





Case Report

A Late Prosthetic Mitral Valve Infective Endocarditis caused by *Micrococcus* Spp. that Fully Recovered by Antibiotics TreatmentImam Mahbub Zam Zam^{1*} , Agus Subagjo¹ ¹Cardiology and Vascular Department, Universitas Airlangga, Surabaya.

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ABSTRACT

Prosthetic valve endocarditis is the most severe form endocarditis with prevalence of 5.7% at 5 years and mortality with medical treatment is 26%-75%. **Case Summary:** Male, 46 years old, with mechanic mitral prosthetic valve >5 years, hemiparesis sinistra due to embolic stroke >4 weeks prior, was suffering from persistent fever >38,5° for 2 weeks without heart failure. Three separate blood cultures came positive with *Micrococcus* spp. and Osler's node was noticed. Echocardiography shown 1.0 cm x 0.9 cm vegetation at mitral prosthetic valve without paravalvular leakage. Patient was assessed as late mitral PVE. **Discussion:** Gentamycin, Levofloxacin, and Erythromycin were given based on susceptibility test continued by Meropenem as therapy of urinary tract infection based on susceptibility test after second blood culture result was negative. The patient underwent 42 weeks of antibiotics course. The patient was discharged with good condition, no signs and symptoms of infection or heart failure, blood test was within normal limit, no vegetations with prosthetic mitral valve functioned normally. This case shows that late PVE caused by *Micrococcus* spp. can be treated by 42 weeks course of antibiotics according to microbial susceptibility test.

Introduction

Prosthetic valve endocarditis (PVE) is the most severe form of infective endocarditis (IE). The prevalence is 3% - 5.7% in 5 years after valve replacement. PVE that occurs >12 months after valve replacement is called late PVE [3]. Prosthetic or native valve endocarditis mortality is 26%-75% with medical therapy and 23%-43% with surgical therapy [2]. PVE caused by *Micrococcus* spp is rarely found.[4]

Several reports successfully treated micrococcus patients with vancomycin, rifampicin and gentamycin [5]. Even though the cure of PVE patients is more difficult than NVE. Miltiadous 2011 reported unsuccessful antibiotics treatment for aortic native valve endocarditis caused by *micrococcus luteus* using vancomycin, rifampicin and gentamycin.[6,7]

We discuss a patient of mechanical mitral valve late PVE caused by *Micrococcus* spp. which is successfully treated by 42 weeks course antibiotics treatment by levofloxacin, gentamycin and erythromycin.

Case Presentation

A 43-year-old male with mitral prosthetic valve installed more than 5 years ago suffered from fever for 2 weeks accompanied by nausea, weaknesses and headache. On examination GCS was 456, general condition was weak, blood pressure was 110/70, heart rate was 100x/min regular, respiration rate was 24x/minute, body temperature was 38.9°C, there was conjunctival pallor and Osler's nodes found. No murmur, gallop or crepitation lung was detected. The chest x-ray shows clear lungs and a shape of a mechanical heart valve in accordance with the form of the bileaflet mechanical valve in the mitral area. Blood examination shown HB 8.68 g/dl; leukocytes 16,450; neutrophil segment 86.73; CRP 48; LED 30; SGOT 122; SGPT 207; Albumin 3.0; BUN 30; creatinin 1.2. Three blood samples were carried out. All three of them were found to be the growth of positive gram bacteria *micrococcus* spp sensitive to Levofloxacin, Gentamycin, and Erythromycin.

The patient was diagnosed of late mitral prosthetic valve infective endocarditis. Transthoracic echocardiography (TTE) showed mitral prosthetic valve with possible stenosis (peak velocity 1.92

m/s; mean gradient 9.86 mmHg; VTI/Prov/VTI LVO 2.4; EOA 1.1 cm²; IPM 194 ms). There is oscillating mass appearance at the prosthetic mitral valve suspicious of vegetation sized 10.0 mm x 9.0 mm and normal LV systolic function (EF by teich 58%; by biplane 57%).

Therapy is given to improve general conditions with fluids, nutrition, symptomatic drugs and packed red cell transfusion. The patient was given warfarin anticoagulant therapy for prosthetic valve with INR showing a fluctuating increase in accordance with the levofloxacin doses. Patients were treated empirically with ampicillin 4x3g and gentamycin 2x75 mg intravenously (iv). After the results of the initial culture were made, antibiotics were adjusted using the combination of levofloxacin 1x750mg iv and gentamycin 2x75mg iv. Over the next 18-28 days, the patients deteriorated and developed acute renal failure. This acute kidney injury seems to be caused by gentamycin & levofloxacin nephrotoxicity. Both then switched to erythromycin 4x500mg.

The results of the TTE evaluation after 27 days antibiotics administration showed no prosthetic valve leak and good function mitral valve appearance (peak velocity 1.34 m/s; mean gradient 2,94 mmHg; VTI/PrMv/VTI LVO 2.1; EOA 2,1 cm²), no valvular and paravalvular leakage, intracardiac vegetation was disappeared.

Second blood culture revealed no bacteria growth. Antibiotics were administered for 6 weeks (42 days). Patient was fully recovered after 42 days in good clinical condition with all laboratory parameters were within normal limits.

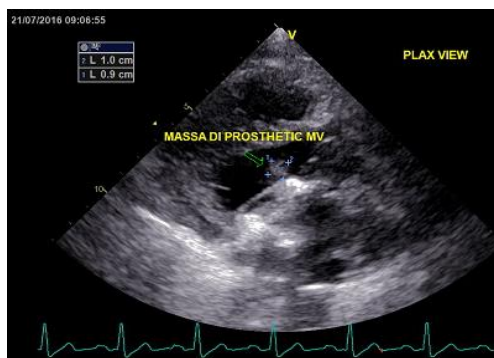


Figure 1. Vegetation in mitral prosthetic valve

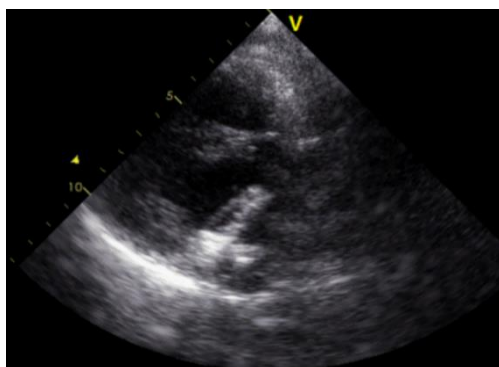


Figure 2. Vegetation in mitral prosthetic valve disappear after 27 days of antibiotics.

Discussion

Fever ($>38^{\circ}\text{C}$) is the most common symptom in $>85\%$ of patients with PVE. Orthopnea, S3 gallop, pulmonary edema or cardiogenic shock can occur if IE causes complications of acute aortic valve regurgitation or acute mitral valve regurgitation with heart failure occurs.

Vegetation in the anterior leaflet of the original mitral valve more often causes embolism than in the aortic valve. The risk of embolism is the same between the original valve and prosthetic [10]. Patient in this case met three minor criteria that is fever (38.9°C), Osler's node and history of prosthetic mitral valve placement. There were no signs or symptoms of heart failure and no worsening of the symptoms of stroke that had been suffered by the patient before. Vegetation, abscess or pseudoaneurism, new malfunctions of the prosthetic valve is three echocardiographic findings in the TTE diagnosis of IE [1]. Vegetation appears as an oscillating mass attached to the valve [12]. Abscess myocardial looked as thick or mass area on myocardial or non-homogeneous perivalvular annulus, lower echo density and possibly accompanied by pseudoaneurysm or fistula.[3]

Other destructive lesions can be seen as perforations, valve prolapse or chordae rupture [12]. In this case, there were 2 major criteria (vegetation and positive blood culture) and 3 minor criteria (fever $> 38.5^{\circ}$, Osler's node and history of prosthetic valve implantation). Patients met the clinical diagnosis requirements of Duke modified ESC 2015 criteria as definite mitral late PVE.

Patients with prosthetic valves are at high risk of endocarditis because the valve surface is alien to the body and the seam connection with annulus.^[8]

The bi-leaflet valve is made from two semilunar plates which are affixed to the valve annulus ring with small hinges. Bioprosthetic valves and mechanical prosthetic valves of metal have the same IE risk ^[14]. In the mechanical valve infection usually starts from the seam connection between a ring and a mechanical valve annulus ^[4]. The spread of infection can cause abscess at the base of the valve connection, in which this connection annulus could cause gap in producing regurgitation and paravalvular leakage.^[14]

The late PVE microbial spectrum resembles IE original valves namely negative coagulase staphylococci, *Staphylococcus aureus*, *Streptococcus viridans* group streptococci, *Enterococcus* species, fungi and *Corynebacterium* species ^[10,11, 14]. The results of the culture of three patients' blood samples were positive for *Micrococcus* spp. These microorganisms are pathogens that are consistent with the cause of PVE but are rare, usually sensitive to penicillin and often incorrectly identified as staphylococcus.^[15]

This bacterium is a normal gram-positive flora in human buccal and skin which forms a yellowish colony. Virulence is actually low but it could be a pathogen and colonize in prosthetic valves. In late PVE aggressive tissue damage rarely

occurs. Truninger et al. showed that patients with non-staphylococcal PVE with stable hemodynamics could be treated with antibiotics alone without increasing the risk of surgery, reinfection or death.^[2]

The main purpose of antibiotics administration is to eradicate infection including vegetation sterilization ^[11]. Combination of antibiotics can provide a faster bactericidal effect and provide activation for blood sterilization (synergy effect) ^[13]. Empirical antibiotic Ampicilin 12g/day, cloxacillin/Oxacillin 12g/hr and Gentamycin 3mg/kg/day administered to patients in late PVE (Class IIa LOE C) until the pathogens are identified by culture and revision antibiotics corresponding sensitivity test results ^[11,1]. If the patient is allergic to penicillin, antibiotic is switched to Vancomycin and Gentamycin (Class IIb, LOE C) ^[16]. Minimum inhibitory concentration (MIC) effective at the site of infection with bacterial density 10^{8-10} colony-forming units (CFU) can be greater than the in vitro test (with a standard inoculum $10^{5.5}$ CFU/MI) ^[1]. Fluoroquinolones and aminoglycosides are less affected by inoculum size is due to its different bactericidal mechanism.^[11]

Anticoagulants should be discontinued in case of a mechanical valve IE experiencing intracranial embolism for at least 2 weeks to prevent hemorrhagic transformation (Class IIa: LOE C).

Warfarin is mandatory for prosthetic valve. In this patient, no contraindication to warfarin because the stroke that occur to the patient was more than 2 weeks. Levofloxacin increases the potency of warfarin so that the INR is maintained at 2.5 - 3.5 by adjusting the warfarin dose. It does not attempt recommended using NOAC and for the resumption of warfarin can be done by providing transitional heparin prior unfractionated.^[11]

Evaluation of therapy in PVE is seen from clinical, laboratory and echocardiography. The fever will resolve in 5-7 days after the appropriate antibiotic administration. If fever persisted may indicate: (1) progressive infection with paravalvular expansion (antibiotics less, septic embolism, extracardiac infection); (2) infection of the urinary catheter or phlebitis; (3) inadequate therapy of resistant organisms; (4) intersection reaction to antibiotic itself ^[9]. If initial blood culture identified the causative microorganism, two sets of blood cultures must be repeated every 48 - 72 hours to evaluate the effectiveness of the therapy until the blood infection disappears ^[11]. Persistent blood culture results after appropriate antibiotics initiation suggest therapy failure.^[13,3]

The timing and type of echocardiography (TTE/TEE) depends on initial findings, the type of microorganism and initial response to therapy. During the treatment, the vegetation may indicate a gradual reduction in size, decreased

mobility and increased echogenicity ^[13,8]. Vegetation can disappear or not change during the acute period or after healing. If significant valve regurgitation that clinically affects hemodynamics was found, especially with regard to deterioration of left ventricular function, large vegetation and intracardiac fistula formation in echocardiography, surgical therapy must be considered.^[8]

Gentamycin is given in a single dose to reduce nephrotoxicity with a total dose of 3 mg/kg/day. Existence of multiple comorbidities including in urology can increase gentamycin nephrotoxicity towards acute renal failure or hemodialysis, hence gentamycin should be stopped when the deterioration of renal function is detected. The potential risk to fulfilled gentamycin therapy for 4 - 6 weeks (28 - 42 days) outweigh the benefits in this case ^[11]. After a stroke, surgical action is indicated for heart failure, uncontrolled infection, abscess or risk of persistent embolism immediately as long as the patient is not comatose and there is no cerebral hemorrhage from CT scan or MRI (Class IIa, LOE B).^[1]

Conclusion

Late PVE occurs >12 months post-installation, is diagnosed clinically in the presence of fever, history of prosthetic valve installation, intracardiac vegetation and blood culture results. Ampicillin, gentamycin and/or vancomycin empirical antibiotics are given first until pathogenic microorganisms are obtained from blood cultures. Antibiotic is given based on sensitivity test for at least 6 weeks. During the treatment period, the signs and symptoms of heart failure, persistent clinical signs of infection, serial echocardiography, and blood culture must be monitored and repeated according to clinical and after completion of antibiotics.

If signs of heart failure, persistent infection, or embolism are found during the treatment period, immediate or elective heart valve replacement surgery should be performed with consideration of the time according to the indication of surgery found. If the patient gets gentamycin and levofloxacin, watch for signs of dangerous nephrotoxicity. Stop gentamycin immediately if the deterioration of kidney function is found. Warfarin can be continued to be given with a fixed INR target of 2.5-3.5 unless there are complications of an embolic stroke, delaying the administration of warfarin for a minimum of 2 weeks. Educate patients about signs and symptoms of recurrence. Do serial TEE after the antibiotics are finished.

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