Case Report

Pneumococcal endocarditis in a 10-year-old child with Marfan syndrome: case report

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Abstract

Endocarditis is a rare disease in children and is associated with high morbidity and mortality. It must be considered for every child with long-term fever without source, especially if there is a risk factor. Among the germs that can be involved, Streptococcus pneumoniae is extremely rare. Streptococcal invasive infections are decreasing since the introduction of vaccination, but all serotypes are not covered.

In this case, we describe a 10-year-old girl affected by Marfan syndrome with pre-existing mitral regurgitation. She was diagnosed with a streptococcal endocarditis. The laboratory identified the strain as Streptococcus pneumoniae serotype 13, a non-vaccinal serotype.

Introduction

Pneumococcal invasive infections have decreased in industrialized countries thanks to the conjugate vaccine. Management of these infections has improved due to prompt diagnosis (improvement in imaging techniques, better and rapid molecular testing) and the correct use of antibiotics (new cutoff minimum inhibitory concentration (MIC)) (1-3).

Streptococcus pneumoniae is a very rare cause of endocarditis and accounts for 3-7% of all cases. It is associated with a high mortality rate (3).

Case report

A 10-year-old girl presented by her parents to the cardiology consultation for fever (maximum 38°C), chills, headache and asthenia for the past 3 days. She was seen the day before by her general practitioner, who prescribed amoxicillin 50mg/kg/day for a suspected sinusitis and received 2 doses.

Among her medical history, she is afflicted by Marfan syndrome (MFS) associated with mitral prolapsus, mild mitral regurgitation and aortic dilatation.

She was seen at the cardiology consultation, where she was followed for the cardiovascular complications of MFS, by her parents initiative. The physical examination was totally normal, especially there was no cardiac murmur. Her vital signs were normal for age. A transthoracic echocardiography was performed and showed an increase of mitral regurgitation, neither a vegetation was seen nor other abnormalities.

Laboratory investigations revealed high inflammatory syndrome: white blood cells 14730/mm3 (normal range: 5000-10000 WBCs per microliter), polynuclear neutrophils 10850/mm3 (normal range: 2500-7500 neutrophils per microliter), C-reactive protein 150 mg/L (normal range; < 3.0 mg/L) and high NT- ProBNP 798 pg/mL (normal range: <125 pg/mL) which can be a sign of acute cardiac failure. She was admitted to the pediatric unit and we decided to stop the antibiotics since no source of infection was found. Chest X-ray and urinalysis were normal.

During the hospitalization fever persisted. Blood cultures were taken at each febrile peak. CRP fluctuated but remained high (between 89 and 130 mg/L). Her vital signs remained normal and she kept an excellent condition. The first 2 days, blood cultures remained negative, on the third day of the therapeutic window rapid growth of *Streptococcus pneumoniae* was observed in 2 blood cultures. She was immediately treated with intravenous amoxicillin clavulanate 100 mg/kg/day for a pneumococcal bacteremia. The blood cultures obtained after that were all negative and the fever quickly dropped.

At first, we concluded that she had an occult pneumococcal bacteremia since the chest X-ray was normal, there were no sign of meningitis, neither sinusitis nor otitis seen by the ENT specialist and the transthoracic echocardiography at admission was normal.

On day 8, the antibiotic therapy was adapted according to the antibiogram, we started amoxicillin 100 mg/kg/day. The same day, a second transthoracic echocardiography performed by her cardiologist to control mitral regurgitation, revealed a soft mass measuring 14x5 mm on the anterior leaflet of the mitral valve (fig 1).

A transesophageal echocardiography then confirmed the endocarditis suspicion and showed a voluminous A3 pericommissural vegetation, valve perforation and a peri-annular abscedation (fig 2).

We increased the doses of amoxicillin to 300mg/kg/day in the context of endocarditis and the patient was referred to a reference center with a pediatric cardiosurgery department for surgical management. She underwent a valvuloplasty on day 10. Unfortunately, peroperative samples were not send for microbiological analysis. The postoperative recovery was uncomplicated.

She was treated with penicillin 500.000 U/kg/day based on the MIC for 4 weeks after the first negative blood culture.

Other additional investigations did not show any complications: no sign of septic embolization seen on the abdominal ultrasonography or cerebral magnetic resonance imaging.

The bacteriological strain was referred to the national reference laboratory and was identified as serotype 13, a non-vaccinal serotype. The patient was immunized according to the Belgian vaccination schedule applied at that

time, including pneumococcal conjugate vaccine PCV7 at 2 and 4 months and PCV13 (since the vaccine had changed that year) at 12 months.

The echocardiography performed before discharge showed stable mitral regurgitation with preserved function and no vegetation.

Discussion

Infectious endocarditis (IE) is a rare disease in children. The estimated incidence ranges from 3,3 per 100000 per year among infants < 1 year to 0,3-0,8 per 100000 per year in older children in the United States and 0,5 per 100000 children per year in Norway (4-7). We did not find any numbers in Belgium.

The major risk factors in the pediatric population are congenital heart diseases, especially cyanotic heart diseases and the use of central venous catheters.

Due to the improved management of children affected by congenital heart diseases, the increasing use of central catheters, the incidence of IE is also increasing these last years. Rheumatic heart disease is an uncommon predisposing factor in developed countries, the incidence of the disease has drastically declined over the decades.

Our patient in this case report had MFS. This is an autosomal dominant genetic disorder caused by mutations in *FBN1* gene, located on the 15q21 chromosome. This gene is coding for the Fibrilline-1, a protein of the conjunctival tissue. The clinical manifestations of this syndrome may involve ophthalmologic, pulmonary, musculoskeletal and cardiovascular systems. The main manifestations in the cardiovascular systems are aortic root dissection, mitral valve prolapse, pulmonary artery enlargement and left ventricular dilatation (8).

Streptococcus viridans and *Staphylococcus aureus* are the major responsible pathogens, accounting for > 90% of IE (6). *Streptococcus pneumoniae* is extremely rare and accounts for 3-7% (3). Serotype 13 is non-vaccinal and is the only case found by the national reference laboratory during these 5 past years. Our patient was immunocompetent and did not have any history of invasive infection in the past. She had an abdominal ultrasonography that confirmed the presence of a spleen.

The clinical manifestations of IE are variable and non-specific. The typical signs like Roth spot and Osler nodes are rarely seen in children. The apparition or modification of a known heart murmur can be a sign of IE, but normal examination, as it was for our patient, cannot rule out the diagnosis. The diagnosis is based on the modified Duke criteria, our patient had 3 minor criteria (table 1), IE was thus suspected (6). When IE is suspected, blood cultures and echocardiography are essential to the diagnosis. Transthoracic echocardiography (TTE) has high sensitivity and is the gold standard for IE diagnosis in children. Transesophageal echocardiography (TOE) should be performed to confirm the diagnosis and demonstrate complications and must be considered for children with prosthetic valve or when there is a high suspicion for IE with a normal TTE. The absence of vegetation does not exclude the diagnosis, it is thus important to repeat the examination if the suspicion remains high. For our patient, the first TTE didn't show any vegetation, maybe because it was the early stage of the disease, TOE should have been performed, especially in front of increased mitral regurgitation.

In our patient, the first blood culture was negative, but she had received two doses of antibiotics before admission which probably turned the first cultures negative. The diagnosis is much more difficult in patients already receiving antibiotics, sometimes for unclear or unjustified reasons.

Once IE is confirmed treatment is complex and long (4-6 weeks to treat effectively). It is empirically based on the microbiologic epidemiology of the country and later on the antibiogram and MIC.

20 to 30% of the patients will need surgery. Indications for cardiovascular intervention are: uncontrolled infection, peri-annular abscedation, valvular perforation, worsening heart failure or vegetation measuring more than 10 millimeters (5, 6, 9). The lesions caused by pneumococcal IE progresses rapidly, thus early surgery can improve the prognosis (3).

Figure 1a : *Transthoracic echocardiography*

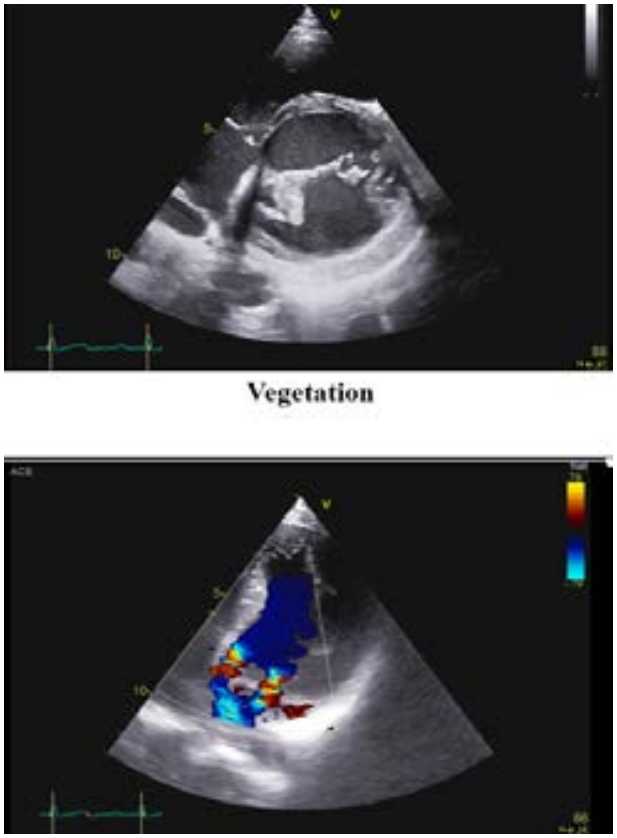
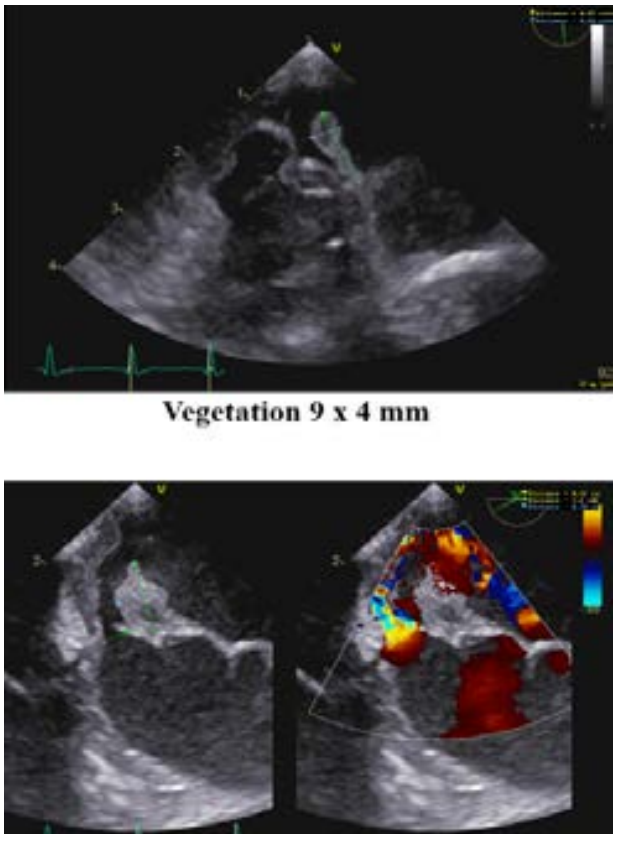


Figure 1b : *Transesophageal echocardiography*



Conclusion

IE is a rare disease in children but associated with a high mortality and morbidity. The incidence is increasing due to improved management of congenital heart diseases.

This diagnosis must be suspected in any children with prolonged fever without source, especially when there is a risk factor. The diagnosis is based on the Modified Duke criteria and is confirmed by blood cultures and echocardiography.

Streptococcus viridans and *Staphylococcus aureus* are the main pathogens found. *Streptococcus pneumoniae* is uncommon due to the vaccine coverage. Because of the global immunization against certain pneumococcal serotypes, we are facing pneumococcal serotypes not met before.

Antibiotics should never be prescribed without having obtained all cultures, otherwise the diagnosis of an invasive bacterial infection may be delayed while prompt management is crucial to reduce mortality and morbidity.

Conflict of interest

The authors have no funding or conflicts of interest to disclose.

REFERENCES:

1. Andrade AL, Toscano CM, Minamisava R, Costa PS, Andrade JG. Pneumococcal disease manifestation in children before and after vaccination: what's new? Vaccine. 2011;29 Suppl 3:C2-14.
2. de Egea V, Munoz P, Valerio M, de Alarcon A, Lepe JA, Miro JM, et al. Characteristics and Outcome of Streptococcus pneumoniae Endocarditis in the XXI Century: A Systematic Review of 111 Cases (2000-2013). Medicine (Baltimore). 2015;94(39):e1562.
3. Ishiwada N, Niwa K, Tateno S, Yoshinaga M, Terai M, Nakazawa M. Pneumococcal endocarditis in children: a nationwide survey in Japan. Int J Cardiol. 2008;123(3):298-301.
4. Gupta S, Sakhuja A, McGrath E, Asmar B. Trends, microbiology, and outcomes of infective endocarditis in children during 2000-2010 in the United States. Congenit Heart Dis. 2017;12(2):196-201.
5. Johnson JA, Boyce TG, Cetta F, Steckelberg JM, Johnson JN. Infective endocarditis in the pediatric patient: a 60-year single-institution review. Mayo Clin Proc. 2012;87(7):629-35.
6. Singh Y, Ganjoo N. Infective endocarditis in children. Paediatrics and Child Health. 2017;27(2):68-74.
7. Jortveit J, Eskedal L, Klcovansky J, Døhlen G, Holmstrøm H. Prevalence of infective endocarditis in children. Tidsskr Nor Laegeforen. 2019;139(2).
8. Yuan SM, Jing H. Marfan's syndrome: an overview. Sao Paulo Med J. 2010;128(6):360-6.
9. Carceller A, Lebel MH, Larose G, Boutin C. [New trends in pediatric endocarditis]. An Pediatr (Barc). 2005;63(5):396-402.

Table 1 : *Duke's criteria*

Major criteria	
I.	Blood cultures positive
	- Typical microorganisms from 2 separate blood cultures : *Viridans streptococci, Streptococcus gallolyticus,* HACEK group, *Staphylococcus aureus* or community acquired enterococci in the absence of a primary focus
	- Microorganisms from persistently positive blood cultures
	- Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre > 1 :800
II.	Imaging positive for IE
	- Echocardiogram positive for IE : vegetation, abscess, pseudoanevrysm, intracardiac fistula, valvular perforation or aneuvrysm , new partial dehiscence of prosthetic valve
	- Abnormal activity around the site of prosthetic valve implantation detected by F-FDG PET/CT (only if the valve was implanted > 3 months) or radiolabelled leukocytes SPECT/CT
	- Definite paravalvular lesions by cardiac CT
Minor criteria	
I.	Predisposition such as predisposing heart condition or drug injection
II.	Fever > 38°c
III.	Vascular phenomena : major arterial emboli, septic pulmonary infarcts, infectious aneuvrysm, intracranial haemorrhage, conjunctival haemorrhages, Janeway's lesions
IV.	Immunological phenomena : glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
V.	Microbiological evidence : positive blood cultures but does not meet a major criterion as noted above or serological evidence of active infection with microorganism consistent with IE