The management of acute endocarditis

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Abstract

Infective endocarditis (IE) is an infection, usually of bacterial aetiology, which can affect any part of the endovascular surface of the heart or large intrathoracic vessels but most commonly affects cardiac valves. Without treatment this condition is invariably fatal and even with treatment is associated with a high incidence of morbidity and mortality.

This article looks at the difficulties in diagnosing IE and the investigations used to confirm the diagnosis. It also lists the major causes of IE and its management.

Keywords

Infective Endocarditis, Blood Cultures, Echocardiography, Duke criteria, Antibiotics, Surgery.

Key Points

- IE can present in a number of different ways so one must keep a high index of suspicion of the diagnosis.
- Key investigations are multiple sets of blood cultures and transoesophageal echocardiography.
- IE is usually a life-threatening condition and without treatment is invariably fatal.
- Treatment is **early** high-dose parenteral antibiotics for long duration.
- Patients with confirmed IE should be managed by a cardiologist, in close liason with a microbiologist.
- Early referral to a cardiothoracic surgeon should be considered if complications arise.

Introduction

Infective Endocarditis (IE) is, by definition, an infection that can affect any part of the endovascular surface of the heart, the large intrathoracic vessels or intracardiac foreign material (see Table 1). Classically it involves one or more of the cardiac valves and is classified as either 'Native Valve Endocarditis' (NVE) and 'Prosthetic Valve Endocarditis' (PVE) or 'left'- and 'right'- sided endocarditis. NVE accounts for the majority of cases (about 70-90%) although the incidence of PVE is increasing as the number of people undergoing valve replacement increases.

- Intracardiac structures
  - Native Valves (most common)
  - Ventricular endocardium (eg VSD*)
  - Atrial endocardium (eg ASD*)
- Intrathoracic vessels
  - Patent ductus arterosus
  - Coarctation of the aorta
  - Arterio-venous shunts
- Intracardiac Foreign Material
  - Prosthetic valves
  - Pacemaker leads
  - Patch material (eg previous VSD surgical repair)
  - Surgical conduits

* VSD: Ventricular Septal defect. ASD: Atrial Septal defect

Table 1. Possible Sites of Infective Endocarditis.

Early infection usually involves the formation of a 'vegetation' consisting of a mass of platelets, red blood cells, fibrin, inflammatory cells and micro-organisms. This can then lead to destruction, ulceration and abscess formation. As IE can rapidly lead to life-threatening haemodynamic compromise or embolic phenomena, it is imperative to be able to diagnose IE, initiate prompt antimicrobial therapy and refer early for life-saving surgical intervention where required.

The annual incidence of IE is between 1.9 - 6.2 cases per 100,000 population.[1, 2] Men are affected more commonly than women. Patients with pre-existing cardiac diseases are at higher risk of developing IE,[3] particularly after dental extraction as a result of transient bacteraemia.[4] This has led to the use of prophylactic antibiotics for patients with certain cardiac diseases when undergoing dental treatment.

Clinical Presentation

Diagnosing IE can be extremely difficult in view of the widespread possible manifestations of the disease. Symptoms may vary from minor constitutional upset to life-threatening septicaemia or pulmonary oedema. The key to making a successful diagnosis is to maintain a high index of suspicion.

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History

It is vital to take a thorough history. One should ask about the presence of any predisposing risk factors for IE (see Table 2) especially existing structural cardiac disease or the presence of a prosthetic valve (up to 5-10 times the risk of IE than patients with native valves).[5] Recently prescribed antibiotic therapy should be noted as this may affect blood culture results. Fever, malaise, anorexia, weight loss, arthralgia and breathlessness are the most frequently presenting symptoms.

Examination

As a number of different systems may be affected it is imperative to perform a full examination looking for both the manifestations as well as the complications of IE (see Table 3).

General

Look specifically for a fever and signs of anaemia. Examine the state of the patient's teeth for poor dental hygiene. Check for signs of intravenous drug abuse. Splenomegaly and clubbing are rare findings.

Cardiac

Assess the pulse for rate: bradycardia (conduction defects) and tachycardia (septic) and character (collapsing with aortic regurgitation (AR)). Look for haemodynamic complications such as heart failure (both left- and right-sided) and hypotension. Look in particular for a low diastolic pressure as seen in acute AR.

Heart murmurs are heard in about 80% of cases. The absence of a murmur does not exclude IE but the finding of a new or changing murmur is highly suggestive of the diagnosis as it suggests progression of valvular regurgitation.

Other Systems

Other systems which may be affected (see Table 3) include the vascular system, usually as a result of embolic phenomena which can occur in up to 40% of cases of IE;[6] the neurological system (confusion is an especially common finding in the elderly); the musculoskeletal system and the skin: Osler nodes, Janeway lesions and splinter haemorrhages. Mycotic aneurysms secondary to septic embolisation of vegetations are uncommon.

- Congenital cardiac disease – especially cyanotic heart disease
- Acquired cardiac disease (eg. aortic stenosis, rheumatic fever)
- Prosthetic intracardiac material – especially prosthetic valves
- Previous episode of IE
- Intravenous drug abuse
- Recent invasive procedures (eg. dental treatment, iv lines)
- Systemic illness (eg. diabetes, sepsis)
- Long-term haemodialysis
- Immunosupression – malignancy, steroid therapy
- Poor dental hygiene

Table 2. Risk Factors for Infective Endocarditis.

Investigations

Blood / Urinary testing

It is imperative to take multiple sets of blood cultures (at least 3 sets of both aerobic and anaerobic) from different sites. FBC, U&Es, ESR, CRP, LFTs should be requested. Other tests can be requested depending on the index of suspicion; atypical serology if Brucellosis, Coxiella or Legionella is suspected, auto-immune profile for SLE, plus tumour markers if an underlying malignancy is thought to be a possibility.

A urinary dipstick should be always obtained, looking for microscopic haematuria.

Electrocardiogram

A 12-lead ECG should be taken looking for conduction abnormalities (associated with the development of an aortic root abscess). Ischaemic changes may be seen and can be a consequence of coronary artery embolisation.

Chest Radiograph

Acute pulmonary oedema, nodular infiltrates, cavitation, multifocal pneumonia and pleural effusions can all be seen. Abnormal chest x-ray findings are seen in the majority (70-85%) of patients with right-sided IE.[7]

- Cardiac
  - Congestive heart failure
  - Direct destruction of a valve
  - Abscess formation
  - Haemodynamic compromise
  - Conduction defects
- Arterial embolism may lead to :
  - Stroke
  - Renal or splenic infarction
  - Lower limb ischaemia
  - Retinal infarction – blindness
- Septic embolism may lead to :
  - Abscesses (eg. cerebral, lung)
  - Septic arthritis
  - Mycotic aneurysms
- Neurological
  - Confusion / stupor
  - Meningitis
  - Seizures
  - Stroke
  - Cerebral abscess
- Mucocutaneous / Immunological
  - Petechiae
  - Splinter haemorrhages
  - Osler nodes
  - Janeway lesions
- Renal
  - Renal infarction
  - Immune-complex mediated glomerulonephritis

Table 3. Complications of Infective Endocarditis

Echocardiography

An echocardiographic study should be performed in all cases of suspected IE.[8,9] Whether a transthoracic (TTE) or transoesophageal (TOE) study is performed first depends on the clinical situation.

Transthoracic Echocardiography (TTE) should usually be performed prior to a TOE. It will provide a great deal of important information, such as the presence of structural heart disease, the quantification of valvular regurgitation (if present) and assessment of LV function.

TTE will identify vegetations in approximately 50% of cases of IE[10] and can allow identification of high-risk patients, thus guiding early treatment decisions. TTE will often give better visualisation of the right heart structures (tricuspid and pulmonary valves) than TOE[11] and is the investigation of choice in suspected right-sided endocarditis.

Transoesophageal Echocardiography is more sensitive and specific (both >90%) than TTE[12] for the diagnosis of IE (see figure 1). It is also much better than TTE in identifying complications associated with IE such as aortic root abscesses and fistulae and can identify the mechanisms causing acute valvular regurgitation.[13] However TOE is an invasive test and therefore will carry some inherent risk including trauma to the teeth, oropharynx and oesophagus as well as the risks associated with the sedation. A TOE may be contraindicated in some patients, for example those with oesophageal problems such as strictures and varices as well as those known bleeding disorders.

Other useful tests

Other imaging modalities such as CT, MRI and Ultrasound (USS) may be required, depending on the mode of presentation. For example neurological manifestation may require a CT or MRI of the head while abdominal pain may justify abdominal imaging.

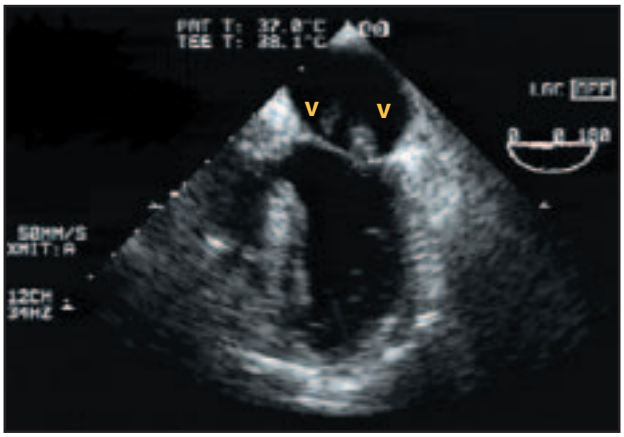

Figure 1. A TOE image of the mitral valve in a patient with two large vegetations (v) attached to the atrial surface of both the anterior and posterior leaflets in a patient with Streptococcal NVE. The patient presented with a splenic infarct and underwent successful mitral valve replacement.

Diagnosis

A diagnostic scheme termed the Duke criteria was introduced in order to help physicians to make the diagnosis of IE[14] (see Table 4). This scheme attempts to stratify patients into 3 categories – "definite", "possible" and "rejected" cases of IE depending on the presence or absence of specific findings with major emphasis on positive blood cultures (for organisms known to cause IE) and echocardiographic findings. A patient is said to have "definite" IE if found to have either two major, one major and three minor, or five minor criteria. "Possible" IE is where findings are consistent with IE but fall short of criteria for rejection. A patient is said to have the diagnosis of IE "rejected" where either the presence of a firm alternative diagnosis is made or where the manifestations of IE resolve after less than 4 days of antibiotic therapy

These criteria have consistently been shown to have a high sensitivity and specificity in helping to diagnose IE.[15] However, use of these criteria should not replace clinical judgement. Treatment may still be required if clinical suspicion is high.

Major criteria

Positive blood culture findings:

- Typical microorganism consistent with IE from 2 separate blood cultures, either viridans streptococci, Streptococcus bovis, or HACEK group
- Community-acquired Staphylococcus aureus or enterococci, in the absence of a primary focus
- Microorganisms consistent with IE from persistently positive blood cultures defined as:
  - 2 positive cultures of blood samples drawn >12 hours apart, or
  - all of 3 or a majority of 4 separate cultures of blood (with first and last sample drawn 1 hour apart)
  - Positive echocardiographic findings:
- Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation
- Myocardial abscess
- Development of partial dehiscence of a prosthetic valve
- New-onset valvular regurgitation

'Minor' criteria

- Predisposing cardiac condition or IVDA
- Fever ≥ 38°C
- Vascular phenomena
- Immunological phenomena
- Suggestive microbiological findings (positive blood culture but not meeting major criteria)
- Echo (consistent with IE but not meeting major criteria)

Table 4. Duke diagnostic criteria for IE

Causes (see Table 5)

Historically the commonest organisms found to be responsible for NVE are *viridans* group Streptococci (about 50% of cases).[16] However, the incidence of *Staphylococcus aureus* continues to increase and recent observational studies confirm that *Staphylococcus aureus* is now the leading cause of NVE.[17] In PVE, the most frequent causal organism is coagulase-negative staphylococci (< 1year post-op) and *viridans* group Streptococci (> 1 year post-op).

In intravenous drug-abusers the commonest organism responsible is *Staphylococcus aureus* (50-60%). Enterococci account for around 10% of all cases of IE, whilst fungi are responsible for between 2-10% of cases. Approximately 5% of cases have negative blood cultures,[18] most often due to previous antibiotic therapy[19] but occasionally as a result of fastidious organisms belonging to the 'HACEK' group (see Table 5) of gram-negative bacilli.

Treatment

Antibiotic Therapy

The initial treatment is high-dose empirical parenteral antibiotic therapy. This should be started immediately following blood cultures and should not be delayed whilst results are pending. UK guidelines recommend intavenous benzylpenicillin and gentamicin unless the patient is either allergic to penicillin or Staphylococcus is suspected, when intravenous vancomycin should replace benzylpenicillin.[20] This antibiotic regimen can be altered once the organism and sensitivities have been identified. If fungal endocarditis is confirmed, treatment is with intravenous Amphotericin B although surgery is nearly always required.

Early referral to a cardiologist in important, as is involvement of a senior microbiologist or infectious disease specialist. The duration of the intravenous antibiotic therapy depends on a number of factors including the organism responsible, the clinical response of the patient to treatment and the occurrence of complications, but should be for a minimum of 2 weeks with daily re-evaluation of the patient being essential to ensure both satisfactory response to treatment and that no complications occur.

- Bacteria
  - Streptococci (esp *Streptococcus viridans*)
  - *Staphylococcus aureus*
  - Staph aureus
  - Coagulase-negative Staphylococcus
  - Enterococcus
  - 'HACEK' group (gram –ve bacilli) :
    - *Haemophilus parainfluenza or aphrophilus*
    - *Actinobacillus actinomycetemcomitans*
    - *Cardiobacterium hominis*
    - *Eikenella corrodens*
    - *Kingella kingae*
- Fungi
- Culture negative

Table 5. Major Causes of Infective Endocarditis.

Surgical Intervention

Indications for surgical treatment are listed in Table 6. Patients with any of these high-risk features should be transferred to a cardiothoracic centre for consideration of early operative intervention.

Outcome

The mortality rate remains disappointing at 25%, despite antibiotic therapy. In some cases death may be attributable to a delay in making the diagnosis. In addition, the increasing frequency of *Staphylococcus aureus* has lead to an increased number of serious complications and higher mortality rates.

Patients with moderate to severe heart failure have the worse prognosis.[21] Other factors associated with a poor outcome are old age, diabetes, aortic or multiple valve involvement, large vegetations, abscess formation or the occurrence of a neurological event. Prognosis is also dependent on the organism involved, with fungal endocarditis having the worst outcome (mortality > 50%), followed by *Staphylococcus aureus* (mortality 40 – 50%) and then viridans group streptococci (mortality 4 – 16%). Right-sided endocarditis has a lower mortality rate (about 10%). PVE has a much worse prognosis then NVE.

- Indications
  - Moderate to severe heart failure secondary to valve dysfunction
  - Unstable prosthetic valve
  - Uncontrolled infection despite optimal antibiotic therapy
  - IE secondary to fungi, brucella, pseudomonas (aortic or mitral valves)
  - *Staphylococcus aureus* PVE with an intracardiac complication
  - Relapse of PVE after optimal therapy
- Relative Indications
  - Perivalvular extension of infection /Intracardiac fistula
  - Poorly responsive *Staphylococcus aureus* NVE (aortic or mitral valves)
  - Relapse of NVE after optimal treatment
  - Culture-negative endocarditis with persistent fever (≥ 10 days)
  - Large vegetations (>10mm) - risk of embolisation
  - IE due to highly antibiotic-resistant enterococci

Table 6. Indications for Surgical Intervention

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