Chapter

Introductory Chapter: Infective Endocarditis - An Introduction

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1. Introduction

Infective endocarditis (IE) is a rare but potentially fatal condition. Almost always it is caused by bacteria, even though fungal endocarditis may occur. The infectious agent enters the bloodstream where it may adhere to the endocardium and predominantly the cardiac valves. While infective endocarditis (IE) may occur in any person, some risk factors are well known. Among these, the most significant are patients with valvular anomalies, prosthetic valves, cardiac implantable electric devices (CIEDs), and intravenous drug users. The clinical presentation may vary greatly depending on factors pertaining to the host as well as the causative microbe. Initial symptoms may be low-grade and unspecific but occasionally fulminant and severe. The diagnosis is often challenging and based on a combination of several clinical, microbiological, and radiological findings. The cornerstone of treatment is high-dose antibiotics, which are generally administered intravenously. However, pharmaceutical treatment alone is sometimes insufficient, and surgical intervention is required. This is particularly true in complicated cases, as well as in prosthetic valve endocarditis and CIED infection.

2. Epidemiology, pathophysiology, and prophylaxis

Bacteremia is a prerequisite for the development of infective endocarditis [1], and it is a more common phenomenon than might be assumed. In fact, transient bacteremia often occurs in various dental and surgical procedures, as well as in toothbrushing, flossing, and even chewing [2]. Despite the ubiquity of transient bacteremia, infective endocarditis is a rare condition with annual incidence in the USA varying between 11 and 15 cases per 100,000 population in the first 12 years of the new millennium [3]. It can thus be surmised that bacteremia alone is insufficient to cause the condition. Data from animal models suggest that the development of IE is dependent on the existence of a valvular lesion, which may be symptomatic, previously unknown or even microscopic, and clinically insignificant. The lesion in turn allows bacteria to adhere to the endocardial surface, promoting the establishment of the principal lesion in infective endocarditis: the vegetation [4].

The degree of valvular damage that is sufficient to cause disease varies greatly depending on the causative agent. *Staphylococcus aureus* has an exceptional status in this regard, owing to its recognized tendency to cause IE in patients without a pre-existing valvular condition. Infectious material in the bloodstream causes an upregulation of the body's inflammatory response. Fractions of the vegetation may come loose and cause embolization of other organs. Additionally, the presence of a vegetation on the endocardial surface may contribute irreversible structural damage [3].

The topic of antibiotic prophylaxis to prevent IE is a subject of controversy. As described above, transient bacteremia is very common in the general population,

while manifest infective endocarditis is rare. Concordantly, striving to administer antibiotics to all individuals at risk for transient bacteremia would be a futile endeavor. Indications for prophylaxis in surgical and dental procedures have varied over the years, but it has never been proven that general prophylaxis is indicated, regardless of whether the procedure is high or low risk. Current recommendations, as put forward by the European Society of Cardiology, assert that antibiotic prophylaxis only be considered in high-risk procedures in patients with a pre-existing heart condition that confers a heightened risk of endocarditis. These include prosthetic valve, cyanotic congenital heart disease, and patients with a previous episode of IE. Antibiotic prophylaxis is not recommended in other forms of valvular or congenital heart disease [5].

3. Clinical symptoms, diagnosis, and imaging

Infective endocarditis is a condition whose presentation may vary greatly, which consequently may make the diagnosis elusive, conferring a significant delay in initiation of treatment. The presenting symptoms stem from several distinct pathophysiological mechanisms, and any combination of these may occur in any given individual:

- Symptoms of disseminated infection
- Symptoms of structural cardiac damage

Definite infective endocarditis
Pathologic criteria
1. Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen
2. Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination
Showing active endocarditis
Clinical criteria
1. Two major criteria
2. One major criterion and three minor criteria
3. Five minor criteria
Possible infective endocarditis
1. One major criterion and one minor criterion
2. Three minor criteria
Rejected
1. Firm alternate diagnosis explaining evidence of infective endocarditis
2. Resolution of infective endocarditis syndrome with antibiotic therapy for < 4 days
3. No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for <4 days
4. Does not meet criteria for possible infective endocarditis, as above

Table 1.
Modified Duke criteria [6].

- Symptoms of an upregulated immune system and circulating immune complexes

- Symptoms of septic embolism to distant organs

These mechanisms are reflected in the diagnostic criteria (the Duke criteria) provided in **Table 1** [6]. To accurately make an IE diagnosis, it is crucial to (a) perform a thorough clinical examination, (b) acquire adequate microbiological samples, and (c) ensure that correct radiological imaging is carried out. As to the latter, the cornerstone of radiological imaging has long been echocardiography: preferably with a transesophageal approach. Other modalities, such as ECG-triggered computerized tomography and positron emission tomography, are sometimes used in clinical practice, but are as yet not included in the Duke criteria [5].

4. Microbiology, antibiotic treatment, and surgery

The most common etiologic agents in IE are Gram-positive bacteria, which are responsible for more than 90% of cases. IE caused by Gram-negative bacteria and fungi does occur but rarely. While traditionally the major bacterial finding has been streptococcal species, later decades have seen a continuing rise of *S. aureus* [3].

Regardless of etiology, treatment consists of a long course of high-dose antibiotics, which are generally administered intravenously for the entire duration. Length of the treatment is usually 2–4 weeks but may be longer in complicated cases—particularly in those involving foreign material in the bloodstream. Due to the high total drug exposure, it is imperative to use pharmaceuticals which are well tolerated by the majority of patients. As in other severe infections, antibiotics of the beta-lactamase class are preferred when applicable. These drugs are distinguished by a combination of high efficacy and good tolerability [7].

Pharmaceutical treatment alone is often insufficient, however. Thoracic surgery is required in 25–50% of cases during acute infection and 20–40% during convalescence. Surgery is effective (a) as a means of source control (b) in preventing embolization and (c) as a means to repair structural cardiac damage [8]. Procedural risk is significant, however, and the decision to operate should be taken on an individual basis and in collaboration with representatives of appropriate clinical and diagnostic specialties. To this end it is recommended that decisions are taken by a unit known as the endocarditis team [9].

5. Conclusion

The aim of this book is to provide a deepened understanding of infective endocarditis which is a complex condition. Due to its diverse clinical features, patients with infective endocarditis may present at any part of the healthcare system, and awareness is crucial in order to establish a rapid and accurate diagnosis. In order to prevent mortality, as well as morbidity arising from embolic events and structural cardiac damage, it is important that appropriate medical and surgical management be initiated promptly in each individual case.

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