Successful medical management of fungal infective endocarditis post VSD closure

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ABSTRACT
Fungal infective endocarditis (IE) is uncommon in postoperative cardiac surgical patients. The fungal IE accounts for 1.3%–6.8% of all IE cases and is considered the most severe form with a mortality rate as high as 45%–50%. There are various predisposing factors for fungal IE which include congenital heart defects, cardiac interventions like pacemaker insertion, degenerative valvular heart diseases, long-term use of broad-spectrum antimicrobial therapy, and long-term use of central venous. Mortality can reach up to 100% without specific treatment. Definitive therapy necessitates surgical debridement of vegetations/mass/abscess followed by long-term treatment with antifungal agents in patients who have symptoms of heart failure despite optimum medical management. We, hereby, report a case of fungal IE which occurred after the closure of a ventricular septal defect and was treated successfully with liposomal amphotericin B.

Keywords: Congenital cardiac surgery, fungal infective endocarditis, low cardiac output, postoperative sepsis

INTRODUCTION
Fungal infective endocarditis (IE) is uncommon in postoperative cardiac surgical patients. The most common fungi that causes IE are Candida and Aspergillus species.[1] The outcome of the fungal IE is generally poor when compared with bacterial endocarditis.

We, hereby, report a case of fungal IE which occurred after the closure of a ventricular septal defect (VSD) and was treated successfully with liposomal amphotericin B.

CASE REPORT
A two-year old male child weighing 8 kg presented with a complaint of respiratory distress and recurrent respiratory tract infections since two months of age. On examinations, air saturation in his room was 96%, heart rate was 110/min and non-invasive blood pressure was 80/50 mm Hg. The child was diagnosed to have a large 19-mm inlet VSD with muscular extension with a left to right shunt and with features of severe PAH and normal biventricular function on transthoracic echocardiographic (TTE) examination.

After the thorough pre-anesthetic check-up, he was posted for VSD closure. After induction of general anaesthesia, transesophageal echocardiographic (TEE) examination confirmed the preoperative findings [Figure 1 and Video 1]. Cardiopulmonary bypass (CPB) was initiated after systemic heparinization and the intraoperative inspection revealed a very large VSD with an almost absent interventricular septum. The VSD was

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DOI: 10.4103/aca.ACA_33_19

How to cite this article: Gourav KK, Mandal B, Mishra AK, Nayanar VK. Successful medical management of fungal infective endocarditis post VSD closure. Ann Card Anaesth 2021;24:95-8.
closed by polytetrafluoroethylene (PTFE) patch. The patient developed severe left ventricular dysfunction which was due to the absence of interventricular dependence between left and right ventricle as a result of large PTFE patch. The pressure of pulmonary artery decreased after surgery to half of systemic pressure. Hence, the CPB was terminated with a high inotropic support, that is, milrinone injections – 0.6 mcg/kg/min (loading dose of 50 mcg/kg given pre-CPB), noradrenaline – 0.05 mcg/kg, and adrenaline of 0.1 mcg/kg/min. Post-CPB, TEE examination revealed no residual VSD with mild mitral regurgitation, normal right ventricular function and poor left ventricular function [Figure 2 and Video 2]. The patient was shifted to the intensive care unit (ICU) with an invasive blood pressure (IBP) of 65/41 mm Hg, CVP 6–8 mm Hg, AV (atrioventricular) sequential pacing of 100 beats per minute. The patient required prolonged inotropic support and was unable to be weaned off from mechanical ventilation for 12 days due to the low cardiac output state. On the 15th postoperative day (POD), the trachea was extubated and inotropes were gradually tapered. The kid was shifted to the ward on the 18th POD. The central venous catheter was removed before shifting to the ward. Ten days later, he developed a high-grade fever which did not subside with antipyretics and antibiotics. We did not find any new murmurs in this patient. Then the patient was re-admitted in ICU for further investigations. His haemoglobin was 9.1 g/dl, total leucocyte count was 11,000/mm$^3$, and platelet count was 170,000/mm$^3$. Blood culture were negative for bacteria but showed a growth of Candida tropicalis. TTE confirmed the diagnosis of IE by showing vegetation that measured 7 × 6 mm on the PTFE patch toward the right ventricle [Figure 3 and Video 3]. The patient was hemodynamically stable with no symptoms of embolic event to any organ systems. The patient was put on aggressive antifungal therapy of injection liposomal Amphotericin B (5 mg/kg/day) and IV Fluconazole (12 mg/kg loading dose followed by 6 mg/kg/day). After two weeks of therapy, his fever subsided and repeated TTE showed a reduction in the size of vegetation. Antifungal therapy was continued for 8 weeks and after completion, no vegetation was seen on TTE and blood culture was negative for any organism [Figure 4 and Video 4]. During the subsequent 1-year follow-up, he is doing well with no signs and symptoms of relapse.

**DISCUSSION**

IE is a dreadful lesion associated with high mortality and morbidity. The incidence of IE in congenital heart disease is 4.1 per 10,000 person-years. Whereas, in patients with VSD, its incidence is 2.4 per 10,000 person-years.[2] The most common etiological agent for IE is bacteria followed by fungi. The fungal IE accounts for 1.3%–6.8% of all IE cases and is considered the most severe form with a mortality rate as high as 45%–50%.[1] It was first reported
The mainstay of antifungal therapy is amphotericin B with or without flucytosine. Liposomal amphotericin B has fewer side effects but can cause electrolyte imbalance like hypokalemia, hypomagnesemia, and hypocalcemia. However, penetration of amphotericin B into abscesses and/or vegetation is limited. Concomitant use of a second agent, such as flucytosine, that acts synergistically may potentiate the resolution of fungal vegetations. Fluconazole, a fungistatic agent, is considered to be less efficacious than amphotericin B and serves as a second-line drug in the treatment of fungal endocarditis. The combination of antifungal agents can be associated with a better clinical outcome when compared with monotherapy in fungal endocarditis. However, combination therapy may result in higher side effects and toxicity levels of drugs.

At present, there is no specific prescribed regimen of treatment for fungal endocarditis. Mortality can reach up to 100% without specific treatment. Definitive therapy necessitates surgical debridement of vegetations/mass/abscess followed by long-term treatment with antifungals in patients who have symptoms of heart failure despite optimum medical management. However, medical treatment alone proved successful in some reports of Candida endocarditis. The mainstay of antifungal therapy today is amphotericin B with or without flucytosine. Liposomal amphotericin B has fewer side effects but can cause electrolyte imbalance like hypokalemia, hypomagnesemia, and hypocalcemia. However, penetration of amphotericin B into abscesses and/or vegetations is limited. Concomitant use of a second agent, such as flucytosine, that acts synergistically may potentiate the resolution of fungal vegetations. Fluconazole, a fungistatic agent, is considered to be less efficacious than amphotericin B and serves as a second-line drug in the treatment of fungal endocarditis. The combination of antifungal agents can be associated with a better clinical outcome when compared with monotherapy in fungal endocarditis. However, combination therapy may result in higher side effects and toxicity levels of drugs.

Two strategies can be adopted to prevent fungal IE; first is personal hygiene of proper hand-washing, care of indwelling CVCs which are universal and helpful in preventing all infections. The second strategy is related to screening of local site fungal infections. Evaluation of colonization before surgery to find out the susceptibility pattern of the isolated pathogen is the best approach.
for the management of Candida endocarditis. Care of CVCs is important for reducing candidemia and Candida endocarditis. High-efficiency particulate air filters can be used to prevent contamination by fungal spores.[8] In patients with high risk, antifungal prophylaxis could be used to prevent fungal infections.[8]

To conclude, the case presents a rare scenario where vegetation of Candida tropicalis developed post VSD closure on PTFE patch and was successfully treated with antifungal therapy.

Clinical pearls
1. Prolonged low cardiac output syndrome in postoperative period predisposes patients to superimposed infection with less virulent organisms because of low immunity
2. In patients with high risk, antifungal prophylaxis could be used to prevent fungal infections
3. A timely medical management of fungal IE can save important lives.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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