

CASE REPORT

Successful Conservative Treatment of Massive Infective Endocarditis with Severe Mitral Valve Regurgitation and Septic Emboli

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ABSTRACT

Management of complicated massive infective endocarditis (IE) in patients who are contraindicated for surgical valve replacement has long been a dilemma for many clinicians. Studies have shown that massive IE patients who were treated conservatively generally result in poorer prognosis. We report two cases of massive native valve infective endocarditis with severe mitral valve regurgitation and septic emboli that has been successfully treated conservatively. Interestingly, despite having a large vegetation and multiple septic emboli complications, none of these two cases had any positive culture or serology. Managing culture negative IE without surgical intervention pose an even greater challenge to the choice and duration of antibiotics with further long-term plans. We hope to share these case series to aid in the management dilemma of similar cases in the future.

Keywords: Massive Infective Endocarditis, Culture Negative, Conservative, Complicated, Septic emboli

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INTRODUCTION

Massive infective endocarditis (IE) with only medical therapy usually results in poorer outcomes compared to a combination with surgical valve replacement. Patients who are indicated but could not proceed with surgery have been reported to have the worst prognosis. Nonetheless, there isn't much literature focusing on the management of critical IE and its multiple complications. Data reporting the outcomes of conservative management in patients who refused surgery are scarce. We report two cases of massive native valve infective endocarditis with severe mitral valve regurgitation and septic emboli that has been successfully treated conservatively.

CASE REPORT

Case 1

A 33-year-old gentleman presented with a one-month history of prolonged fever associated with paroxysmal migratory arthritis. He also had a reduced appetite and weight loss of 8kg over this one-month period. He is a paddy farmer with no other past medical history or high-risk behavior.

Upon admission, the patient was lethargic, dehydrated and jaundiced. His blood pressure (BP) was 92/52 mmHg, heart rate (HR) 106 bpm, temperature (T) 37.8 °C with oxygen saturation (SPO₂) of 98% under room air. There was a grade 3 pansystolic murmur over the mitral region radiating to the left axilla, clubbed fingers, mild splenomegaly, Roth spot over the right eye with multiple dental caries and gingivitis.

Blood investigation showed leukocytosis at 28.5 x 10⁹/L (neutrophil predominant) and a raised CRP of 10 mg/L. Echocardiography showed a severe mitral regurgitation with vegetation at the anterior mitral valve leaflet measuring 21.5mm² and left ventricular ejection fraction of 67% (Fig. 1).

The patient was diagnosed as infective endocarditis with multiorgan involvement. He was started on intravenous (IV) gentamycin and ceftriaxone for 2 weeks, and IV cloxacillin for 6 weeks. He was also referred for early mitral valve replacement. However, he strongly refused surgical intervention after being duly informed about the risks and benefits of both surgical and conservative managements.

Multiple blood samples for bacterial and fungal culture and sensitivity (C&S) taken prior to antibiotic therapy and throughout the admission showed no growth. *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*,



Figure 1: Vegetation at the anterior mitral valve leaflet measuring 21.5mm²

Eikenella, and Kingella (HACEK) study, melioidosis, brucella, legionella, mycoplasma, antistreptolysin O test (ASOT), HIV, hepatitis B, hepatitis C, syphilis, leptospirosis serology as well as autoimmune screening such as Anti-nuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA), Complement C3, C4 were all negative. CT angiography of the brain showed no evidence of intracranial aneurysm.

After eight days of admission, the patient developed bilateral acute lower limbs ischaemia secondary to distal emboli of IE. CT Angiography revealed multilevel bilateral lower limb arterial thrombosis involving both common iliac arteries, down to the dorsalis pedis artery and posterior tibialis artery. He subsequently underwent bilateral femoral embolectomy and profundaplasty. Repeated cultures including cultures from emboli were negative.

After completing six weeks of antibiotics via peripherally inserted central catheter (PICC), the patient was subsequently discharged home as he still refused surgical intervention. Six months post discharge, the patient remained asymptomatic and afebrile. A repeat echocardiography showed a reduction in vegetation size to 9.7mm². (Fig. 2) Trans-Oesophageal Echocardiography (TOE) was not done as the diagnosis for this patient was sufficient by Trans-Thoracic Echocardiography (TTE).

Case 2

A 14-year-old teenage girl with no past medical illness, presented with intermittent high-grade fever for two weeks associated with headache, non-productive cough, abdominal pain, joint pain, reduced effort tolerance and poor oral intake.

On arrival, she was lethargic, febrile at 38.2°C, with a BP of 93/52mmHg, HR of 139bpm, and SpO₂ of 99% under room air. There was a pansystolic murmur best heard at apex, tenderness at epigastric and left iliac region, Janeway lesions over the soles and Roth's spot in the eyes.

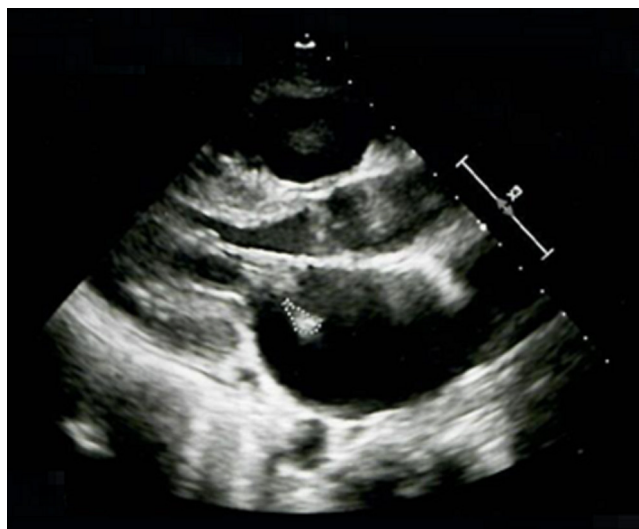


Figure 2: Reduction in vegetation size to 9.7mm²

Urgent echocardiography revealed severe mitral regurgitation, chordae damage with vegetation seen at the posterior mitral valve leaflet measuring 34mm² and ejection fraction of 78%. (Fig. 3) CT scan showed segmental splenic and territorial renal infarcts with jejunal ischaemia and multiple peripherally located lung nodules. There were also multiple intracranial hemorrhages with mass effect secondary to ruptured mycotic aneurysm.



Figure 3: Vegetation seen at the posterior mitral valve leaflet measuring 34mm²

Additionally, the patient also had leukocytosis at 12 x 10⁹/L with a raised CRP of 132 mg/L, ESR 111 mm/hr, and Anti-Deoxyribonuclease B titres: 449U/mL (normal range 0–375). Extensive septic workout including serial blood bacterial and fungal C&S, HACEK study, melioidosis, ASOT, HIV, hepatitis C, hepatitis B, syphilis, brucella, legionella, coxiella, cerebrospinal fluid C&S, urine C&S, throat C&S, urine C&S, stool C&S were all negative. Autoimmune screening such as ANA, anti-dsDNA, C3, C4 were all negative as well.

The patient was diagnosed as infective endocarditis

complicated with distal septic emboli to the spleen and ruptured mycotic aneurysm. IV gentamicin, piperacillin/tazobactam and cloxacillin were given via PICC for six weeks each, making a total of ten weeks on antibiotics. She underwent a total of four craniotomies for blood clot evacuation and excision of the intracranial mycotic aneurysm due to recurrent intraparenchymal bleed. Conservative measures were opted for the splenic lesion.

After completing ten weeks of IV antibiotic in total, the patient's fever subsided but echocardiography showed no reduction in the size of the posterior mitral valve vegetation. A delayed index valve intervention was decided as the patient is young, and her heart may still undergo physiological changes as she gets older. She was successfully discharged after 2.5 months of hospitalization with intramuscular benzathine penicillin 1.2mU monthly until age of forty years. Six months post discharge, the patient remained asymptomatic and afebrile. A repeat echocardiography at 6-months post discharge showed a small organized vegetation measuring 1.3mm². (Fig. 4) TOE was not done as the young girl was very fragile and uncooperative. Subjecting her to another TOE under general anaesthesia again after her multiple craniotomies was deemed too stressful to the young girl and her family.



Figure 4: Reduction in vegetation size to 1.3mm²

DISCUSSION

Massive IE is defined as >10mm² (left sided valves) and > 20mm² (right sided valves). The brain and spleen are the most frequent sites of embolism in IE, followed by lung, renal, major arterial beds and coronary arteries. Embolism may occur as high as 40% in IE cases, but its incidence decreases by half after antibiotic initiation. Management of massive IE still needs to follow the latest guidelines which is prolonged IV antibiotic and early surgical intervention for the best patient outcomes. (1) Indication of surgery in these two cases include: large vegetation >10mm², severe mitral regurgitation, septic emboli, young and no comorbidity.

However, in cases where urgent or early surgical intervention could not be done (ie: patient refusal or deferment due to small body size as in our case series),

the role of conservative management with prolonged IV antibiotics becomes very challenging. Patients who are indicated but could not proceed with surgery, have been reported to be associated with a high in-hospital mortality and extremely high long-term mortality rate (2).

With conservative management, the above two cases were successfully treated with prolonged antibiotics of six weeks and ten weeks respectively. Interestingly, despite having a large vegetation and multiple septic emboli complications, none of the two cases had any positive cultures to aid in the causative organism and antibiotic sensitivity. It is common for patients in rural areas to take oral antibiotics from their local general practitioner prior to hospital presentation. This may have contributed to the negative cultures. The second case had a longer antibiotic duration than the first case due to having clinical signs of nosocomial infections which responded well to gentamycin and piperacillin/tazobactam. Hence gentamycin and piperacillin/tazobactam were given over a prolonged period of 6 weeks respectively. To the best of our knowledge, these two patients are by far amongst the worst reported cases of IE which had been successfully treated conservatively. The success in treating these two cases with conservative management is probably due to the insertion of PICC and an individualized team co-management (cardiology, cardiothoracic surgeons, neurologist, neurosurgeons, vascular surgeons, anaesthesiologist, radiologist).

PICC has been recommended for patients who require prolonged IV access. (3) Not only can it reduce the risk of peripheral thrombophlebitis, it is also associated with a significantly lower incidence of catheter-related bloodstream infection as compared to peripheral IV catheters and central venous catheters (4).

Managing culture negative IE can be problematic as the duration and choice of antibiotics in such cases remains a dilemma. The most common organism of culture negative massive IE are *Coxiella burnetii*, *Bartonella* species, and *Chlamydia psittaci*. If cultures for bacterial and fungal are negative in suspected cases, the serum should be analysed for *Bartonella*, *Coxiella*, and *Chlamydia* species antibodies, autoimmune antibodies and the excised valve or embolus should be analysed by microscopy, culture, histology, and relevant polymerase chain reaction (PCR). (5) The emboli for both cases were sent for cultures. Relevant serology and PCR were not sent due to the unavailability of these tests at the local hospital setting.

CONCLUSION

When facing patients with massive IE vegetation, severe valvular lesion, systemic complications, and patient refusal for surgical intervention, prolonged antibiotics is the only choice while continuously reminding patients

on the risks. The usage of PICC with minimum of 6 weeks antibiotic duration is highly recommended. These two cases are by far among the worst reported IE cases to be successfully treated conservatively with prolonged antibiotic via PICC. However, life-long follow-ups of these patients are still required to determine the long-term outcomes of such managements.

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