Winning the Battle Against Pseudomonas aeruginosa Endocarditis: A Case Report

Pseudomonas aeruginosa Endokarditine Karşı Savaşı Kazanmak: Vaka Sunumu

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Abstract

Infective endocarditis is a major risk for patients with congenital heart disease and has high mortality and morbidity rates, even though there have been many advances in antimicrobial therapy and surgical intervention techniques. Gram positive microorganisms, such as staphylococcus and streptococcus species, are the most commonly isolated organisms. *Pseudomonas aeruginosa* is a rare causative organism for infective endocarditis. It usually affects the right side of the heart, which is usually seen in intravenous drug users. Incidence of pseudomonas endocarditis has increased due to a higher frequency of drug abuse, heart surgery and bacteremia. Mortality from pseudomonas infective endocarditis remains high despite optimal use of available antibacterial agents and also the treatment plan is very challenging as there is no consensus to date. We report a patient with tetralogy of Fallot and recurrent *P. aeruginosa* endocarditis after corrective cardiac surgery. We wish to emphasize the importance of surgical intervention and also recall the significance of lenghtening the antipseudomonal combination therapy.

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Key words: Infective endocarditis, congenital heart disease, pediatric

Özet

Enfektif endokardit, konjenital kalp hastalığı bulunan hastalarda, antimikrobiyal ve cerrahi alanında olan gelişmelere rağmen önemli bir morbidite ve mortalite nedenidir. Stafilokok ve streptokok gibi gram pozitif mikroorganizmalar en sık izole edilen etkenlerdendir. *Pseudomonas aeruginosa* enfektif endokarditin nadir görülen patojenlerindendir. Genellikle ilaç bağımlılarında görülmektedir ve kalbin sağ tarafını etkilemektedir. Artan ilaç bağımlılığı, kalp cerrahisi ve bakteriyemi nedeniyle pseudomonas endokarditinin sıklığı da artış göstermiştir. Pseudomonasa bağlı enfektif endokarditin yol açtığı mortalite, uygun antimikrobiyel ajanların kullanımına rağmen halen yüksek seyretmektedir ve tedavi planı üzerinde henüz tam olarak uzlaşılamadığından zorlayıcı olmaya devam etmektedir. Bu vaka sunumunda Fallot tetralojisi olan bir hastanın cerrahi sonrası tekrarlayan *P. aeruginosa* endokarditi sunularak cerrahinin ve antipsödomonal kombinasyon tedavinin uzatılmasının önemi vurgulanmıştır.

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Anahtar kelimeler: İnfektif endokardit, konjenital kalp hastalığı, pediyatrik

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Introduction

Infective endocarditis is an infection of the endocardial surface of the heart which is a major problem for patients with congenital heart disease and has high mortality and morbidity rates despite advances in antimicrobial treatment and surgery (1). Gram positive microorganisms such as staphylococcus and streptococcus species are the most common causative organisms. *Pseudomonas aeruginosa* is rarely reported as an etiological agent for infective endocarditis. It

usually affects the right-side of heart, which is encountered in intravenous drug users. Other rare conditions that might cause pseudomonas endocarditis are heart surgery and *P. aeruginosa* bacteremia (2,3).

Treatment of *P. aeruginosa* endocarditis is a point of discussion and as yet there has been no concensus on treatment. In our case, the importance of surgical intervention and the significance of lenghtening the antipseudomonal combination therapy in case of pseudomonas endocarditis is emphasized.

Case Report

A 2-year old boy was admitted to our hospital with the diagnosis of Fallot Tetralogy for corrective surgery and complete correction was made and a patch was used for the ventriculoseptal defect. Seven days after the operation, he became febrile and no vegetation or collection was detected by transthoracic echocardiographic scans performed on the same day. The white blood cell count was 28 x 10^9 / L, C-reactive protein was 8.6 mg/dL (N:0-0.8), and erythrocyte sedimentation rate was 10 mm/hour. Blood cultures were taken and sulbactam-ampicillin and amicasin therapy was started empirically. *Pseudomonas aeruginosa* was isolated from blood culture. His antimicrobial therapy was then arranged as meropenem and amikacin Repeated blood cultures on 10^{th} and 13^{th} postoperative days (first and third day of meropenem and amicasin therapy) also revealed *P. aeruginosa*. On the fourth day of meropenem and amikacin, he became afebrile. Control blood cultures were negative after the fifth day of anti-pseudomonal therapy. Antibiotics were stopped after day 28 of treatment and he was discharged.

Two months later, he became febrile again. There was vegetation on the patch on control transthoracic echocardiography and therapy for infective endocarditis was started - as vancomycin, ceftazidime and netilmicin empirically because of previous *P. aeruginosa* endocarditis, and on the third day of hospitalization pseudomonas was isolated from blood culture once again and ceftazidime was changed to meropenem according to susceptibility result of the culture. On the third week of therapy, ciprofloxacin was added to the therapy regimen due to persistance of vegetation on echocardiograpy. At the second month of therapy, because of persistance of vegetation on the patch, vegetation on the tricuspid valve and patch was removed and a new patch was placed. After an additional 34 days of meropenem, ciprofloxacin and aminoglycoside therapy, the patient was discharged.

One month after discharge, the patient was readmitted to our hospital with the complaint of fever. A transthoracic echocardiography revealed vegetations in the right ventricle. Meropenem and amikacin therapy was initiated and *P. aeruginosa* was isolated once more. Surgery was performed on the third day of hospitalization and vegetations from the right ventricle were removed and also *P. aeruginosa* was isolated from surgical material. He became afebrile after surgery and therapy was modifed to ceftazidime, amikacin and ciprofloaxcin. He was discharged after 68 days of antimicrobial therapy.

There was no relapse after this combination of prolonged medical therapy and surgical treatment at 6 months follow up period.

Discussion

Gram-negative bacilli are responsible for 5.3-12% of endocarditis. *Pseudomonas aeruginosa* is present in 30 to 50% of these cases and the majority are observed in intravenous drug users. Also, patients with catheters and prosthetic heart valves are at increased risk for *P. aeruginosa* endocarditis (4). In a study by Ishiwada et al, *P. aeruginosa* was found to be responsible for 2.1% of infective endocarditis of patients with congenital heart disease (2). Risk factors for pseuodomonas endocarditis are valvular heart abnormalities, congenital heart diseases, heart surgery, intravenous drug usage, presence of central catheters, hemodialysis, cardiac catheterization, gastrointestinal and genitourinary procedures (5).

P. aeruginosa usually affects tricuspid valves and the right ventricle, causing symptoms and signs of septic pulmonary emboli. Management of *P. aeruginosa* endocarditis is difficult, especially when causing left-sided disease, as infection is acute, aggressive and poorly responsive to antibiotics. There is no consensus on the duration of antibiotic therapy. In our case, the antimicrobial therapy period was 21 days in the initial course, 34 days in the first relapse and 68 days in the last attack supported by surgical intervention. In case of pseudomonal endocarditis, failure of treatment could be caused by the emergence of resistance during the period of therapy and might also caused by discordance of in vitro and *in vivo* antimicrobial susceptibilities (6). Recent studies suggest that left-sided *P. aeruginosa* infective endocarditis is an aggressive disease with mortality rates ranging from 50 to 85% in patients treated with medical therapy alone. One of the challenging aspects of pseudomonal endocarditis treatment is the requirement of higher concentration of antimicrobial agents, as penetration of the antimicrobial agent is decreased to the bacterial cell because of polyanionic glycocalyx biofilm formation of *P. aerugi-*

nosa (7). It is stated that reduced antibiotic penetrance within left-sided vegetations contributes to strikingly higher mortality of left-sided disease compared to right sided disease (8).

Medical treatment is usually composed of a combination of two anti-pseudomonal agents, usually an extended-spectrum penicillin with an aminoglycoside. Meropenem has the broadest antibacterial spectrum of any β-lactam agent available and has greater intrinsic activity in vitro against clinical isolates of *P. aeruginosa* than quinolone and comparable anti-pseudomonal β-lactam antimicrobials such as ceftazidime and piperacillin (9). One of the advantages of β -lactam antimicrobials is their ability to reach high concentrations within vegetations and this is important for treatment success (8). Aminoglycoside and β-lactam antibiotics have demonstrated *in vitro* synergy in endocarditis caused by *P. aeruginosa* (10).

In our case, carbapenem plus aminoglycoside therapy is not eradicative in the repeated episodes and in the last attack cure was achieved by anti-pseudomonal β-lactam, quinolone and aminoglycoside combination with a long course of therapy in addition to surgery.

We would like to notify that pseudomonal endocarditis with prosthetic or foreign material could not be eradicated without surgical removal. Even after surgical removal, anti-pseudomonal therapy should be prolonged to prevent relapses. When antimicrobial therapy is a matter of concern, quinolones could be an option as a combination agent even in children.

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