Infectious endocarditis (pediatrics)

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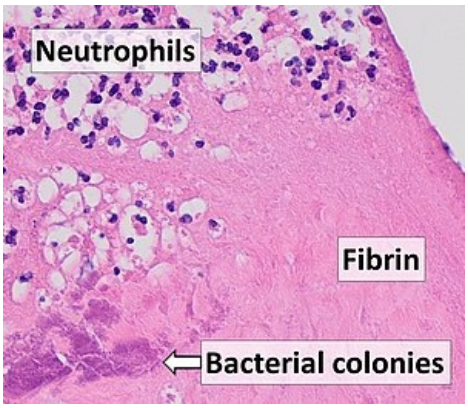
Infectious endocarditis (IE) is a disease caused by an infectious agent that affects the endocardium, heart valves and adjacent structures. Inflammation can be caused by bacteria, fungi, chlamydia, rickettsiae or viruses.



Histopathology of vegetation of bacterial endocarditis, HE

Risk factors

Risk factors in children:

- Congenital heart defects;
- Rheumatic heart defects (rarely);
- iatrogenic – long-established central venous catheters;
- intravenous drug use;
- bicuspid aortic valve;
- mitral valve prolapse with regurgitation;
- St.p. cardiac operations using conduits and vascular prostheses, with artificial valves.[1]

In congenital heart defects, IE occurs most often in:

- Fallot tetralogy,
- ventricular septum defect,
- aortic stenosis,
- open lychees.

A significantly lower risk is for pulmonary stenosis and IE is practically not found in arterial septum defects.

- Bicuspid aortic valve is a common seat of IE regardless of whether it causes stenosis or regurgitation.
- With mitral valve prolapse, patients are at risk of IE if the valve regurgitates.

IE is rare in newborns, infants and small toddlers with the exception of iatrogenic IE in critically ill children with catheter infection. As we get older, the risk of IE increases in individuals with heart disease.

Etiology

In children, the most common causative agent of IE are:

- **viridating streptococci** (*Streptococcus viridans*),
- Staphylococci
- enterococcal more rarely.
- Coagulase negative *staphylococcus epidermidis* are typical insoles of IE after cardiac surgery.
- Gram negative microorganisms and fungi cause IE rarely. They usually affect individuals with imunosupression, patient with artificial valves and addicts. Funicular IE is also a serious complication of long-established central venous catheters usually after repeated use of broad-spectrum antibiotic.

Pathogenesis

An important factor in the development of IE is the presence of turbulent blood flow, which disrupts the endothelium. However, vegetation can also be formed as a result of the Venturi effect at the site of slow blood flow. A cluster of platelets and fibrin is then formed in the damaged endothelium, which is subsequently colonized by the infectious agent. The bacteremia occurs in connection with various diagnostic or therapeutic interventions. Transient bacteremia can also occur when brushing teeth or biting solid food. This mechanism explains the development of IE in patients where a clear cause of bacteremia cannot be identified.

The main macroscopic findings are endocardial vegetation. They contain microbes and are covered with a layer of fibrin and leukocytes. Less virulent bacteria nest in thrombi, where fibrin protects them from phagocytosis and antibiotics.

Adjacent affected tissue is edematous, cellular infiltrated, and poorly vascularized, which impairs antibiotic penetration. Vegetation fragility is the cause of recurrent bacteriemia and embolization into the lungs or systemic circulation, depending on the site of cardiac involvement and the presence of intracardiac shunts. Embolization into the lungs mimics pneumonia, an unrecognized lung abscess can perforate the vascular system with subsequent fatal bleeding. Skin, kidney, spleen and brain are most commonly affected by systemic embolization. With prolonged illness, the heart valves are destroyed. Virulent bacteria (Staphylococcus aureus) cause rapid destruction of the valve or invasion of the myocardium leads to the formation of abscesses. Septic embolizations

into the coronary arteries are also a common finding. Infective endocarditis significantly activates the humoral and cellular immune systems. For example, circulating immunocomplexes are responsible for the development of glomerulonephritis.[1]

Classification

- IE on native valves,
- IE in drug addicts (predisposes to tricuspid valve involvement with the risk of pulmonary embolization),
- IE on valve prostheses (early / late onset - the limit is two months after surgery).

The division of IE into acute and subacute is already obsolent and is not used. Dividing according to the causative agent is recommended. Microorganisms with low virulence (eg α-hemolytic streptococcus) usually cause the "subacute" form, while Staphylococcus aureus and other pyogenic bacteria cause the "acute" form.

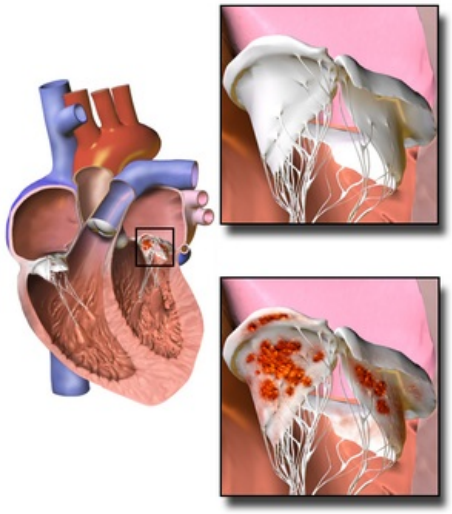
Risk of infectious endocarditis

high risk;

- valve prostheses (lifetime),
- st.p. heart surgery (within 6 months after surgery),
- aortic defects,
- Fallot's tetralogy,
- mitral insufficiency,
- PDA,
- VSD,
- aortic coarctation,
- Marfan's syndrome ,
- IE in anamnesis.

medium risk;

- mitral stenosis,
- tricuspid valve defects,
- mitral valve prolapse,
- hypertrophic cardiomyopathy.



Endocarditis

Clinical manifestation

We always suspect IE in high-risk patients (see above) in a febrile condition. Mitigated forms of IE should always be in mind after treatment with antibiotics, which was given out of embarrassment, and febrile illness may subside. Endocarditis is most often manifested by higher temperatures and non-specific problems such as myalgia, arthralgia, headaches, fatigue. If the disease lasts, we find splenomegaly , the skin is colored with a touch of white coffee (caffé au lait). Other late symptoms include embolism in the periphery: chipped subungual hemorrhages, petechiae of the skin or subconjunctival, red spots on the palms (*Janeway spots*), painful indurations on the fingertips (*Osler nodes*). Embolization may be revealed by eye background examination (retinal hemorrhagic lesions = Roth spots) or hematuria.

In up to 30% of patients, the first clinical sign of IE may be an acute embolic cause. The internal carotid artery is most often affected. Clinical signs include hemiplegia, aphasia, mental disorders, and rarely blindness caused by damage of the retinal arteries. In general, left heart IE causes peripheral embolism followed by ischemia, sterile embolism infarction, infectious embolism abscesses, or fungal aneurysms. Embolization from the right heart to the lungs is often asymptomatic due to good lung filtration properties or symptoms of pulmonary embolism with subsequent cough, listening and X-ray findings in the lungs.

Sometimes there may be a picture of Löhlein's nephritis with hematuria, proteinuria and decreased glomerular filtration. It is a manifestation of microembolization in the kidneys or a consequence of focal or diffuse glomerulonephritis, which causes deposits of immunocomplexes in the glomeruli. Up to 20% of children have neurological symptoms: meningitis, brain abscesses, toxic encephalopathy.

Significant findings are a new or altered heart murmur due to valve involvement, more rarely, the inflammatory process can affect the cardiac conduction system and cause AV block. Heart failure is the most common cause of death.

CAVE!!! It is always necessary to keep in mind the mitigated forms of IE when treated with antibiotics, which was given out of embarrassment, then the febrile may subside!

Diagnostics

Lab tests

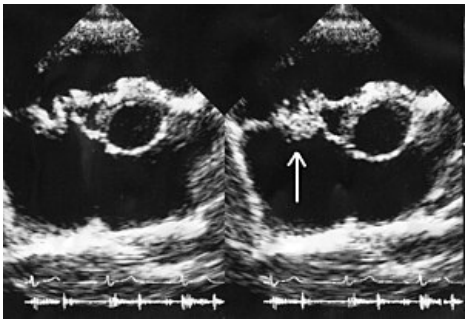
From common laboratory findings, high sedimentation , leukocytosis, microscopic hematuria, proteinuria, positive rheumatoid factor , and increased CK values indicate a diagnosis of IE. We often find anemia and hypergammaglobulinemia. The correct sampling of blood cultures is crucial for the diagnosis and treatment of IE. We collect 3 blood cultures within 24 hours and in case of negative findings on the second day of incubation, another 2 blood cultures are collected. If IE is clinically suspected, we also collect blood cultures from subfebrile or

afebrile patients. Blood culture negativity may be due to previous antibiotic treatment, IE caused by rickettsiae, chlamydiae, viruses or slow-growing organisms. Molecular biological methods such as PCR provide another possible refinement of IE diagnostics. Negative blood cultures may also support the diagnosis of sterile thrombotic endocarditis most commonly associated with antiphospholipid syndrome.

False positivity of blood cultures is caused by contamination during non-sterile sampling. These are most often coagulase-negative staphylococci, corynebacteria, transiently colonizing enterobacteria, pseudomonads, etc. Repeated findings, isolation of the same strain from other biological samples and the corresponding clinical picture testify to etiological agents.

Echocardiography

Echocardiography is a very valuable method for confirming IE. This examination reliably detects vegetation on the endocardium and valves and is also important in monitoring the development of possible valve regurgitations or other cardiac findings. We also use transesophageal echocardiography for unclear findings. Echocardiographic diagnosis of IE on an artificial valve is very difficult, because vegetation is often hidden in the shadow of a strong signal caused by echodensic material.


Vegetation on trikuspid valve (ECHO)

CAVE!!! Neither a negative echocardiogram nor a negative blood culture exclude the diagnosis of IE!

Special examinations

If embolization into the pulmonary or systemic circulation is suspected, special CT scans, MRIs to detect or rule out septic emboli or abscesses are indicated.

We always consult a dentist or ENT (= ORL) doctor to rule out a focal infection. Remediation of the infectious lesion is carried out during the treatment of IE.

Diagnostic criteria

Currently recommended are criteria for the diagnosis of IE by Durack of Duke University in the USA (so-called Duke criteria), which are based on a combination of clinical, laboratory and echocardiographic findings. According to these criteria, patients with suspected IE are divided into 3 categories: proven IE, possible IE, and excluded IE.

main criteria

- *positive blood culture: a* typical IE microorganism (including *Streptococcus viridans* including nutritional variants or *Streptococcus bovis,* or *HACEK* microorganisms; *Staphylococcus aureus* or *Enterococcus spp.* if no other primary source of infection was detected) was detected from 2 different blood samples / if positive blood cultures were detected: the same finding in 2 blood cultures collected between 12 hours and more or the same finding in 3 or 3 of 4 blood cultures if the interval between the first and last collection was greater than 1 hour
- *signs of endocardial involvement:* echocardiographic finding corresponding to IE (fluttering intracardiac structures on the valve or surrounding structures at the site of accelerated blood flow, or on foreign material for which there is no other anatomical explanation; abscess; new paravalvular dehiscence at the site of the artificial valve) / newly formed valve regurgitation

secondary criteria

- *predisposition:* structural heart disease, drug abuse,
- *temperatures* ≥ 38.0 ° C,
- *vascular symptoms:* embolization, septic pulmonary infarction, intracranial hemorrhage, conjunctival haemorrhage and skin petechiae,
- *immunological symptoms:* glomerulonephritis, Osler's nodules, Roth spots, rheumatoid factor,
- *microbiological finding:* positive blood culture that does not meet the above main criteria, or serological evidence of active infection corresponding to IE,
- *echocardiographic finding* corresponding to IE, but which does not meet the above main criteria.

IE Diagnosis (Duke criteria):

proven IE

- pathological criteria (at least 1 criterion): proven microorganism by culture or histology in vegetation or vegetation embolization or intracardiac abscess, or histological evidence of active IE in vegetation or intracardiac abscess,
- clinical criteria: 2 main criteria, or 1 main and 3 secondary criteria, or 5 secondary criteria.

possible IE

- 1 main + 1 secondary criterion / 3 secondary criteria

excluded IE

- proven other diagnosis explaining the symptoms of the disease / disappearance of IE symptoms within 4 days of antibiotic treatment / absence of IE findings during surgery or autopsy after antibiotic treatment within 4 days

Treatment

In empirical treatment or in case of blood culture negativity, we choose the combination of oxacillin 200 mg / kg / day for 4 hours + gentamicin 3 mg / kg / day for 12 hours iv, for patients allergic to penicillins then vancomycin 40 mg / kg / day for 6 hours. + gentamicin 3 mg / kg / day 12 hours i.v.

With positive blood culturewe take into account the type of proven microbe, its sensitivity and MIC. As a rule, when penicillin-sensitive streptococci are detected, we administer Penicillin G 200,000–400,000 IU / kg / day every 4 hours, ev. + gentamicin. When detecting enterococci and other resistant streptococci, we administer ampicillin 200–300 mg / kg / day for 6 hours iv + gentamicin. Gram negative IE (HACEK) is treated with a combination of cephalosporins III. generation, eg ceftriaxone 100 mg / kg / day 12 hours iv or ampicillin 200-300 mg / kg / day 6 hours iv + gentamicin 3 mg / kg / day 12 hours iv, Mycotic IE is treated with amphotericin B : test initial dose is 0.1 mg / kg, with good tolerability we increase the dose to 0.5 mg / kg for 1 day and continue for at least 6-8 weeks with a maintenance dose of 1 mg / kg / d iv It is usually necessary to supplement the surgical performance (replacement of infected valve, excision of infected tissue).

In general, we always choose bactericidal ATB, when combining them we take care to achieve a synergistic effect. Periodic determination of serum bactericidal activity and monitoring of serum concentration is important, especially for potentially toxic antibiotics (gentamicin, vancomycin). We prove the effectiveness of ATB therapy by eradicating bacteremia in blood culture. Occasional monitoring of blood culture is important for the first 8 weeks after the end of treatment, as most relapses occur during this period.

With the treatment, we can follow the available guidelines in more detail, from current recommendations such as the American Heart Association ([www.americanheart.org]).

Prevention

IE prevention involves the targeted use of antibiotics to all at-risk individuals prior to surgical or diagnostic procedures that are known or suspected to cause transient bacteriemia. These are usually operations in the oral cavity, nasopharynx, digestive or urogenital tract.[1] IE prevention has significantly reduced the incidence of this devastating infection since its introduction. The most important thing is to prevent bacteremia in children with structural heart disease. Pay particular attention to the timely treatment of all dental conditions, including minor tooth decay, even the first dentition, for increased oral hygiene, vigorous therapy of purulent skin conditions and respiratory bacterial infections. However, IE prevention does not mean flat-rate treatment of all and non-bacterial infections with antibiotics or continuous use of antibiotics. Cardiac patients are provided with identification cards with established principles. In summary, the most effective prevention of IE is early and complete correction of the heart defect.

patients requiring routine IE prevention

- with congenital heart disease except atrial septal defect,
- with rheumatic or other valve defect,
- with obstructive hypertrophic cardiomyopathy,
- with mitral valve prolapse and concomitant regurgitation. [1]

patients requiring IE risk prevention

- the first 6 months after cardiac surgery and interventional catheterization,
- lifelong in patients with artificial valves, including bioprostheses and allografts, after aortopulmonary window surgery
- in complex cyanotic heart defects (functionally single ventricle, Fallot's tetralogy, transposition of large arteries)
- after undergoing IE.

patients not requiring IE prevention

- isolated atrial septal defect ,
- atrial septal defect and open duct 6 months after surgery without residual findings,
- mitral valve prolapse without regurgitation,
- past Febris rheumatica or Kawasaki disease without valvular involvement,
- functional murmurs,
- implanted stimulator or defibrillator,
- coronary bypass.

performances that do not require IE prevention

- dental procedures, accompanied by bleeding from the gums or mucous membranes, including professional cleaning of tartar,
- tonsillectomy and adenotomy,
- operations affecting the intestinal mucosa or respiratory system,

- bronchoscopy with rigid bronchoscope.
- esophageal dilatation and sclerotization of esophageal varices ,
- gall bladder surgery,
- bladder catheterization if infection is present *,
- urological surgery if infection is present *,
- prostate surgery,
- incision and drainage of infected tissues *,
- vaginal delivery if infection is present *,
- vaginal hysterectomy.

* – in addition to the recommended prophylaxis, antibiotics are given for these procedures according to their sensitivity

performances that do not require IE prevention

- dental procedures in which there is no bleeding from the gums or mucous membranes, e.g. treatment of tooth decay above the gum level,
- loss of the first dentition,
- diagnostic cardiac catheterization,
- endotracheal intubation,

bronchoscopy with flexible bronchoscope including biopsy *, endoscopic examination of the GIT, including biopsy *, transesophageal echocardiography, cesarean section, if no infection is present: uncomplicated labor, cervical dilatation and curettage, insertion and removal of the IUD *.

* – except for the risk group of patients

References

Related articles

- Infectious endokarditis

Reference

1. LEBL, J – JANDA, J – POHUNEK, P. *Klinická pediatrie.* 1. edition. 2012. ISBN 978-80-7262-772-1.

Source

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