

# Right-sided infective endocarditis in patients with uncorrected ventricular septal defect and patent ductus arteriosus: Two case reports

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## Key Clinical Message

Uncorrected left-to-right shunt congenital heart defect is a predisposing factor for infective endocarditis (IE), especially right-sided IE which has different clinical manifestations and complications from left-sided IE. Prompt diagnosis by means of transthoracic echocardiography and timely antibiotics management for IE are encouraged to prevent multiorgan failure and fatal pulmonary embolism.

## KEYWORDS

pulmonary embolism, right-sided infective endocarditis, uncorrected ventricle septal defect, vegetation

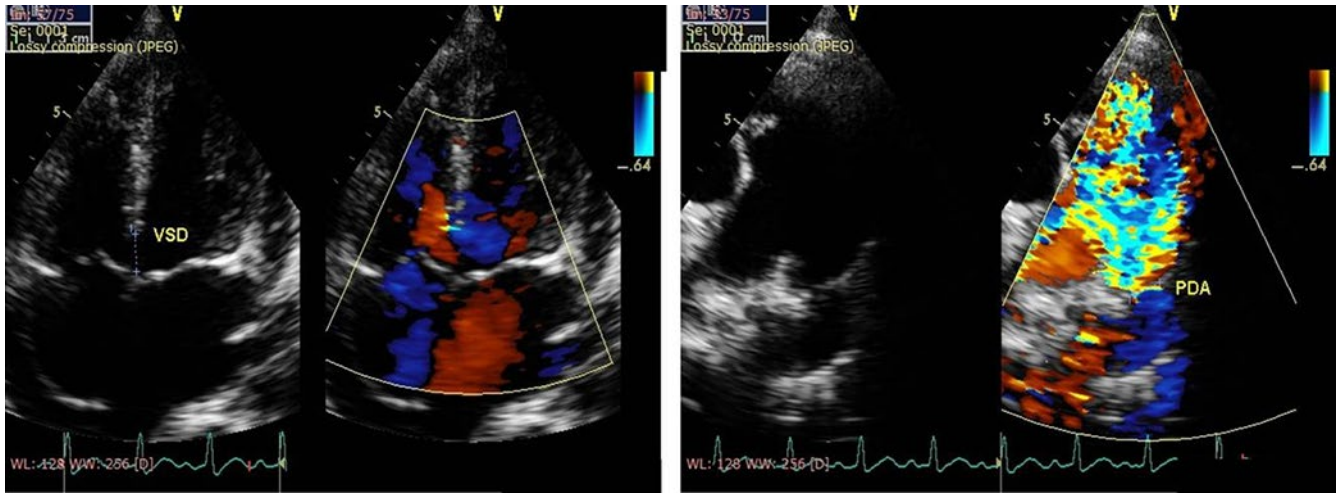
## 1 | INTRODUCTION

Infective endocarditis (IE) is a rare and potentially fatal disease. Its incidence varies between 1.4 and 12.7 cases in 100 000 persons per years.<sup>1</sup> Congenital heart disease is a predisposing factor for IE. The incidence of IE among ventricular septal defects (VSD) was 0.2%-2%.<sup>2,3</sup> In patent ductus arteriosus (PDA), the risk for developing IE is lower as compared to patients with VSD.<sup>4</sup> The presence of both defects concomitantly may increase the risk for IE, especially in patients with uncorrected defects. The right-sided IE, which involves the tricuspid or pulmonary valve, accounts for 5%-10% of the entire IE.<sup>5</sup> Intravenous drug users, congenital heart disease patients, and instrumentation of the right heart are predisposing factors for right-sided IE.<sup>5,6</sup> Among congenital heart disease, VSD is the most frequent anomaly in right-sided IE.<sup>6</sup> As the clinical manifestations and complications differ from left-sided IE, prompt diagnosis and timely

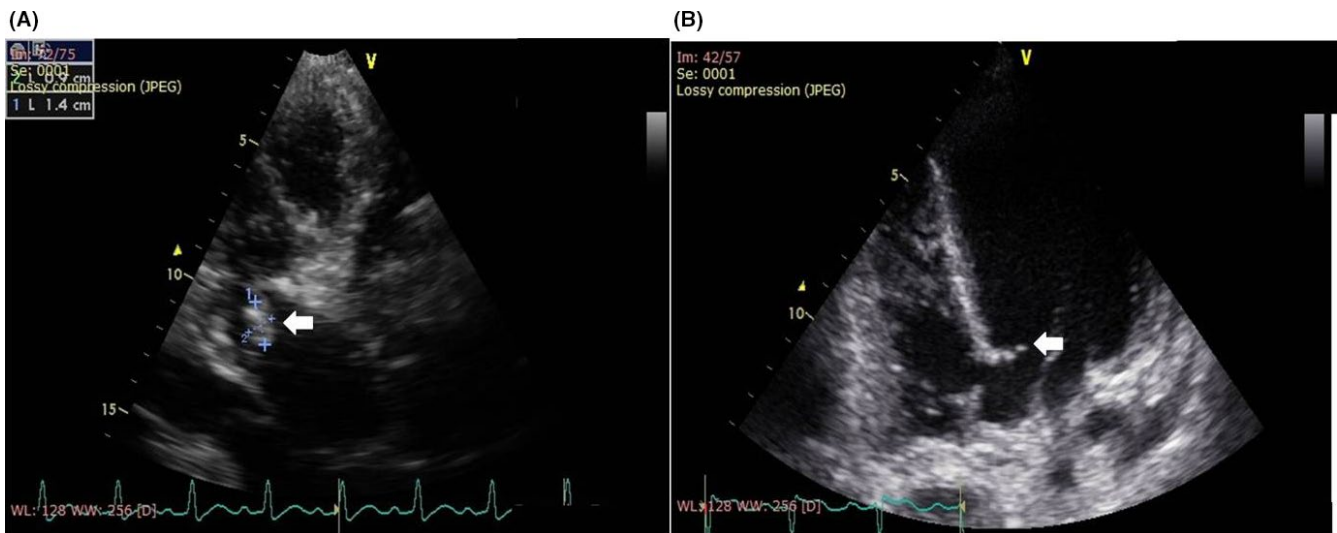
management are encouraged to prevent multiorgan failure and fatal pulmonary embolism. We herein report two adult cases with uncorrected left-to-right VSDs and PDAs which were complicated by right-sided IE.

## 2 | CASE REPORT 1

A 26-year-old female came to the emergency department of our hospital with a chief complaint of worsening shortness of breath over the past 1 month accompanied by palpitation and general weakness. The shortness of breath was aggravated by strenuous activity and relieved by taking a rest. The patient had visited primary health care and a local hospital, which resulted in only mild improvement. Two weeks prior to current admission, she developed multiple red spots over her extremities without itching or pain. From previous hospital, she was diagnosed as heart failure and given oral furosemide



**FIGURE 1** The transthoracic echocardiography showed ventricular septal defect (left figure) and patent ductus arteriosus (right figure)



**FIGURE 2** A, The transthoracic echocardiography showed vegetation (white arrow) attached to the pulmonary valve. B, The transthoracic echocardiography showed new vegetation (white arrow) attached to the left ventricular site of VSD

20 mg q.d., digoxin 0.125 mg q.d., ramipril 2.5 mg q.d., and spironolactone 25 mg q.d.

During admission, her physical examination showed blood pressure of 100/60 mmg Hg, regular heart rate of 112 beats per minute, respiratory rate of 24 times per minute, and axillar temperature of 36.5°C. The patient was pale and underweight, with body mass index of 16.4 kg/m<sup>2</sup>. There was no increased jugular venous pressure. Cardiac examination revealed cardiomegaly with palpable apex of the heart shifted leftward. A loud pansystolic murmur was heard at the lower left sternal border, and systolic ejection murmur was heard in the upper left sternal border. The lung examination was within normal limit. Splenomegaly was found (Schuffner II). Multiple petechiae were observed over her extremities. Slight peripheral edema was observed. No cyanosis or clubbing fingers were detected.

Laboratory investigation revealed anemia with hemoglobin level of 5.8 g/dL. The serum albumin level was 2.47 g/dL. The liver and kidney function tests were normal. The NT-proBNP was 7711 pg/mL. A thorax X-ray showed cardiomegaly with normal lung area. We immediately performed a transthoracic echocardiography (TTE). The TTE revealed a bidirectional with predominant left-to-right shunt perimembranous VSD and PDA (Figure 1). It showed 14 mm × 9 mm vegetation attached to the pulmonary valve (Figure 2A). The left ventricle was dilated and hypertrophied (LVIDd 54 mm). Its systolic function was normal with ejection fraction of 78%. The right atrium and ventricle were dilated with moderate-to-severe tricuspid regurgitation (transvalvular gradient 84 mm Hg) and high probability of pulmonary hypertension.

Patient was diagnosed as bidirectional with predominant left-to-right shunt VSD and PDA, high probability of

pulmonary hypertension NYHA functional class II, possible IE (based on modified Duke criteria), anemia, and hypoalbuminemia. We gave oral sildenafil 20 mg t.i.d. and intravenous furosemid 40 mg b.i.d for alleviating symptoms of pulmonary hypertension. For possible IE, the blood samples from 3 different sites (right arm, right leg, and left leg) were withdrawn for bacterial culture examination, in order to guide the antibiotics treatment. At first, we administered intravenous empirical antibiotics, that is, ampicillin and sulbactam 3 g q.i.d and gentamycin 120 mg q.d. The result of blood culture showed *Streptococcus viridans* was identified from the right arm, *Streptococcus porcinus* from the right leg, and *Streptococcus mitis/oralis* from the left leg. Antibiotics were then continued according to blood culture and sensitivity study. We gave antibiotics until 14 days before performing full evaluation. For anemia, three bags of packed red cell transfusions were given and her hemoglobin level rose to 9.3 g/dL. There was no bleeding manifestation. For hypoalbuminemia, we corrected with intravenous albumin until normal level.

In the treatment course, multiple petechiae and peripheral edema were diminished. Her hemoglobin level reached 11.5 g/dL, platelet count increased to  $99 \times 10^3/\mu\text{L}$ , and albumin level was within normal level. Clinically, the patient's condition was improved. After 14 days course of intravenous antibiotics and supportive treatment, the TTE was performed to evaluate the vegetation. Despite clinical improvement, the vegetation persisted and attached to the pulmonary valves with the size of 18 mm  $\times$  11.5 mm. The intravenous antibiotic therapy was extended for 14 more days with similar antibiotics. Afterward, another TTE was performed and showed the persistence of the vegetation and the presence of new vegetation with the size of 10 mm  $\times$  10 mm attached to the VSD (Figure 2B). The patient remained hemodynamically stable and clinically well. During long-term antibiotics treatments (28 days), the daily mobility of patient was good, therefore, the deep vein thrombosis was prevented. The medical team decided to perform surgical therapy for her to remove the vegetation and close the defect. Transcatheter coiling of PDA was performed prior to surgical intervention. Unfortunately, the patient then refused the surgery. The patient decided to continue the medication at district hospital and reported to be doing well after 1.5 years since hospital discharge.

### 3 | CASE REPORT 2

A 32-year-old male came to our hospital emergency department with a chief complaint of prolonged fever lasting for more than two months. Two weeks prior to admission, he felt fever more frequently. He was admitted previously to another hospital and underwent a full course of antibiotics (intravenous ceftriaxone 1 g b.i.d), however the fever persisted. At

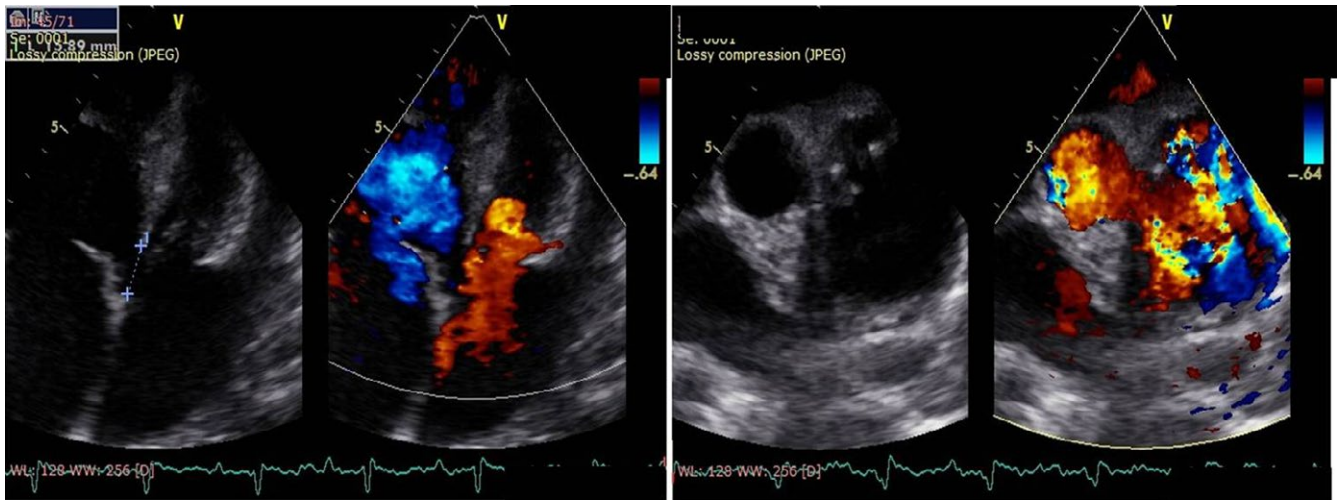
the day of current admission, the patient complained shortness of breath along with fever. The congenital heart disease in this patient had already been identified since his childhood; however, he refused the surgical correction and never again visited the medical services. He was an intravenous drug user.

Physical examination revealed blood pressure was 130/80 mm Hg, heart rate was 88 beats per minute, respiratory rate was 22 times per minute, and body temperature was 38.1°C. He looked pale and underweight. Cardiac examination revealed cardiomegaly with a grade 4/6 pansystolic murmur loudly heard at the lower left sternal border. The lung examination indicated slight basal rales. Hepatosplenomegaly was found in the abdominal examination. Multiple petechiae were identified over his four extremities, accompanied by peripheral edema. No cyanosis or clubbing fingers were detected.

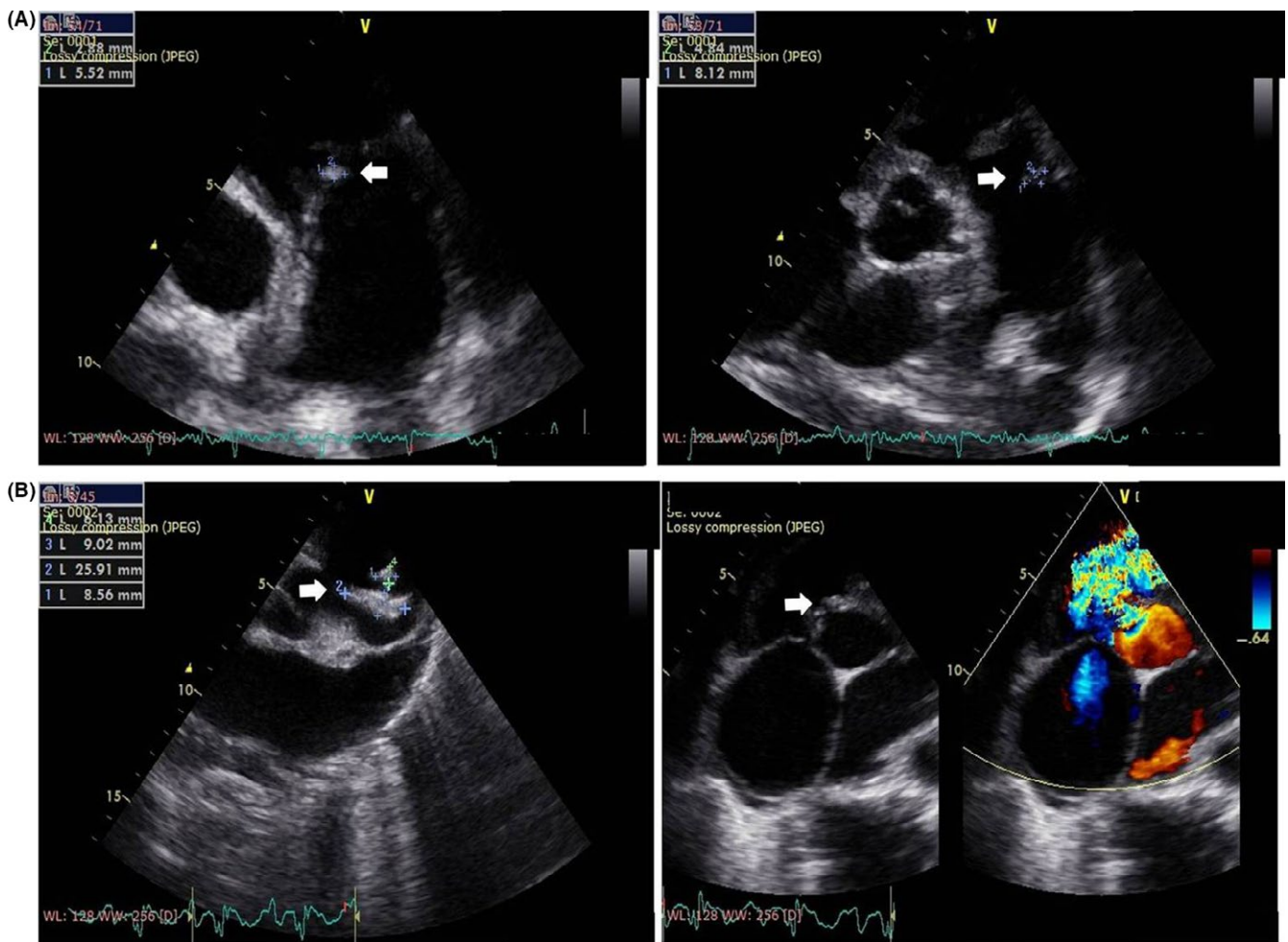
The laboratory examination showed hemoglobin level was 7.6 mg/dL, leukocyte count was  $11.68 \times 10^3/\mu\text{L}$ , and platelet count was  $108 \times 10^3/\mu\text{L}$ . The serum albumin was 2.2 g/dL. The liver and kidney functions were normal. The NT-proBNP level was 6604 pg/mL. Chest X-ray revealed cardiomegaly with signs of pulmonary edema. Abdominal ultrasound revealed splenomegaly. We immediately performed TTE. The TTE showed a large left-to-right shunt perimembranous VSD and a left-to-right shunt PDA (Figure 3). The multiple vegetations with the size of 4.8 mm  $\times$  8.1 mm, 7 mm  $\times$  14 mm, and 2.8 mm  $\times$  5.5 mm were identified. The vegetations were attached to the pulmonary valves, the wall of main pulmonary artery, and the VSD (Figure 4A). Both atrial and ventricular dimensions were dilated. The left ventricular systolic ejection fraction was 76%. Mild tricuspid regurgitation (transvalvular gradient 40 mm Hg) and intermediate probability of pulmonary hypertension were detected.

Patient was diagnosed as left-to-right shunt VSD and PDA, intermediate probability of pulmonary hypertension NYHA functional class II, and prolong fever due to possible IE (based on modified Duke criteria), with anemia and hypoalbuminemia. We gave oral sildenafil 20 mg t.i.d. and intravenous furosemid 40 mg b.i.d for alleviating symptoms of pulmonary hypertension. For possible IE, the blood samples from 3 different sites (right arm, right leg, and left leg) were withdrawn for bacterial culture examination, in order to guide the antibiotics treatment. After taking blood samples, we administered intravenous empiric antibiotics, that is, ampicillin and sulbactam 3 gq.i.d. and gentamycin 80 mg q.d. Blood culture examination from multiple sites showed no growth of bacteria; therefore, we continued empirical antibiotics for 14 days. For anemia, the patient received transfusion of four bags of packed red cells.

In the treatment course, the fever was diminished, the hemoglobin level increased to 11.0 mg/dL, leukocyte count was found slightly increase to  $12.65 \times 10^3/\mu\text{L}$ , and platelet count was  $99 \times 10^3/\mu\text{L}$ . Albumin level also increased after



**FIGURE 3** The transthoracic echocardiography showed ventricular septal defect (left figure) and patent ductus arteriosus (right figure)



**FIGURE 4** A, The transthoracic echocardiography showed vegetation (white arrow) attached to the pulmonary valve (left figure) and to the wall of pulmonary artery (right figure). B, The transthoracic echocardiography showed multiple vegetation (white arrow) attached to the pulmonary valve (left figure) and VSD (right figure)

intravenous albumin infusion. Clinically, the patient condition was stable. At day fourteen, the TTE evaluation revealed persistence of the multiple vegetations on the pulmonary

valves, main pulmonary artery, and the VSD with each size of 3.6 mm × 6.4 mm, 3.2 mm × 7.5 mm, 9.5 mm × 11 mm, and 8.8 mm × 8.5 mm (Figure 4B). The intravenous antibiotic

therapy was extended for 14 more days with similar antibiotics. During in-hospital long-term antibiotics treatment (28 days), patient mobility was preserved such that deep vein thrombosis was avoided.

At day 27 of hospitalization, the patient complained of sudden chest pain, difficulty of breathing, and profuse hemoptoe. Fresh blood of approximately 600 mL was coughed. Physical examination revealed blood pressure of 90/60 mm Hg, heart rate of 140 beats per minute, respiratory rate of 36 times per minute, and normal temperature. Vesicular sound on the right lung field was significantly decreased along with additional coarse crackles on the left lung field. While providing fluid resuscitation for him, emergency TTE was performed revealing a positive McConnell's sign. The patient was assessed as unstable acute pulmonary embolism. He experienced cardiac arrest and a cardiopulmonary resuscitation was performed, however, it failed and he was pronounced dead.

## 4 | DISCUSSION

Uncorrected VSD and PDA are predisposing factors for IE, especially right-sided IE. In our cases, the first patient was fulfilled modified Duke criteria with the finding of two major criteria (intracardiac vegetation and positive blood culture) and 1 minor criterion (predisposing factor of congenital heart disease). The second patient satisfied 1 major criterion (intracardiac vegetation) and 2 minor criteria (predisposing factor of congenital heart disease and prolonged fever), referring to the diagnosis of possible IE.<sup>7</sup> Both cases had multiple vegetations in pulmonary valves and the wall of VSD, which were where the site of turbulent flow in left-to-right shunt occurred. This perpetual turbulent flow was damaging for endothelial cell, which may lead to vegetation formation. In both cases, the antibiotics were unsuccessful to remove the vegetation.

Around 80%-90% of IE cases result from staphylococcal, streptococcal, and enterococcal infection.<sup>8,9</sup> *Staphylococcus aureus* is the most frequent microorganism in right-sided IE among intravenous drug users, whereas *Streptococcus viridans* is the predominant microorganisms in nondrug users.<sup>10</sup> *Streptococci* were found from the blood cultures of the first patient. *Streptococcus viridans* and *Streptococcus mitis/oralis* are commensal bacteria in the oral cavity and gastrointestinal tract.<sup>11</sup> Other blood culture revealed the growth of *Streptococcus porcinus*, a member of beta hemolytic streptococcus originating from genitourinary tract of female in reproductive age.<sup>12</sup> Single bacterial growth from blood culture of polymicrobial IE may result from growth competition in blood agar media. Previous report revealed that from 1011 cases of IE, 5.9% were caused by polymicrobial infection.<sup>13</sup> The mortality between patients with polymicrobial vs monomicrobial infection does not significantly differ.<sup>13</sup>

The blood cultures from the second patient did not show the growth of bacteria, possibly due to a previous antibiotics course.

In addition to the left-to-right shunt VSD, a left-to-right shunt PDA contributes to the increase in blood flow through pulmonary artery which promotes pathologic pulmonary vascular shear stress and circumferential stretch. In both cases, left-to-right shunt through VSD and PDA caused volume overload in the right ventricle and increased blood flow through the pulmonary valve into pulmonary vasculature.<sup>3</sup> This high flow caused endothelial disruption in the turbulence loci, via increasing shear stress and circumferential stretch, and ignited the formation of vegetation during bacteremia. The same mechanism was applied for high flow through VSD which was a predisposing state for vegetation formation on the defect. The endothelial disruption facilitates fibrin deposition and aggregation with subsequent vegetation formation.<sup>9</sup>

Surgical intervention for right-sided IE may be performed by considering several conditions such as right heart failure due to severe tricuspid regurgitation with poor response to medication, persistence of infection that does not respond to appropriate antibiotics, tricuspid valve vegetation of >20 mm, and recurrent pulmonary embolism.<sup>14</sup> Most reports showed high success rate of antibiotics treatment for right-sided IE.<sup>15</sup> The need for surgical intervention is <30%.<sup>15</sup> However, our cases were unresponsive with appropriate antibiotics treatments; therefore, the surgery was planned. Unfortunately, one patient refused the surgery and another patient was succumbed to death due to fatal acute pulmonary embolism suspected from the right-sided vegetations. During their hospital stay, both patients were active and mobile. No unilateral leg edema was identified in our second patient; therefore, he had low probability of having deep vein thrombosis as the cause of pulmonary embolism.

## 5 | CONCLUSION

These two cases represent uncorrected left-to-right shunt congenital heart diseases which were complicated by right-sided IE. Concomitant left-to-right shunt VSD and PDA serve as predisposing factor for vegetation formation in the right heart. Our cases emphasize the significance of prompt diagnosis and timely management for IE in patients with uncorrected congenital heart disease because it has the potential for fatal outcome.

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## CONFLICT OF INTEREST

There is no conflict of interest.

## AUTHORSHIP

PDS: acted as Internal Medicine Resident, took care the patients, and wrote the manuscript as primary author. ABH: acted as Internist-Cardiologist, participated in ward supervision, reviewed and approved the manuscript. DWA: acted as Cardiologist, participated in ward supervision, reviewed and approved the manuscript. HM: acted as Cardiologist-Echocardiography Consultant, interpreted the echocardiography data and reviewed the manuscript. LKD: acted as Cardiologist-Echocardiography Consultant, interpreted the echocardiography data, and participated in clinical advice for the patients.

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