Mini Review

CrossMark
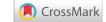
Infective endocarditis: an overview

Abstract

Infective endocarditis (IE), a microbial infection of the endothelial surface of the heart, most commonly affects the valve leaflets and carries increased morbidity and mortality.IE can also occur on foreign material, such as permanent pacemaker leads and prosthetic cardiac valves and grafts. Management of prosthetic valve endocarditis is particularly challenging.

YK Arora

Senior Consultant, Department of Cardiology, National Heart Institute, India

Correspondence: YK Arora, Senior Consultant, Department of Cardiology, National Heart Institute, India, Email dryagi08@gmail.com

Introduction

The characteristic lesion of IE is a vegetation, a mass of platelets in which micro-organisms and inflammatory cells are enmeshed. This may be visible on echocardiography and may embolise, leading to infarction and seeding of infection. The clinical presentation varies considerably and is dependent on the organism involved, the site of infection, any underlying cardiac disease and the patient's immune response. It may therefore present acutely to hospital with sepsis, heart failure and evidence of embolisation, or more insidiously in primary care with persistent fever and malaise. Acute IE is typically caused by Staphylococcus aureus (the commonest pathogen), whereas the sub acute variety can be caused by viridans streptococci, enterococci, coagulase-negative staphylococcus and Gram-negative coccobacilli. Sometimes, there is an identifiable source of bacteraemia (such as a dental procedure or indwelling venous line).[1]

Epidemiology & classification

The epidemiology of endocarditic has changed significantly in recent years. Traditionally, it was seen in younger patients with rheumatic valve disease. As rheumatic fever declines in industrialised nations, it is increasingly a disease of the elderly and those with prosthetic heart valves or cardiovascular implantable devices. The overall incidence was thought to have remained steady over the past 30 years, with about three to 10 episodes per 100,000 person-years, rising to 14.5 episodes per 100,000 person-years in those aged 70-80 years. Recent evidence suggests that the incidence may be rising over the last 5 years; the reason for this remains unknown.[2,3] IE is commonly classified according to its speed of onset (acute vs subacute), according to site (left- or right-sided) or into native or prosthetic valve/prosthetic device IE. It may also be defined by the route of acquisition (associated with or without indwelling lines, community acquired or from IV drug use).

Clinical features & diagnosis

The presenting features are varied and delayed diagnosis is common,[1] the condition may be acute and fulminant, or subacute and chronic. Most patients (90%) will have fever and malaise, often with weight loss. Most have heart murmurs (85%), although the classical 'changing murmur' is rarer. New regurgitation murmurs are highly suspicious. Classical features of IE may be present in up to 50% of patients. These include splinter haemorrhages under the fingernails, Janeway lesions, Osler's nodes, Roth's spots or finger clubbing. These stigmata are less frequent in earlier presentations of the disease. Patients may also present with stroke, or peripheral or pulmonary emboli as vegetations break away. A high index of suspicion is appropriate in patients with prosthetic valves, pacemakers and indwelling lines.[1]

Investigations include routine blood tests, blood cultures and transthoracic echocardiography. The blood test may show anaemia of chronic disease, leucocytosis, renal failure and a high CRP and ESR. The blood cultures require three 10ml samples from different sites at different times with meticulous aseptic technique, before administration of antibiotics. Yield from appropriately taken cultures is high. If cultures remain negative, microbiologists can advise on special media or special microbiological techniques for organism identification, such as PCR.

Echocardiography

Transthoracic echocardiography (TTE) has a sensitivity of about 50% and transoesophageal echocardiography (TEE), more than 90%. Vegetations, abscesses, valve regurgitation and prosthetic valve dehiscence may be seen. Infection on pacing leads is more difficult to visualise. A TTE is advised as the initial test, followed by TEE in the majority of cases of suspected or positive TTE. In cases of negative or non-diagnostic TTE, a TEE should always be performed. The Duke criteria are commonly used in clinical practice. They do not replace clinical judgment. Diagnosis requires two major criteria, one major and three minor, or five minor criteria.[4]

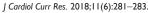### Endocarditis Diagnostic Criteria--Duke Criteria

Diagnostic: 2 Major Criteria and 0 Minor Criteria

Diagnostic: 1 Major Criteria and 3 Minor Criteria

Diagnostic: 0 Major Criteria and 5 Minor Criteria

Major diagnostic criteria

Positive blood culture for typical Infective Endocarditis organisms (strep viridins or bovis, HACEK, staph aureus without other primary

site, enterococcus), from 2 separate blood cultures or 2 positive cultures from samples drawn > 12 hours apart, or 3 or a majority of 4 separate cultures of blood (first and last sample drawn 1 hour apart).. Echocardiogram with 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, or abscess, or new partial dehiscence of prosthetic valve or new valvular regurgitation.

Minor diagnostic criteria

Predisposing heart condition or intravenous drug use, Temp >38.0°C (100.4°F). Vascular phenomena: arterial emboli, pulmonary infarcts, mycotic aneurysms, intracranial bleed, conjunctival hemorrhages, Janeway lesions

Immunologic phenomena: Glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor.

Microbiological evidence: Positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with endocarditis (excluding coag neg staph, and other common contaminants).

Echocardiographic findings: Consistent with endocarditis but do not meet a major criterion as noted above.

Treatment

The basis of treatment is prolonged combined bactericidal antibiotic therapy along with surgical intervention when indicated. Antibiotics should be initiated once blood cultures are taken. Early determination of the organism and sensitivities allows adjustment of therapy, especially as resistance is increasing.[1] Therapy usually lasts two to six weeks for native valve IE (NVE) and six weeks or more for prosthetic valve IE (PVE). A multidisciplinary approach in treatment is important, including cardiology, cardiothoracic surgery and microbiology input. Synergistic combinations of antibiotics are used to maximise effect. Aminoglycosides shorten the therapy duration.[4] The 2015 European Society of Cardiology guidelines gave full details of recommended antibiotic regimens.4 Most regimes comprise of a penicillin for four to six weeks, with an aminoglycoside (gentamicin) for up to two weeks, although in streptococcal NVE, treatment may be shorter. Staphylococcal IE, either NVE or PVE, is treated with vancomycin, rifampicin and gentamicin. The indications and use of aminoglycosides have changed and they are given once daily owing to renal toxicity.

Surgery

Despite antibiotic treatment, up to half of patients with IE will require valve surgery. This carries considerable risk, but can be lifesaving. Surgery may be required acutely, but if possible, should be delayed for valve sterilisation with antibiotics (usually at least for two weeks). Indications for surgery include:

1. Heart failure (refractory pulmonary oedema, cardiogenic shock)

2. Uncontrolled infection (abscess, enlarging vegetation, persistent cultures)

3. Prevention of embolism in certain clinical situations.

Managing PVE and Cardiac Device Related IE (CDRIE)

The diagnosis of PVE and CDRIE is more challenging because blood cultures may be negative and interpreting the echocardiogram difficult.PVE makes up 20% of all IE cases. Early PVE (less than 1 year postoperation) is often caused by nosocomial infection with staphylococci Gram-negative organisms and fungi; late PVE more closely mirrors the microbioligical profile of NVE.1 Early PVIE is usually managed surgically in high risk subgroups because antibiotic therapy is rarely effective (Table 1).[5]

Table 1 Principles of prevention of infective endocarditis.

	Prevention
1	Main principles of prevention of infective endocarditis
2	The principle of antibiotic prophylaxis when performing procedures at risk of IE in patients with predisposing cardiac conditions is maintained.
	Antibiotic prophylaxis must be limited to patients with the highest risk of IE undergoing the highest risk dental procedures. (dental procedures requiring manipulation of the gingival or periapical region of the teeth Or perforation of the oral mucosa)
	a. Patients with a prosthetic valve, including transcatheter valve, or a prosthetic material used for cardiac valve repair.
	b. Patients with previous IE.
	c. Patients with congenital heart disease.
	1. Any cyanotic congenital heart disease,
	2. Congenital heart disease repaired with prosthetic material whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if there remains residual shunt or valvular regurgitation.
3	Good oral hygiene and regular dental review are more important than antibiotic prophylaxis to reduce the risk of IE.

Streptococcal late PVE may be managed medically, but these patients have to be carefully monitored due to the risk of relapse. CDRIE may be localised to the generator pocket, with local erythema and swelling, or may infect the pacing leads in the right-sided heart chambers and valves. Staphylococcal species are the most common culprits. Treatment is with IV antibiotics for four to six weeks and the device leads must be removed. Re-implantation of the device is best delayed, if possible, until the infection is treated. It carries a poor prognosis as it frequently occurs in elderly patients with multiple co-morbidities.

Prognosis

Overall inpatient mortality from endocarditis varies from 15-30%.[1] Those at highest risk should be managed in a specialist centre with full input from the 'endocarditis team'. The major determinants of poor outcome are patient characteristics (old age, prosthetic valve, and diabetes), complications (stroke, renal or heart failure), the infecting organism (Staph aureus and fungi carry worse prognosis) and echocardiographic findings, such as vegetation size and valve dysfunction or dehiscence. If three adverse factors are present, mortality approaches 79% (Table 2).

Table 2 Recommended prophylaxis for dental procedures at risk

Recommended prophylaxis for dental procedures at risk			
Situation	Antibiotic	Single-dose 30-60 minutes before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or ampicillin	2 g orally or iv	50 mg/kg orally or ivh
Allergy to penicillin or anpicillin	C lindamycin	600 mg orally or iv	20 mekg orally or iv'

a. Alternatively, cephalexin 2 g i.v. for adults or 50 ingfkg i.v. for children, cefazolin or ceftriaxone I g Iv for adults or 50 rnekg for children.
b. Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after inuike of penicillin or arnpicillin due to cross-scnsitivity,
c. Paediatric doses should not exceed adult doses

Acknowledgments

Conflicts of interest

Authors declare that there is no conflicts of interest.

References

1. Habib G, Hoen B, Tornos P et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J.* 2009;30(19):2369−2413.

2. Wang A. The changing epidemiology of infective endocarditis: the paradox of prophylaxis in the current and future eras. *J Am Coll Cardiol.* 2012;59(22):1977−1978.

3. Dayer MJ, Jones S, Prendergast B, et al. Incidence of infective endocarditis in England, 2000-13 a secular trend, interrupted time-series analysis. 2015;28(385):1219−1228.

4. Habib G, Lancellotti P, Antunes MJ ,et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J.* 2015;36(44):3075−3128.

5. Richey R, Wray D, Stokes T, et al. Prophylaxis against infective endocarditis: summary of NICE guidance. *BMJ.* 2008;336(7647):770−771.