Case Report

Infective Endocarditis in a β-thalassemia Major Child

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Key Words : *Infective endocarditis, ²-thalassemia, tricuspid valve.*

Abstract:

Almost all patients who develop infective endocarditis (IE) had history of congenital or acquired heart disease.We report a 9 years old boy who was diagnosed as β-thalassemia major since age 1.5 years, admitted to hospital with chief complaint of difficulty of breathing for 1 week before admission, accompanied by fever. Holosystolic murmur of grade 3/6 was found in the lower left sternal border along with hepatosplenomegaly. Chest x-ray depicted right ventricle enlargement and opaque densities in the middle field of left lung. Blood culture showed growth of Staphylococcus aureus. *Echocardiography detected thickening tricuspid valve with oscillating mass in the tricuspid valve, severe pulmonary hypertension, and minimal pericardial effusion. Diagnosis of IE was made. After clinical improvement he was discharged with good condition. The diagnosis of IE in children without heart defects is difficult to establish and right-sided IE is rare in children that a high suspicion index should be considered.*

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Introduction:

Infective endocarditis (IE) is an infection of endocardium.[1] The incidence in children varied between 0.8–3.3/1000 in general hospital and 20–56/1000 in cardiac center.[2] Infective endocarditis is classified based on clinical condition and pathogens as native-valve IE, prosthetic-valve IE, IE in intravenous drug users, and health care-associated IE. Health care-associated IE tends to increase.[3, 4] Infective endocarditis is more common in male, with male and female ratio is 2:1.[2,3,5] Diagnosing IE in patient without heart defect is a challenge. The mechanism of right-sided IE in this patient is similar with those Intravenous drug users (IDU).

Case History:

A 9 years old boy was admitted to our hospital with chief complaint of difficulty of breathing for 1 week before admission, accompanied by fever and cough. There was no wheeze or stridor. He was diagnosed as β-thalassemia major since age 1.5 years. He received regular packed red cell transfusion every two weeks and desferioxamine as iron chelating agent. He experienced intermittent fever since one month ago after receiving transfusion in a district hospital. He was hospitalized there for 8 days and discharged with improvement. After five days at home, he had an episode of fever again and admitted to another district hospital. He was hospitalized there for two weeks; got hospital acquired pneumonia, and then referred to our hospital. In the last two years he felt easy fatigability and limited his activities himself.

In the physical examination, he was moderately ill with severe malnutrition, cooley facies, fever, holosystolic murmur grade 3/6 was found in the lower left sternal border, crackles in both lung fields, and hepatosplenomegaly. There was no eyelid and extremities edema, no petechiae on the skin, mucous membranes, no Osler's node, Janeway's lesions or Splinter hemorrhages. Pulpitis was found in numerous of his teeth. Blood test revealed hemolytic anemia, leukocytosis with elevated segmented polymorphonuclear cell. His tuberculin skin test confirmed negative result. His

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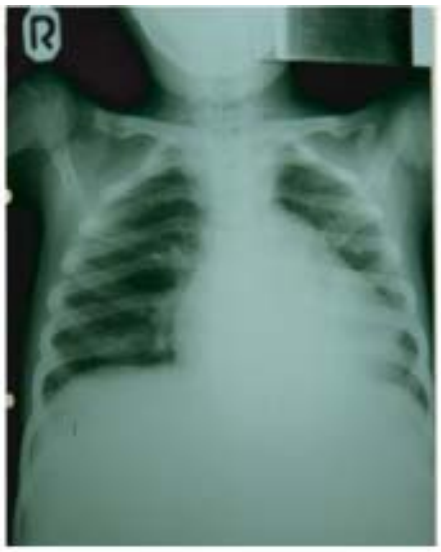
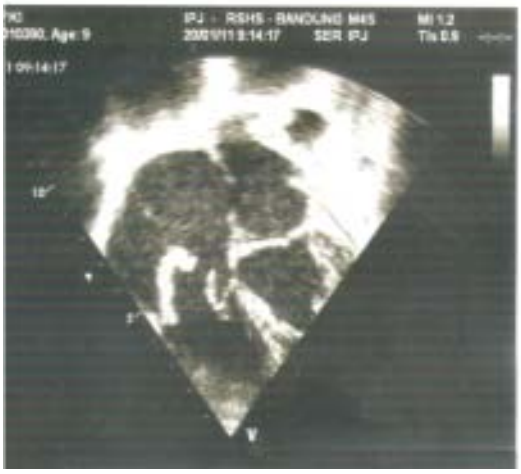
chest x-ray depicted right ventricle enlargement and opaque densities in the middle field of left lung. Electrocardiography revealed sinus tachycardia. Blood culture showed growth of *Staphylococcus aureus*. Echocardiography detected thickening of tricuspid valve with oscillating mass 1.2 x 2.6 cm sized in the tricuspid valve and severe pulmonary hypertension (pulmonary arteries pressure gradient 60 mmHg), and minimal pericardial effusion.

Initially he was diagnosed and treated as a patient with typhoid fever. The diagnosis of IE was made on day 10 of hospitalization, when his pneumonia resolved, but congestive heart failure (CHF) developed. He received empirical antibiotics (cefotaxime) while awaiting the results of blood culture. Digoxin, captopril, and furosemide were added. Cefazolin was given for 5 weeks. Teeth extraction was planned to be performed after clinical improvement. Clinical improvement was seen in day 17 of hospitalization. Repeated echocardiography showed reduced size of vegetation, right atrium and right ventricle dilatation, moderate to severe tricuspid regurgitation, poor cooptation and thickened of posterior and anterior leaflet, mild pulmonal valve regurgitation, good ventricle function and no pericardial effusion. Digoxin, captopril and furosemide discontinued. In the day 51, there was definite clinical improvement, drugs discontinued and he was discharged. His last echocardiography revealed shortened septal leaflet without vegetation.





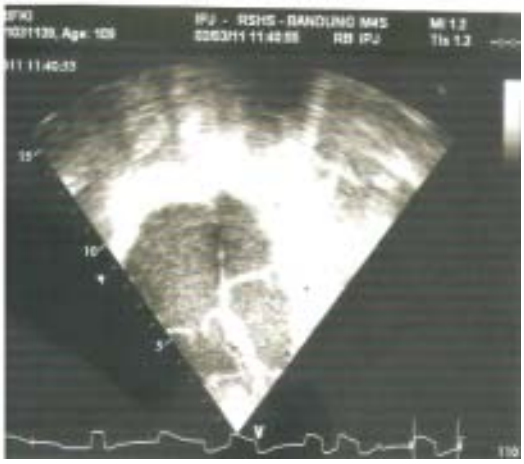


Fig.-1:

Discussion:

The principal pathophysiology of IE is presence of defect or structural lesion of endocardium and bacteriemia, even transient. Endocardial defects are usually congenital or acquired lesions, such as rheumatic heart disease. Injury of endocardium can be caused by blood turbulence from high pressure to low pressure, flow through orifice or small defects, central vein cathetherization, inflammation such as rheumatic carditis, or degenerative process in adults. Such endothelial damage induces platelet adhesion and thrombus formation, called as non bacterial thrombotic endocarditis (NBTE).[1, 3, 6-9]When bacteriemia occurs, bacteria will attach to the NTBE area. Bacterial colonization will enhance thrombus formation, local inflammation, and damage adjacent structures.[1, 3, 5, 10] Bacteriemia can occur as a result of procedures or trauma at mouth, oropharynx, gastrointestinal or urogenital tract, even in trauma of chewing or teeth brushing.[1,3,6,7,11]

Infective endocarditis risk factors are rheumatic heart disease, congenital heart defects especially after heart procedures, and mitral valve prolapse, neonates, infants, and intravenous drug users.[2,12] Infective endocarditis can occur in children without previously cardiac defects in 20% cases.[13, 14]Right-sided IE rarely occurs with 5–10% incidence from all cases, especially in HIV or immunosuppresed patients. Infections related with low sterility of intravenous (IV) injection, contaminated IV drugs, and immunity abnormalities. *Staphylococcus aureus* is the etiology of 60%–90% cases.[3]

Our patient received regular blood transfusion and intravenous furosemide and no previous cardiac defects. Thalassemia patients could experience myocarditis, pericarditis, pulmonary hypertension, or cardiomyopathy due to infection, chronic anemia, and hemosiderosis.[15-18] There was pulmonary hypertension, tricuspid regurgitation, and cardiomegaly which can occur before IE. The predisposing factor is endothelial damage as a result of thalassemia and repeated IV drugs.

A diagnosis of IE is made based on history, clinical manifestation, and laboratory studies. From history taking, it took the presence of heart defects, rheumatic heart disease, recent dental procedure or mouth minor surgery, urogenital diseases, IV drug administration, central venous cathetherization, prosthetic valves. Patients experienced fever, cough, joint pain, chest pain, myalgias, and shortness of breath, loss of appetite, fatigue, night sweating, weight loss, and neurologic symptoms. In the physical examination, we can find fever, tachycardia, petechiae, Osler's nodes, splinter hemorrhages, Roth's spot, Janeway's lesion, new murmur or changes of previous murmur, splenomegaly, and clubbing fingers, arthritis, glomerulonephritis, myocardium abscess, and CHF may be present.[1-3, 5, 13, 19]Prolonged fever is common in 90%-100% patients.[2, 3, 20, 21]CHF may be present in 29%-39% patients.[5] Negative blood culture can be found in 4%-31% from all IE patients.[14, 22, 23]There are three categories of diagnostic possibilites using the modified Duke criteria: definite, possible, and rejected. A diagnosis of definite IE is made by pathologic evidence and fulfillment of pathologic evidence of IE (microorganism demonstrated by culture and histologic examination) and clinical criteria is met by the presence of two major criteria, one major and three minor criteria, or five minor criteria. Major criteria are blood culture positive for IE and evidence of endocardial involvement. Minor criteria are (1) predisposition, predisposing heart condition, or injection drug users, (2) fever, temperature >38°C, (3) vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions, (3) immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor, (4) microbiologic evidence: positive blood culture but does not meet a major criterion or serologic evidence of active infection with organism consistent with IE.[3, 5, 7, 24]

Infective endocarditis diagnosis in this patient is made based on history, clinical symptoms, and in the presence 1 major criterion (positive echocardiography for IE) and 3 minor criteria (fever, IV drug administration, and positive blood culture).

Antibiotic administration in infection due to *Staphylococcus aureus* should be considering whether methicllin susceptible *S. aureus* (MSSA) or methicllin resistant *S. aureus* (MRSA). Standard therapy for IE caused by MSSA is ²-lactamase

(nafcillin, oxacillin, and flucoxacillin 200 mg/kg/24 hour IV in 4–6 doses combined with or without gentamicin 3 mg/kg/24 hour IV for 3–5 days, maximally 2 weeks. In patient allergic to penicillin, vancomycin 40 mg/kg/24 hours IV in 2–4 doses for 4–6 weeks combined with or without gentamicin for 3–5 days, maximally 2 weeks. Another alternative is cefazolin 100 mg/kg/24 hours IV in 3–4 doses combined with or without gentamicin.[24] IE caused by MRSA given vancomycin 40 mg/kg/24 hours IV in 2–3 doses for 4–6 weeks combined with or without gentamicin for 3–5 days, maximally 2 weeks.[2, 3, 5, 7, 22]CHF in right-sided IE is rare, but can occur due to increased pulmonary resistance, severe right-side valvular regurgitation, or obstruction.[3] He was given cefazolin for 6 weeks and gentamicin for 2 weeks. Antibiotic selection consistent with presumptive infection caused by MSSA, and resistance test showed sensitivity to cephalosporine. Therapy for CHF is given when symptoms of CHF developed, and discontinued once clinical and following echocardiography showed improvement.

Monitoring IE patients covered response of therapy and complications. Surgical procedure performed when poor response of therapy and complications developed.[35, 24] Prognosis of right-sided IE is good with mortality in hospital <10%.[3] Indications of surgical procedure in right-sided IE are CHF due to severe tricuspid regurgitation and poor response to diuretic drugs administration, difficult-to-eradicate organism, or persistent bacteremia after adequate antibiotic therapy for 7 days, and persistent tricuspid vegetation >20 mm, and reccurent pulmonary embolism with or without CHF.[3] In children, preserving native valve is primary choice.[2] Our patient had good response to therapy, that tricuspid valve repair was deferred with long term follow up.

Recurrence of IE is the next important point. Once a child recovered from IE, then he was on high risk of recurrence, as much as 2.7%–22.5%.[3,5-7,24] Prevention step of IE is oral hygiene care and prophylactic antibiotic in certain medical procedures, one of them is dental procedure. Prophylactic antibiotic administration is recommended in dental procedure such as teeth extraction. Amoxicillin or ampicillin 50 mg/kg/24 hours oral or IV is given. In patients allergic to penicillin, clindamycin 20 mg/kg oral or IV can be given 30-60 minutes before procedure.[3,5-7,9, 11,24,25] There were several differences of guidelines in developed countries.[26-29] He was included in high-risk category of recurrence of IE. Counseling of oral hygiene and teeth extraction plan is to be given to the patient and parents along. Sterility of IV access and drug administration should be maintained.

Conclusion:

The diagnosis of IE in children without heart defects is difficult to establish and right-sided IE is rare in children that a high suspicion index should be considered.

Conflict of Interest - None.

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