# A case report of infective endocarditis in a 10-year-old girl

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## Abstract

Infective endocarditis is a rare disease in children, and it can result in significant morbidity and mortality. The epidemiology of infective endocarditis in children has shifted in recent years with less rheumatic heart disease, more congenital heart disease survival, and increased use of central venous catheters in children with chronic illness. Less commonly, infective endocarditis occurs in children with no preexisting cardiac disease or other known risk factors. We present a "case of" 10 year-old girl with no known cardiac disease or any other risk factors who was diagnosed with infective endocarditis according to modified Duke criteria. Blood cultures grew haemophilus parainfluenza. She had prolonged fever for 2 weeks after starting antibiotics, even though her blood culture became sterile 48 hours after treatment. We emphasize the importance of maintaining high index of suspicion for endocarditis in febrile children, even those without cardiac anomalies or other apparent risk factors.

## Case Report

A 10-year-old previously healthy girl presented to the hospital with bacteremia. The patient was initially admitted to the hospital 2 days prior with 3 days of fevers (up to 40°C), emesis and fatigue that were thought to be related to a viral illness. She was discharged home 24 hours later after her condition slowly improved. A blood culture, which was obtained during that hospitalization, resulted positive at 48-hours for gram-negative rods, so family was called and the patient was re-admitted. The patient had no chronic diseases, and took no medications. She was born full-term with no complications and her growth and development were age-appropriate. On admission she had a temperature of 38.5°C, a pulse of 96 beats/minute, a blood pressure of 98/65 mmHg, a respiratory rate of 20 breaths/minute, and an oxygen saturation 98% in room air. Her physical examination was significant for an alert and oriented child who was mildly dehydrated. She had a regular heart rate and rhythm, and normal first and second heart sounds without murmurs. Her lungs were clear to auscultation bilaterally, and her abdomen was soft, non-distended, and non-tender without hepatosplenomegaly. She had a normal dentition with no tooth decay. She had no skin rash or petechiae. The rest of her examination findings were unremarkable. A complete blood count revealed a normal white blood cell count of $7.3x10^3$ /$mm^3$ (4-12), anemia with a hemoglobin and hematocrit of 10 g/dL (11-14) and 29.1% (32-42) respectively, and thrombocytopenia with platelets $103x10^3$/$mm^3$ (140-440). Electrolytes showed a sodium of 135 mmol/L (138-145), a potassium of 3.1 mmol/L (3.7-5.6), a blood urea nitrogen of 11 mg/dL (10-18), a creatinine of 0.5 mg/dL (0.4-1), and a calcium of 8.3 mg/dL (9-11). Her C-reactive protein (CRP) was elevated at 10.8 mg/dL (normal <1 mg/dL). Her urinalysis showed no hematuria. A second blood culture was obtained before she was started on intravenous (IV) ceftriaxone. Her first and second blood cultures (48 hours apart) were identified later as beta-lactamase negative *Haemophilus parainfluenza*. She developed a new regurgitant heart murmur two day after admission, so a transthoracic echocardiogram (TTE) was obtained due to concern of infective endocarditis (IE). This showed a vegetation on the mitral valve. She had a transesophageal echocardiogram, which confirmed a 13x10-mm vegetation below the posterior leaflet of the mitral valve and resultant mild to moderate mitral valve regurgitation (Figure 1).

High dose ceftriaxone 100 mg/kg/day divided every 12 hours was continued. She had daily fevers (38.3-39.1 C) during her entire hospital stay. Blood cultures became sterile 48 hours after starting ceftriaxone. However, they were obtained daily for a week due to persistent fevers. They remained negative for bacterial growth. Abdominal ultrasound was normal with no hepatic, renal, or spleen abscess. A TTE was repeated twice and showed stable size vegetation, stable mitral regurgitation, and normal cardiac function. Computed tomography of head showed no evidence of embolic stroke and the patient's neurological status and examination remained normal. It was determined that her daily fevers were due to the large size of the vegetation and difficulty to eradicate the organism, not due to treatment failure or complications. Prophylactic surgery to prevent a primary embolic event was not indicated in this case per American Heart Association (AHA) guidelines.[1] She was discharged home despite persistent fevers after 11 days of hospital stay to continue IV ceftriaxone therapy at home for 4 weeks with a close follow up with her primary care physician, pediatric infection disease specialist, and cardiologist. She became afebrile at home two weeks after treatment started. Repeated echocardiogram a month after discharge showed stable mild to moderate mitral valve regurgitation with a small echo density attached to the posterior leaflet of the mitral valve likely representing a fibrinous material and not an active vegetation.

## Discussion

Infective endocarditis (IE) is a rare disease in children, and it can result in significant morbidity and mortality. The epidemiology of IE in children has changed in recent years as congenital heart disease (CHD) becomes the main predisposing factor from the developed world and rheumatic heart disease becomes much less frequent.[1-5] There is increased incidence of IE in children with no preexisting heart disease likely due to increased use of central venous catheters (CVC) especially in premature children with chronic illness.[1,3] However, in up to 10% of cases, IE is seen in children with no known structural heart disease or other risk factors[1] similar to this case. Viridans streptococci and staphylococcus aureus remain the most common pathogens responsible for pediatric IE with or without

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CHD.[1-7] On the other hand, a small percent (5%) is caused by a group of fastidious gram-negative organisms known as HACEK (*Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species).[1,5] Culture-negative IE, which is estimated to be in 5% of cases as well, has been described in patients with clinical and echocardiographic evidence of IE with blood culture yields no organisms.[1,5] Damaged cardiac endothelium and transient bacteremia are believed to be the main two factors in the pathogenesis of IE. Damaged endothelium, resulted usually from turbulent blood flow in CHD, causes a sterile platelets-fibrin thrombus (nonbacterial thrombotic endocarditis). It is then the transient bacteremia (from dental procedure or daily activities like toothbrushing) that colonize this thrombus and replicate to from the infected vegetation.[1,5,8] The pathogenesis of IE in children with no preexisting cardiac disease and no CVC or other known risk factors (as seen in this case) is not fully understood. These children might have asymptomatic undiagnosed mild structural cardiac anomalies.[3]

The clinical presentation of IE has been traditionally classified as subacute and acute presentation. Subacute IE presents as prolonged low-grade fever for weeks or even months with other symptoms like fatigue, chills, myalgia, and weight loss.[1,5,7] Acute IE on the other hand presents with high fever and rapid deterioration if not recognized in a timely manner.[1,5] Patient might have mixed features similar to this case as patient presented acutely, but was clinically stable overall and did not deteriorate. The diagnosis is based on well-known modified Duke criteria (Tables 1 and 2). This case met the criteria for definite diagnosis (2 major clinical criteria). Laboratory abnormalities that can be seen in IE are elevated acute phase reactants (erythrocyte sedimentation rate and C-reactive protein), anemia, thrombocytopenia, hematuria, and positive rheumatoid factor.[1,5] Cardiac echocardiography is essential for the diagnosis and monitoring vegetation size and cardiac function. It is important to notice that absence of vegetation on echocardiography does not necessary "rule" out IE.[5] Patients usually require a prolonged course (4-6 weeks) of antibiotics intravenously. The blood culture in this patient resulted positive for haemophilus parainfluenza; beta-lactamase negative, she was already on IV ceftriaxone for her bacteremia and she was continued on a high dose 100 mg/kg/day divided every 12 hours. Ceftriaxone is the recommended drug for HACEK per The AHA guidelines.[1] It important to mention that caring for these children with IE should be a collaboration between pediatric hospitalist, infectious disease specialist, cardiologist, and cardiac surgeon. The AHA has released new guidelines in 2015 with detailed antibiotic regimes and surgical indications.[1] Cardiac complications include congestive heart failure, valvular dysfunction, intra-cardiac abscess, and heart block.[1,5,7] Extracardiac complications include among others sepsis, extra-cardiac infections (*e.g.* osteomyelitis and renal

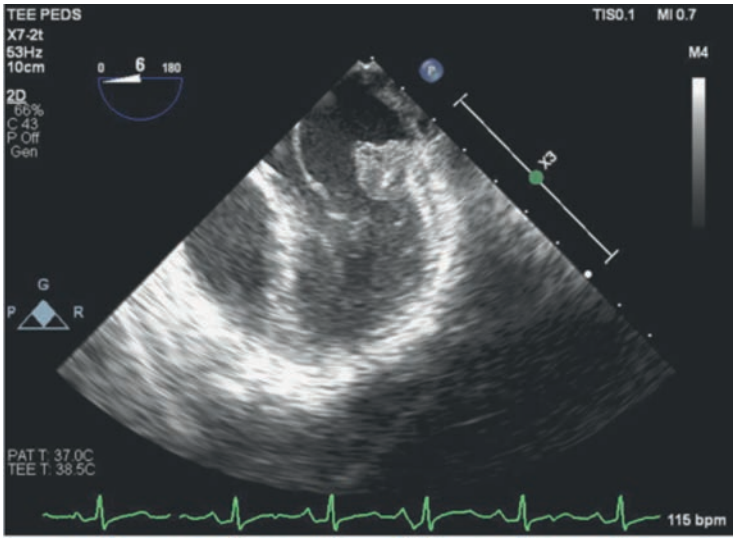


**Figure 1. Transesophageal echocardiogram, 4-chamber view. There is a large vegetation seen below the posterior leaflet of the mitral valve.**

**Table 1. Modified Duke criteria for diagnosis of infective endocarditis.**

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| **Definite infective endocarditis** |
| Pathological criteria:<br>Microorganisms (culture or histology in a vegetation or intracardiac abscess), or<br>Pathological lesions (vegetation or intracardiac abscess)<br>Clinical criteria:<br>Two major criteria, or<br>One major criterion and three minor criteria, or<br>Five minor criteria |
| **Possible infective endocarditis** |
| Consistent findings that do not meet definite definition but not rejected |
| **Rejected** |
| Alternative diagnosis, or<br>Resolution of manifestations with antibiotic therapy for ≤4 days, or<br>No pathological evidence at surgery or autopsy |

Adapted from Li *et al*., 2000.2

**Table 2. Definition of modified Duke clinical criteria for diagnosis of infective endocarditis.**

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| **Major criteria** |
| 1. Positive blood culture for infective endocarditis. |
| 2. Evidence of endocardial involvement (positive echocardiogram or new valvular regurgitation) |
| **Minor criteria** |
| 1. Predisposing heart condition or intravenous drug use |
| 2. Fever |
| 3. Vascular phenomena (e.g. arterial emboli, septic pulmonary infarcts, etc.) |
| 4. Immunologic phenomena (e.g. glomerulonephritis, Osler nodes, etc.) |
| 5. Microbiological evidence (does not meet a major criterion definition) |

Adapted from Li *et al*., 2000.2

abscess), immune complex depositions (*e.g.* glomerulonephritis), and embolization (*e.g.* stroke).[1,5,7] Finally, the AHA recommend to focus mainly on oral and dental hygiene rather than antibiotics prophylaxis in preventing IE. Antibiotics prophylaxis recommended before high-risk dental procedures for cardiac conditions with the highest risk for adverse outcome from IE and these include:[1] i) cardiac valve repair with a prosthetic valve or material; ii) previous IE; iii) certain CHD (*e.g.* unrepaired cyanotic CHD, and repaired CHD with prosthetic material or device during the first 6 months after the procedure); iv) recipients of cardiac transplants who develop cardiac valvulopathy.

## Conclusions

The following conclusions shoud be considered:

- Infective endocarditis should always be suspected in febrile children even without known cardiac disease or other apparent risk factors like central venous catheters.
- Infective endocarditis might cause prolonged fever after starting treatment.
- Congenital heart disease is the principal predisposing factor for infective endocarditis, with more cases in children without pre-existing heart disease due to widespread use of central venous catheters.
- *Viridans streptococci* and *Staphylococcus aureus* remain the main culprit pathogens.

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