

Infective Endocarditis (IE) in Children — Symptoms and Treatment

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Infective endocarditis is a common serious infectious pathology in children. The most commonly identified organisms are of the streptococcus and staphylococcus species. Patients always have a fever. Other signs of infective endocarditis include Roth spots, splinter hemorrhages, and Osler nodes. Blood cultures and echocardiography are very important in the establishment of the diagnosis. The diagnosis of infective endocarditis is based on the presence of major and/or minor criteria from the modified Duke's criteria for infective endocarditis. Antibiotic therapy is essential and life-saving.



Overview

Infective endocarditis is defined as the bacterial infection of the endothelial lining of the heart. This infectious process can involve the heart valves, the mural endocardium or, in case of a ventricular septal defect, the defect itself. The involvement of the cardiac valves results in valvular insufficiency which might be complicated by congestive heart failure.

Epidemiology of Pediatric Infective Endocarditis

Infective endocarditis is quite a common condition in the pediatric population with an estimated incidence of 1 case per 1000.

Pediatric infective endocarditis has been found to have an equal incidence in both sexes and has been reported in all ethnicities and races. The incidence of infective endocarditis peaks in young children and infants.

Despite recent advances in antibiotic treatment for infective endocarditis, the mortality rate remains as high as 25 %. This high mortality rate is attributed to the delayed diagnosis in most of the cases. Survivors might develop a diverse range of complications such as valvular heart disease, myocardial abscess, complete heart block or pericardial disease. If emboli form inside the heart, they can be septic. Once the heart pumps these septic emboli, they can cause other infectious diseases such as osteomyelitis, meningitis,

and pneumonia.

Risk Factors for Infective Endocarditis

In the past, rheumatic heart disease as a complication of **streptococcal throat infections** was a common cause of infective endocarditis. After the introduction of penicillin and other adequate antibiotics for streptococcal infections, rheumatic heart disease became a rare condition.

Nowadays, the most common predisposing factor for infective endocarditis is **congenital heart disease**. Up to approximately 90 % of children who develop bacterial endocarditis have some form of a preexisting cardiac abnormality.

Other possible risk factors for infective endocarditis in the pediatric population include:

1. Prolonged hospitalization.
2. Chronic use of indwelling catheters, especially in premature babies.
3. Valvulopathy and the presence of prosthetic valves in cardiac patients.
4. Surgical shunts.
5. Previous episodes of bacterial endocarditis.

Etiology of Pediatric Infective Endocarditis

The forms of infective endocarditis include:

1. Gram-positive bacteria are the most commonly identified organisms in infective endocarditis. *Streptococcus viridans*, *Staphylococcus aureus* and coagulase-negative staphylococci account for most of the cases.
2. Enterococci is a common cause of infective endocarditis, and it is well known for its resistance to medications.
3. HACEK group of organisms that include *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella* or *Kingella*. They are important causes of infective endocarditis in neonates.
4. Fungal infective endocarditis causes severe disease that is associated with poor prognosis and complications.

Patients presenting with typical symptoms of infective endocarditis and characteristic signs on their echocardiography but are found to have a negative blood culture most likely have received antibiotics recently with the diagnosis being a culture negative infective endocarditis.

Pathophysiology of Pediatric Infective Endocarditis

The semiology of infective endocarditis is attributed to the local infectious process of the heart endothelial cell surface and the embolic septic phenomena.

The initial step in the pathogenesis of endocarditis is the preexisting presence of an abnormal valve or abnormal communication between two heart chambers, such as a ventricular septal defect. This abnormal communication is usually associated with abnormal blood flow that can eventually cause an injury to the endothelial cell surface. When the endothelium is injured, platelets and fibrin products are attracted to the site of injury and a thrombus is formed. At this stage, the thrombus is still sterile.

The next pathogenic step is the presence of bacteremia. Bacteremia can happen because

of a recent dental procedure, the use of indwelling catheters, the presence of another infectious process in another organ such as pneumonia, or due to intravenous drug abuse in adults. Once bacteremia happens, the immune system gets activated. The activated immune cells, along with the bacteria, are known to adhere to the sterile thrombus and bacteria can then grow inside the thrombus. At this stage, the patient is said to have infectious vegetation.

The infectious process can then damage the involved valve or cause rupture of the chordae tendineae. If this happens, acute heart failure can ensue which is associated with significant mortality. Other symptoms of the condition are due to vasculitis. Vasculitis happens because of the circulating activated immune complexes which can adhere to and attack other endothelial surfaces in the body distant from the heart.

Clinical Presentation of Pediatric Infective Endocarditis

Patients who have infective endocarditis are usually toxic, have a fever and the duration of their symptoms is typically less than two weeks. Previous medical history is relevant in some cases because of the association between some preexisting structural heart conditions and infective endocarditis.

Patients also develop fatigue, sweats and can have anorexia. Due to the circulating immune complexes, other organs might be involved. In that scenario, patients can develop myalgia, arthralgia, headaches or confusion.

In addition to the previously mentioned picture of acute infective endocarditis, patients can also present with subacute bacterial endocarditis. In that scenario, patients usually have a flu-like illness that lasts for more than two weeks. Subacute bacterial endocarditis is more common in patients with congenital heart disease.

Common findings on physical examination include:

- Fevers are virtually present in almost all cases of infective endocarditis.
- Heart murmurs are auscultated in most patients. Aortic regurgitation murmur is the most common finding.
- Hepatosplenomegaly
- Congestive heart failure
- Petechiae can be also observed on clinical examination of the upper and lower limbs, in addition to the trunk and back.
- Splinter and retinal hemorrhages, the latter known as Roth spots, and Osler painful nodes are due to vasculitis. They are rare and not considered as specific of infective endocarditis.

Causes	Presentation
<i>Staphylococcus aureus</i>	Acute very ill, abscess formation
Coagulase-negative <i>Staphylococcus</i>	Subacute, chronic fevers
Gram-negative rods	Subacute, chronic fevers
Fungal	Acutely very ill, highest mortality

Diagnostic Workup for Pediatric Infective Endocarditis

Necessary workup for infective endocarditis:

1. Blood cultures are very important in the diagnosis of infective endocarditis. At least three different blood samples should be obtained for culturing purposes. The time between one culture and the next should be based on how sick the child is. A child who is very ill should have the three blood cultures performed with a minimum gap between the first and last sample, typically less than one hour.
2. A complete blood count is also indicated in infective endocarditis. Anemia is a common finding, followed by leukocytosis. Erythrocyte sedimentation rate and c-reactive protein, both markers of inflammation, are usually elevated.
3. Patients who have subacute bacterial endocarditis might have a positive result for the rheumatoid factor or other autoantibodies. Due to the immune response in infective endocarditis,
4. Urinalysis can reveal signs suggestive of kidney injuries such as proteinuria or hematuria. The most common form of kidney injury in infective endocarditis is glomerulonephritis.
5. Echocardiography is essential for the diagnosis of infective endocarditis because two of the major criteria depend on echocardiography findings. In infants and young children, transthoracic echocardiography is usually sufficient. Older children and adolescents should undergo transesophageal echocardiography.

Diagnostic criteria: The Modified Dukes Criteria

The criteria have been classified into major and minor criteria. The patient is considered to have definite infective endocarditis if he or she has any of the following:

- 2 major criteria
- 1 major and 3 minor criteria
- 5 minor criteria

The major criteria for the diagnosis of infective endocarditis include:

1. A positive blood culture on two separate occasions that show growth of a typical infective endocarditis bacterial organism.
2. The presence of vegetation, an abscess around a heart valve or dehiscence of a prosthetic valve on echocardiography.
3. Identification of a new valvular insufficiency, i.e., new regurgitation or new-onset murmur.

The minor criteria include:

1. Predisposing heart disease such as congenital heart disease or rheumatic heart disease
2. The presence of a fever of more than 38 C.
3. Vasculitic phenomena such as the presence of major cerebral hemorrhage, conjunctival hemorrhages, and Janeway lesions.
4. Immunologic phenomenon such as the presence of Osler nodes or Roth spots.
5. Positive blood culture of an atypical organism.

Treatment of Pediatric Infective Endocarditis

If left untreated, infective endocarditis has a mortality rate as high as 100 %. The treatment for infective endocarditis should be always based on the blood culture results and the causative organism's antibiotic sensitivity profile. Patients with confirmed streptococcal infective endocarditis should receive penicillin G for four weeks or ceftriaxone for two weeks. Patients with penicillin-resistant streptococcal infective endocarditis should receive penicillin plus gentamicin.

When the case of infective endocarditis involves a prosthetic valve, penicillin plus gentamicin is the combination of choice for streptococcal infective endocarditis regardless of the antibiotic sensitivity profile.

Methicillin-susceptible *Staphylococcus aureus* (MSSA) is a common cause of infective endocarditis. The antibiotic of choice for MSSA is nafcillin with or without gentamicin. Nafcillin or oxacillin should be continued for at least 6 weeks. Patients with confirmed methicillin-resistant *Staphylococcus aureus* infective endocarditis should receive vancomycin for six weeks.

Patients who develop acute cardiac failure, severe and worsening valvular insufficiency or an abscess need urgent surgical intervention.

References

Gewitz M. Pediatric Bacterial Endocarditis. Background, Pathophysiology, Etiology. <http://emedicine.medscape.com/article/896540>. Published January 6, 2017. Accessed March 14, 2017.

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