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ISOLATED RIGHT-SIDED PULMONARY VALVE INFECTIVE ENDOCARDITIS IN AN UNREPAIRED TETRALOGY OF FALLOT: A PAEDIATRIC CASE REPORT

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ABSTRACT
Isolated pulmonary valve infective endocarditis is an uncommon form of right-sided infective endocarditis, especially in children. It is rarely seen even among patients with congenital heart disease, making early diagnosis difficult because the presenting features often resemble severe respiratory infection or sepsis. We report the case of a 4-year-old girl with unrepaired tetralogy of Fallot who presented with persistent high-grade fever, cough, respiratory distress and thrombocytopenia. She was initially managed as sepsis with lower respiratory tract infection. Despite broad-spectrum antibiotics, fever persisted and inflammatory markers remained elevated. Repeated clinical assessment and echocardiography demonstrated vegetation over the pulmonary valve, confirming isolated right-sided pulmonary valve infective endocarditis. She received prolonged intravenous antibiotic therapy with gradual resolution of fever, improvement in inflammatory markers and recovery of platelet counts. This case highlights the importance of maintaining a high index of suspicion for infective endocarditis in children with cyanotic congenital heart disease who have persistent fever despite appropriate antimicrobial therapy. Early echocardiographic evaluation and timely treatment can improve clinical outcomes.

KEYWORDS: Apical debris extrusion; TruNatomy; ProTaper Gold; GenEndo; nickel-titanium rotary instruments; root canal preparation; Myers and Montgomery model

INTRODUCTION
Infective endocarditis (IE) is an uncommon but potentially life-threatening infection involving the endocardial surface of the heart. Although the disease most frequently affects the left-sided cardiac valves, isolated pulmonary valve infective endocarditis (PVIE) is exceptionally rare and accounts for less than 2% of all cases of infective endocarditis [1].
Recent advances in microbiological techniques and cardiac imaging have improved the diagnosis of infective endocarditis. The 2023 European Society of Cardiology (ESC) guidelines recommend early clinical suspicion, blood culture sampling and echocardiographic assessment in patients with persistent fever or underlying structural heart disease, as delayed diagnosis is associated with worse clinical outcomes [2]. Likewise, the updated Duke–International Society for Cardiovascular Infectious Diseases (Duke-ISCVID) criteria have incorporated newer microbiological and imaging findings, thereby improving the diagnostic approach to infective endocarditis [3]. Subsequent validation studies have confirmed the reliability of these revised criteria in routine clinical practice [4].
Congenital heart disease remains one of the major predisposing factors for infective endocarditis in children. Abnormal intracardiac blood flow causes endothelial injury, which facilitates bacterial adherence and subsequent vegetation formation. The risk is particularly high in children with unrepaired cyanotic congenital heart disease because of persistent turbulent blood flow and altered haemodynamics [5,6].
Tetralogy of Fallot (TOF) is one of the common cyanotic congenital heart defects associated with infective endocarditis. However, isolated involvement of the pulmonary valve is exceptionally uncommon even in these patients. Only a few paediatric cases have been reported, and most of the available literature consists of isolated case reports or small case series [7,8]. Consequently, pulmonary valve endocarditis is often overlooked during the initial evaluation, particularly when children present with respiratory symptoms and features suggestive of sepsis.
The clinical presentation of isolated PVIE is usually non-specific. Children commonly present with prolonged fever, cough, respiratory distress and raised inflammatory markers, which can easily mimic severe lower respiratory tract infection or bloodstream infection. Failure to respond to appropriate antimicrobial therapy, persistent inflammatory markers and repeat echocardiography demonstrating valvular vegetation are important clues that should prompt clinicians to consider this uncommon diagnosis [9–11].
We report the case of a four-year-old girl with unrepaired tetralogy of Fallot who presented with persistent fever, thrombocytopenia and respiratory distress. She was initially managed as severe sepsis with lower respiratory tract infection. Persistent fever despite broad-spectrum antimicrobial therapy prompted repeat cardiac evaluation, which demonstrated isolated right-sided pulmonary valve infective endocarditis. This case highlights the importance of

maintaining a high index of suspicion for infective endocarditis in children with cyanotic congenital heart disease who continue to have fever despite appropriate treatment. It also emphasises the value of repeated echocardiographic assessment in establishing an early diagnosis of this rare but potentially life-threatening condition [12].

Case Presentation

A four-year-old girl, a known case of unrepaired tetralogy of Fallot (TOF), was brought to our emergency department with fever for 10 days, cough and cold for four days, and fast breathing for one day. The fever was high grade, intermittent and associated with chills and rigors. It was partially relieved with medications. Her cough was associated with rhinorrhoea, and there was no history of vomiting, loose stools, seizures, skin rash or poor oral intake. Before presentation to our hospital, she had received treatment at multiple healthcare centres with oral cefixime, azithromycin and doxycycline, but there was no significant clinical improvement. Outside laboratory investigations showed anaemia, leucocytosis, elevated C-reactive protein and a weakly positive scrub typhus IgM, following which she was referred to our centre for further management.

She was diagnosed with tetralogy of Fallot during infancy. Her previous echocardiogram had shown a large subaortic ventricular septal defect with bidirectional shunting, more than 50% overriding of the aorta, severe valvular and infundibular pulmonary stenosis, a tiny patent foramen ovale with left-to-right shunt, a small muscular ventricular septal defect and right ventricular hypertrophy. No intracardiac vegetation had been noted on the earlier study. She had not undergone corrective cardiac surgery. There was no previous history of infective endocarditis or prolonged unexplained fever.

She was born preterm by lower segment caesarean section because of oligohydramnios with a birth weight of 1.7 kg. She cried immediately after birth and did not require neonatal intensive care admission. Her developmental milestones were appropriate for age, and she was immunised according to the National Immunisation Schedule. There was no history of parental consanguinity or congenital heart disease among family members.

On admission, she was conscious, alert and in significant respiratory distress. Her respiratory rate was 45 breaths/minute, heart rate was 122 beats/minute and oxygen saturation was 77% on room air, which improved to 98% with supplemental oxygen. Subcostal, intercostal and suprasternal retractions were present. Cardiovascular examination revealed a pansystolic murmur, while bilateral air entry was equal on chest auscultation. The abdomen was soft without organomegaly, and the neurological examination was unremarkable. In view of persistent respiratory distress and hypoxaemia, we shifted her to the paediatric intensive care unit (PICU) for close monitoring and further management.

At the time of admission, our initial clinical impression was severe lower respiratory tract infection with sepsis in a child with underlying cyanotic congenital heart disease. She was started on oxygen support, intravenous ceftriaxone, azithromycin, oseltamivir, bronchodilator nebulisation and supportive care. Despite treatment, she continued to have intermittent fever, worsening thrombocytopenia, markedly elevated inflammatory markers and raised cardiac biomarkers. She also required escalation of respiratory support from a non-rebreathing mask to high-flow nasal cannula because of persistent respiratory distress. Blood investigations showed persistent leucocytosis, C-reactive protein of 223 mg/L, procalcitonin of 19 ng/mL and thrombocytopenia, with the platelet count falling to 43,000/mm³.

As the fever persisted despite broad-spectrum antimicrobial therapy and there was no satisfactory clinical response, we reconsidered our initial diagnosis. The prolonged fever in a child with unrepaired tetralogy of Fallot, together with persistently elevated inflammatory markers and a cardiac murmur, raised our suspicion of infective endocarditis. We therefore planned repeat echocardiographic evaluation, which subsequently demonstrated vegetation involving the pulmonary valve, confirming isolated right-sided pulmonary valve infective endocarditis.

Figure 1 . Image showing the child at time of admission

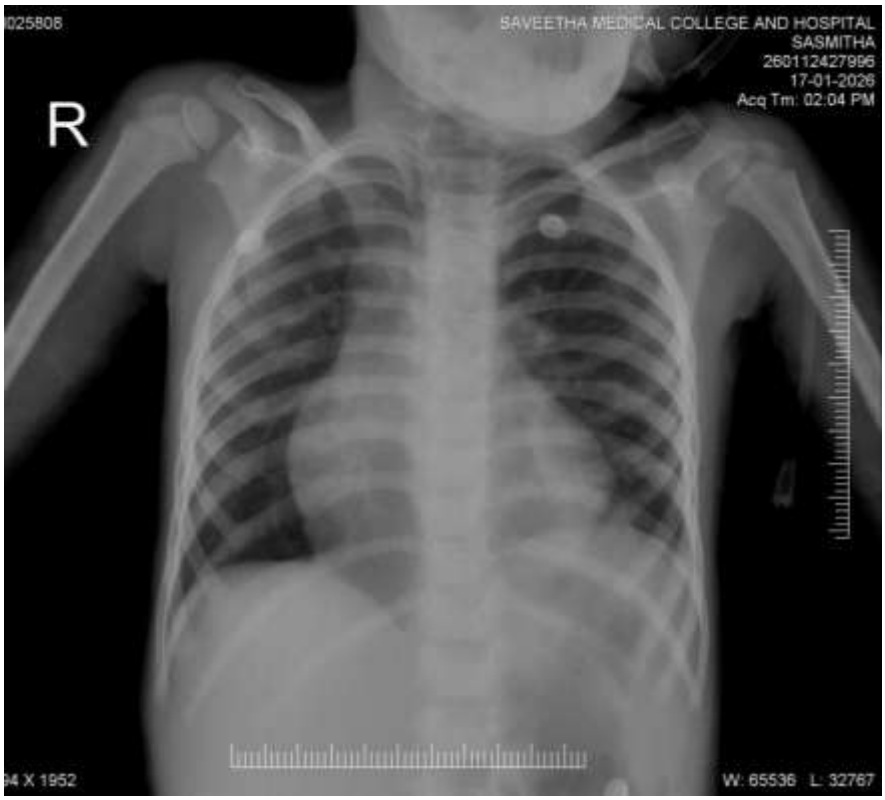

Figure 2 . Chest radiograph of child showing Boot shaped heart

Investigations

On admission, initial laboratory investigations showed anaemia with leucocytosis and neutrophilic predominance. The inflammatory markers were significantly elevated, with a C-reactive protein (CRP) level of 223 mg/L and a procalcitonin level of 19 ng/mL. Thrombocytopenia was noted, with the platelet count decreasing to 43,000/mm³ during the early course of illness. Cardiac biomarkers were also elevated, including N-terminal pro-brain natriuretic peptide (NT-proBNP) of 9360 pg/mL, troponin I of 1.76 ng/mL and creatine kinase-MB (CK-MB) of 6.65 ng/mL, suggesting associated myocardial stress. A scrub typhus IgM performed outside our hospital was reported as weakly positive. However, the overall clinical picture and the lack of sustained improvement with empirical therapy prompted us to consider an alternative diagnosis.

Serial laboratory investigations showed persistent elevation of inflammatory markers during the initial phase of admission despite broad-spectrum antimicrobial therapy. Platelet counts gradually improved from 43,000/mm³ to 50,000/mm³, 53,000/mm³, 75,000/mm³ and finally to 101,000/mm³ with treatment. Similarly, CRP decreased from 223 mg/L to 88 mg/L, followed by 48.8 mg/L and 38.5 mg/L. Serum procalcitonin also reduced from 19 ng/mL to 3.49 ng/mL during the hospital stay, indicating a favourable response to therapy. NT-proBNP showed a declining trend from 9360 pg/mL to 4580 pg/mL on serial assessment.

Chest radiography showed features consistent with lower respiratory tract involvement without evidence of pulmonary abscess or septic pulmonary emboli. Electrocardiography did not reveal any significant rhythm abnormality. Because the child continued to have fever despite appropriate antimicrobial therapy, repeat transthoracic echocardiography was performed. This demonstrated a mobile vegetation attached to the pulmonary valve, consistent with isolated right-sided pulmonary valve infective endocarditis in the background of unrepaired tetralogy of Fallot. The previously known congenital cardiac defects, including a large subaortic ventricular septal defect, overriding aorta, severe valvular and infundibular pulmonary stenosis, right ventricular hypertrophy and a tiny patent foramen ovale, were again confirmed. No vegetation was identified on the left-sided cardiac valves. These echocardiographic findings, together with the clinical presentation and laboratory evidence of ongoing infection, fulfilled the diagnostic criteria for infective endocarditis.

To exclude other causes of persistent fever and systemic inflammation, autoimmune investigations including antinuclear antibody (ANA), perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA) and cytoplasmic ANCA (c-ANCA) were also planned during the course of admission. Ultrasonography of the abdomen was requested as part of the evaluation for possible extracardiac complications.

Differential Diagnosis

When the child was admitted, our first diagnosis was severe lower respiratory tract infection with sepsis because she had prolonged fever, cough, respiratory distress, raised inflammatory markers and thrombocytopenia. The weakly positive scrub typhus IgM from the outside hospital also made us consider scrub typhus as a possible cause. However, the child continued to have fever despite appropriate antibiotics, and her clinical condition did not improve as expected.

Acute myocarditis was another possibility because the cardiac biomarkers, including NT-proBNP and troponin-I, were elevated. However, the child did not have features suggestive of myocardial dysfunction on echocardiography, and the

raised cardiac markers were considered more likely to be related to severe systemic infection and the underlying congenital heart disease.
We also considered infective endocarditis because the child had unrepaired tetralogy of Fallot, prolonged fever and persistently raised inflammatory markers. The previous echocardiogram had not shown any vegetation. Since the fever continued despite broad-spectrum antibiotics, we repeated the echocardiographic examination. This showed vegetation over the pulmonary valve, which confirmed isolated right-sided pulmonary valve infective endocarditis. The clinical findings together with the echocardiographic features were consistent with infective endocarditis.
Thus, the final diagnosis was isolated right-sided pulmonary valve infective endocarditis in a child with unrepaired tetralogy of Fallot presenting with sepsis and lower respiratory tract infection.

Treatment
The child was admitted to the paediatric intensive care unit because of persistent respiratory distress and hypoxaemia. Oxygen support was started initially and later escalated to high-flow nasal cannula as her respiratory distress increased. She received intravenous fluids with careful fluid restriction, bronchodilator nebulisation and supportive care.
Empirical antimicrobial treatment was started with intravenous ceftriaxone along with oral azithromycin and oseltamivir. As the child continued to have fever and inflammatory markers remained high, the antibiotic was changed to intravenous piperacillin–tazobactam. After infective endocarditis was diagnosed, intravenous vancomycin was added to provide adequate coverage for gram-positive organisms. Oral doxycycline, which had already been started because of the initial possibility of scrub typhus, was continued until the clinical picture became clear.
Respiratory management included nebulised bronchodilators, inhaled budesonide and hypertonic saline according to the child's clinical condition. Magnesium sulphate was given during the early phase because of significant wheeze and respiratory distress. Oxygen requirement gradually decreased over the next few days, and she was successfully weaned from high-flow nasal cannula to room air.
Nutrition was maintained through nasogastric tube feeds during the acute phase and later changed to oral feeds as her respiratory status improved. Fluid intake was carefully monitored throughout the hospital stay. After cardiology review, propranolol was started for the underlying tetralogy of Fallot. Regular monitoring of vital signs, urine output, inflammatory markers and serial echocardiography was continued to assess her response to treatment.

Outcome and Follow-up
The child remained in the paediatric intensive care unit for close monitoring and continued treatment. During the first few days, she continued to have intermittent fever, respiratory distress and thrombocytopenia. However, after escalation of antibiotic therapy and supportive management, her general condition gradually improved. The fever became less frequent and finally settled. Her respiratory distress reduced, and oxygen requirement gradually came down. She was successfully weaned from high-flow nasal cannula to room air while maintaining satisfactory oxygen saturation.
Serial laboratory investigations also showed improvement. The platelet count increased progressively from 43,000/mm³ to 101,000/mm³. Inflammatory markers showed a steady fall, with CRP decreasing from 223 mg/L to 38.5 mg/L and procalcitonin from 19 ng/mL to 3.49 ng/mL. NT-proBNP levels also showed a downward trend during treatment, suggesting improvement in the inflammatory process and cardiac stress.
The child tolerated oral feeds well after improvement in respiratory status and remained haemodynamically stable throughout the later part of her hospital stay. No new neurological deficit, embolic event or other major complication was noted during admission. She continued to receive intravenous antibiotics under close monitoring by the paediatric and paediatric cardiology teams.
She was planned for regular outpatient follow-up with the paediatric cardiology team for repeat clinical assessment and serial echocardiography to monitor the response of the pulmonary valve vegetation to antimicrobial therapy. She was also advised to continue follow-up for definitive surgical management of her unrepaired tetralogy of Fallot after complete recovery from the acute infection.

DISCUSSION
Infective endocarditis involving the pulmonary valve is rare in both children and adults. Even among patients with right-sided infective endocarditis, isolated pulmonary valve involvement is uncommon. Most published reports are single cases or small case series, which shows how infrequently this condition is encountered in routine practice [13,14]. Our patient had unrepaired tetralogy of Fallot, making this case even more unusual because pulmonary valve endocarditis is reported only occasionally in children with congenital heart disease.
Children with cyanotic congenital heart disease have a higher risk of infective endocarditis because abnormal blood flow causes repeated injury to the endocardium. This damaged surface allows circulating bacteria to attach and form vegetations. Even then, the pulmonary valve is usually spared because it is exposed to lower pressure and lower oxygen content than the left-sided valves. This explains why isolated pulmonary valve infective endocarditis remains an uncommon diagnosis, even in children with congenital heart disease [15,16]. In our patient, severe pulmonary stenosis and abnormal flow across the right ventricular outflow tract might have contributed to endothelial injury and vegetation formation.
One of the important learning points from our case was the difficulty in making the diagnosis during the early stage of illness. The child came with prolonged fever, cough, respiratory distress and thrombocytopenia. These findings suggested severe lower respiratory tract infection with sepsis, and this was our initial working diagnosis. The weakly positive scrub typhus IgM added further confusion. As a result, the child was initially managed with broad-spectrum antimicrobial

therapy and supportive care. However, the fever continued and the inflammatory markers remained high. This made us reconsider the diagnosis and look for another cause of persistent fever. Similar diagnostic difficulty has also been described in previous reports of pulmonary valve infective endocarditis, where the initial presentation resembled pneumonia or sepsis rather than infective endocarditis [13,17].

A careful clinical examination played an important role in our patient. The presence of an underlying cyanotic congenital heart disease, persistent fever despite appropriate antibiotics and a cardiac murmur made us suspect infective endocarditis. We therefore repeated the transthoracic echocardiogram, which demonstrated vegetation over the pulmonary valve. The earlier echocardiogram performed before this illness had not shown any vegetation. This shows that a single negative echocardiographic study does not completely exclude infective endocarditis, especially when clinical suspicion remains high. Repeated echocardiography should be considered whenever the child fails to improve as expected [2,3,4].

The diagnosis in our patient was based on the overall clinical picture, laboratory findings and echocardiographic evidence of pulmonary valve vegetation. We did not rely on one investigation alone. Instead, we combined the history of prolonged fever, underlying congenital heart disease, raised inflammatory markers and repeat imaging findings before arriving at the final diagnosis. This approach is also supported by the recent ESC guidelines and the updated Duke-ISCVID diagnostic criteria, which recommend interpreting microbiological, clinical and imaging findings together rather than in isolation [2–4].

The management of isolated pulmonary valve infective endocarditis is not different from that of other forms of infective endocarditis. Early intravenous antibiotics remain the mainstay of treatment, while surgery is reserved for selected patients with persistent infection, severe valve destruction, recurrent embolic events or heart failure [2]. Our patient showed gradual clinical improvement with intravenous antimicrobial therapy and supportive care. The fever settled, respiratory distress improved, inflammatory markers decreased and platelet counts recovered during the hospital stay. Since she responded well to medical treatment and did not develop haemodynamic instability or major complications, surgical intervention was not required during the acute phase. Similar successful medical management has also been reported in several recently published case reports [13,18].

Children with tetralogy of Fallot remain at risk of recurrent infective endocarditis until definitive correction of the underlying cardiac defect. Therefore, long-term follow-up is important even after recovery from the acute infection. Our patient was advised regular follow-up with the paediatric cardiology team for serial echocardiography and further planning for definitive surgical repair of tetralogy of Fallot after complete resolution of infection.

Our case adds to the limited paediatric literature on isolated pulmonary valve infective endocarditis. It also reminds us that persistent fever in a child with unrepaired congenital heart disease should not always be explained by respiratory infection alone. When the child does not improve as expected, we should reassess the diagnosis and repeat echocardiography if needed. Early recognition and timely treatment can prevent complications and improve outcomes in this rare condition.

Strengths of our case

- Rare paediatric case of isolated pulmonary valve infective endocarditis.
- Occurred in unrepaired tetralogy of Fallot, which is rarely reported.
- Demonstrates the value of repeating echocardiography when fever persists despite treatment.
- Good clinical recovery with timely medical management alone, avoiding emergency surgery.

Limitation

The exact causative organism could not be clearly established from the available records, which limits microbiological correlation. However, the diagnosis was supported by the clinical presentation, serial laboratory findings and echocardiographic evidence, and the child showed a good response to appropriate antimicrobial therapy.

Learning Points

- Isolated pulmonary valve infective endocarditis is a rare form of infective endocarditis in children, even among those with congenital heart disease.
- Persistent fever in a child with unrepaired tetralogy of Fallot should prompt us to consider infective endocarditis, especially when there is poor response to appropriate antibiotics.
- Repeating echocardiography is important when clinical suspicion remains high despite an initially negative study.
- Serial inflammatory markers and platelet counts are useful in monitoring the response to treatment but should always be interpreted along with the clinical condition.
- Early diagnosis, prolonged intravenous antibiotic therapy and close follow-up can lead to a favourable outcome even in this uncommon condition.

Patient's Perspective

The child was too young to share her own experience. Her parents told us that they were worried because the fever continued even after treatment at different hospitals. They became more anxious when her breathing became fast and she had to be admitted to the intensive care unit. They were relieved after the diagnosis was made and the child started improving with treatment. They understood the need for prolonged antibiotic therapy and regular follow-up for both infective endocarditis and her underlying congenital heart disease.

TruNatomy (Dentsply Sirona, Ballaigues, Switzerland) departs from conventional rotary-file design through a reduced core mass, a 0.03 taper at its finishing file, and a “parallelogram” cross-section intended to maximize flexibility and limit

dentinal-wall engagement while preserving canal anatomy.10 ProTaper Gold (Dentsply Sirona), a heat-treated evolution of the original ProTaper Universal system, retains a multiple variable-taper design while gaining flexibility and cyclic-fatigue resistance through advanced thermomechanical processing.11 GenEndo (Gen Endo, India) is a single-file rotary system increasingly adopted in general and specialist practice across South Asia, built around continuous rotary motion with a distinct rake angle and taper progression; comparative data on its apical-extrusion behaviour, however, remain limited.12

Given the widespread clinical use of all three systems and the scarcity of direct comparative data — particularly involving GenEndo — this study was undertaken to evaluate and compare the quantity of apically extruded debris generated by TruNatomy, ProTaper Gold, and GenEndo during instrumentation of mandibular premolars, using the well-validated Myers and Montgomery experimental model.13

REFERENCES

1. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2023 ESC Guidelines for the management of infective endocarditis. Eur Heart J. 2023;44(39):3948-4042.
2. Fowler VG Jr, Durack DT, Selton-Suty C, Athan E, Bayer AS, Chamis AL, et al. The 2023 Duke-ISCVID criteria for infective endocarditis. Clin Infect Dis. 2023;77(4):518-26.
3. Holland TL, Baddour LM, Bayer AS, Hoen B, Miro JM, Fowler VG Jr. Infective endocarditis. Nat Rev Dis Primers. 2016;2:16059.
4. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. Circulation. 2015;132(15):1435-86.
5. Baltimore RS, Gewitz M, Baddour LM, Beerman LB, Jackson MA, Lockhart PB, et al. Infective endocarditis in childhood: 2015 update. Circulation. 2015;132(15):1487-515.
6. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: Guidelines from the American Heart Association. Circulation. 2007;116(15):1736-54.
7. Li W, Somerville J. Infective endocarditis in the grown-up congenital heart patient. Eur Heart J. 1998;19(1):166-73.
8. Niwa K, Siu SC, Webb GD, Gatzoulis MA. Progressive aortic root dilation in adults with congenital heart disease and implications for infective endocarditis. Heart. 2002;87(3):262-6.
9. Cahill TJ, Prendergast BD. Infective endocarditis. Lancet. 2016;387(10021):882-93.
10. Yuan SM. Right-sided infective endocarditis: recent epidemiologic changes. Int J Clin Exp Med. 2014;7(1):199-218.
11. Ramadan FB, Beanlands DS, Burwash IG. Isolated pulmonary valve infective endocarditis in adults: a case report and review of the literature. Can J Cardiol. 2000;16(10):1282-8.
12. Gonzàlez-Alujas MT, Evangelista A, Santamarina E, et al. Diagnosis and management of infective endocarditis by echocardiography. J Am Soc Echocardiogr. 2004;17(6):614-24.
13. Moss R, Munt B. Injection drug use and right-sided endocarditis. Heart. 2003;89(5):577-81.
14. Millar BC, Moore JE. Emerging issues in infective endocarditis. Emerg Infect Dis. 2004;10(6):1110-6.
15. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy and management of complications: A scientific statement from the American Heart Association. Circulation. 2015;132(15):1435-86.