the disease. The site of infection as well as antimicrobial susceptibility profiles should be consi-

dered for appropriate antibiotics choice and decision to perform a surgical intervention.

ABSTRACT

*Arcanobacterium haemolyticum*은 주로 청소년이나 젊은 연령층에서 인후염을 일으키나, 드물게 피부·창상감염, 골수염, 수막염, 심내막염, 패혈증과 같은 심부감염을 일으키기도 한다. 최근 저자 등은 승모판탈출증이 있던 환자에서 전신 색전을 동반한 *A. haemolyticum*에 의한 아급성 심내막염으로 항생제 투여와 판막치환술로 성공적으로 치료한 예를 경험하였다. 이는 면역능력이 정상인 환자에서 발생한 *A. haemolyticum*에 의한 심내막염으로 수술적 치료를 병행하여 성공적으로 치료된 첫 증례로, 문헌고찰과 함께 보고하는 바이다.

*Arcanobacterium*이 심부감염을 일으킬 수 있다는 것이 점차 알려지면서 최근 보고가 늘고 있으나, 아직까지 항생제 감수성 검사 기준이나 치료 지침이 정해진 바가 없다. 따라서 관심을 가지고 정확한 균종 동정을 위한 노력이 필요하고, 각 균주에 대한 감수성 검사를 토대로 질환 초기에 적절한 항생제가 투여될 수 있도록 하며 동시에 감염 부위를 고려하여 수술적 치료의 병행 여부를 결정하는 것이 중요하겠다.

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