Inflammation of the heart

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Endocarditis is best viewed as an inflammation of the endocardial surface of the heart which includes the heart valves, mural endocardium and the endocardial surface that covers implanted material (prosthetic valves, pacemakers, defibrillator leads and catheters).

In most cases the inflammation is caused by bacterial or fungal infections. Endocarditis is rarely related to non-infectious causes such as cancer (marantic endocarditis) or immunological conditions (Libman Sacks endocarditis).

EPIDEMIOLOGY

Infective endocarditis (IE) is a serious condition. The incidence is about 30 to 100 episodes of IE per million patient-years. The estimated annual incidence is three to nine cases per 100 000 of the population in industrialised countries. This incidence did not change despite preventative efforts.

The epidemiological profile has changed in a number of ways: The patient age has increased, rate of healthcare associated cases (nosocomial and non-nosocomial) has increased, degenerative valvular disease has increased and not only has prosthetic valvular procedures increased, but the use of cardiac implanted devices has significantly increased. There has also been an increase in *Staphylococcus aureus* IE especially in patients on haemodialysis, intravascular devices and in patients with diabetes mellitus. Human immunodeficiency virus infection and intravenous drug use have contributed to healthcare associated cases of IE.

PATHOGENESIS

Normal cardiac endothelium is naturally resistant to colonisation by bacteria. The conventional model explains the development of IE in that the first step is damage to the endothelium caused by jet lesions due to turbulent blood flow or by damage due to electrodes or catheters. A fibrin-platelet aggregate develops into a vegetation, which is initially sterile but eventually is colonised by bacteria to form the typical infected vegetation. The bacteria that cause IE have surface adhesion molecules that mediate adherence to the vegetation. These vegetations can be multiple and involve more than one valve. Vegetations grow rapidly, become fragile and embolise easily and can infiltrate the valvular ring to form a ring abscess. This conventional model does not adequately explain how intracellular organisms cause IE and it is suggested that the patient's immune response may also play a role.

In the past IE was classified according to its mode of presentation such as acute, subacute and chronic. It is now categorised according to the underlying cardiac condition, location of the IE, presence or not of intracardiac devices or the mode of acquisition.

DIAGNOSIS

It is essential that both a high index of suspicion and a low threshold for investigations are kept in mind in a patient with suspected IE. There are two groups of circumstances when IE should be suspected:

1. The development of a new cardiac murmur; Embolic events without a cause, sepsis of unknown origin, fever and evidence of an infection.
2. Fever associated with intracardiac material, fever associated with known valvular problem or known congenital heart disease, fever associated with a recent intervention that can cause a bacteraemia, fever with heart failure, fever with new conduction disturbance on the echocardiogram (ECG), fever with vascular or embolic phenomena (Roth spots, splinter haemorrhages, Janeway lesions, Osler nodes etc.), fever with focal or non-specific neurological symptoms or signs, fever with abscess of kidney, spleen cerebral etc. of unknown cause. It is better to use the Duke criteria for the diagnosis of IE. The Duke criteria for IE have a sensitivity and specificity of about 80% and are therefore the reference criteria for diagnosis. However, these criteria should not replace clinical judgement for the diagnosis of IE.

DUKE CRITERIA FOR DIAGNOSIS OF INFECTIVE ENDOCARDITIS

DEFINITE DIAGNOSIS

PATHOLOGICAL CRITERIA

Micro-organisms identified by culture or histological examination of a vegetation that has embolised or an intracardiac abscess specimen.

CLINICAL CRITERIA

Two major, or one major plus three minor or five minor criteria are needed for the clinical diagnosis of IE.

MAJOR CRITERIA

1. Cultured micro-organism typically identified with IE on two separate blood cultures (viridance *Streptococci, Streptococcus bovis,* HACEK group, *Staphylococcus aureus* or community-acquired *Enterococci* in the absence of a primary focus. A single positive blood culture for Coxiella burnetti or an IgG antibody titre for Q-fever of > 1:800.
2. ECG demonstrating a vegetation on valve or supporting structure or an abscess in the heart.
3. A new valvular regurgitant murmur. (Worsening or changing pre-existing murmur is not a criterion)

MINOR CRITERIA

1. Predisposition to IE (pre-existing heart condition, intravenous drug use).
2. Fever defined as > 38°C.
3. Vascular phenomena: Arterial emboli, septic pulmonary infarcts, mycotic aneurysms, intracranial haemorrhage, conjunctival haemorrhage and Janeway lesions.
4. Immunological phenomena: Glomerulonephritis, Osler's nodes, Roth spots and a positive rheumatoid factor.
5. Microbiological evidence such as positive blood culture with an organism not typical associated with IE.

POSSIBLE DIAGNOSIS

Clinical criteria (see above): One major criterion and one minor criterion or three minor criteria is not enough to diagnose or reject the diagnosis of IE.

REJECTED DIAGNOSIS

A firmly established alternative diagnosis or resolution of IE-like syndrome with antibiotic therapy for ≤ four days or criteria for IE not met or no pathological evidence of IE at °surgery or autopsy with antibiotic therapy for ≤ four days will reject a diagnosis of IE.

A recent systematic review using the Duke criteria for diagnosis of IE in a difficult group

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of pregnant and postpartum patients could find 90 confirmed cases of which 51 occurred during pregnancy and 39 in the postpartum period. The most common microorganisms were *Streptococci* and *S-taphylococci* most commonly affecting the mitral valve. Maternal mortality was 11% and foetal mortality 14%. IE is a rare but life-threatening condition during pregnancy and the postpartum period that requires a high index of suspicion for the early diagnosis and treatment.

MICROBIOLOGICAL INVESTIGATIONS

Streptococci and *staphylococci* now accounts for about 80% of the cases of IE. *Staphylococci* are now the most frequently identified micro-organism in several types of IE. In the last five decades *Staphylococcus* infections have increased, coagulase negative *Staphylococcus* has increased and *Staphylococcus aureus* has also increased, especially in intravenous drug abuse. *Streptococcus* viridans and culture negative cases have decreased. Enterococcal infections have increased.

Central to the diagnosis is blood cultures: At least three sets of blood cultures (aerobic and anaerobic) taken within two hours of suspecting IE. It has also been suggested that blood be taken for rheumatoid antibody titre and for Coxiella burnetti, Brucella, Bartonella species, Aspergillus species, the HACEK group (haemophilus species, aggregatibacter actinomycetemcomitans, cardiobacterium hominis, eikenella corrodens and kingella kingae) and tropheryma whipplei.

Blood cultures can be negative in 2.5%-30% of cases (many estimate it to be 10%) probably due to previous antibiotic administration, or infection with intracellular organisms, fungi or fastidious pathogens.

ECHOCARDIOGRAPHY

ECG is an accurate method to demonstrate endocardial involvement in IE. Initially a transthoracic ECG (TTE) is done as a rapid procedure as confirmation of the suspected IE. A transesophageal ECG (TEE) is recommended where there is a high suspicion of IE, but the transthoracic echo is negative or the presence of prosthetic valves or intracardiac devices. Many believe that even if the TTE is positive a TEE should be done to detect a small abscess when the TTE demonstrated a vegetation because this may influence the management. Follow-up ECGs are necessary to monitor complications and response to treatment and some regard it as mandatory. Sometimes the ECG can be positive for other conditions than vegetations in IE such as thrombi, prolapsed cusp and cardiac tumours (e.g. myxoma). Multislice CT and magnetic resonance imaging (MRI) are complementary to ECG and do not replace it.

The role of positron emission tomography scans in the evaluation of IE in the setting of pacemaker/defibrillator leads and prosthetic valves are being evaluated.

MANAGEMENT

Despite therapeutic advancements, IE is still associated with poor prognosis and poses therapeutic challenges. Antibiotic therapy should be started as soon as IE is suspected and the appropriate microbiological studies have been done. Antibiotic treatment remains the mainstay of treatment with surgical intervention being used in about 50% of cases and a recent trend of earlier surgical intervention as new evidence becomes available. Initially the antibiotic choice will be empiric and then modified as soon as the microbiological results are known.

±80%

of IE cases are due to *Streptococci* and *Staphylococci*

The recommendations from guidelines are still for the older type of antibiotics despite an emerging resistance pattern of the responsible organisms. The empirical use of a combination of a beta-lactam antibiotic plus gentamycin is still used for native valve IE and is given for a minimum of two to six weeks but longer for prosthetic valve IE. *Staphylococcal* IE is suspected in severe sepsis picture, intravenous drug use or diabetes or prosthetic valve IE and then the use of vancomycin is suggested instead of penicillin. There is little evidence of oral antibiotic treatment of IE. More detailed antibiotic use is detailed in Guidelines on the Management of IE.

Surgical indications have increased in the management of patients. The main indications of surgery are the development of heart failure (mainly due to valvular destruction), uncontrolled infection and systemic embolisation. Reported rates of surgery remain heterogeneous and the beneficial effect on mortality is still difficult to show and is caused by scarcity of randomised clinical trials. Many patients with IE also have co-morbidities which increase the operative risk. The management of IE have evolved into a team effort of many specialist disciplines to provide the best possible outcome.

NEUROLOGICAL COMPLICATIONS

Neurological complications, such as stroke, cerebral haemorrhage, infectious aneurysms, cerebral abscess and meningitis, are common and occur in 60%-80% of patients with IE. These cerebral complications are mostly due to vegetation emboli. In almost half of these cases the neurological complications are silent and only detected by special investigations such as a CT scan of the brain or MRI. *Staphylococcus aureus* is the organism most commonly involved in these cerebral complications.

OUTCOME

In-hospital mortality ranges from 15% to 22% and the five-year mortality is about 40%. However, mortality rates do vary across different subgroups of patients. For instance, mortality is about 10% in patients with right-sided lesions or those with oral *streptococci* or left-sided native valve IE whereas in-hospital mortality can be 40% or more in patients with prosthetic-valve IE due to *Staphylococcus aureus.* Heart failure, cerebral complications and embolic events and healthcare associated IE also has a worse prognosis. The long-term survival rate from IE irrelevant of treatment options is around 70%. Mortality rates have not changed significantly in the last decades mainly attributable to changing demographics and causes of IE.

POST-ACUTE MANAGEMENT

Mortality and morbidity extends beyond successful hospital treatment. There are still risks of death, recurrence of the IE and even the need of valvular surgery after initial successful therapy. Therefore patients need to be closely monitored clinically, biologically and with ECG evaluation.

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