Mimics of Infective Endocarditis

Patients' Profiles and In-Hospital Outcome

Data from Kasr Al-Aini Infective Endocarditis Project

A Thesis Submitted for Partial Fulfillment of Masters Degree of Cardiology

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Their words of inspiration and encouragement still linger on

.....To my parents

Thesis abstract

Key Words: infective endocarditic, mimic diseases, over or under diagnosis.

Background: IE is a disease characterized by high morbidity and mortality. Rapid diagnosis, effective treatment, and prompt recognition of complications are essential to good patient outcome. Differentiating IE from its mimics is important to avoid over or under diagnosis of IE with the consequent catastrophic implications.

 Aim of the study:

Through analyzing the database of Kasr Al-Aini infective endocarditis project, (IEP) the main aim of this work was to Identify the spectrum of diseases that could mimic IE, Detect clinical, laboratory and echocardiographic features that may aid in differentiating infective endocarditis from other mimicking diagnoses. Also to determine the inhospital and long term outcome of endocarditis-like diseases.

Methods:

The data of 197 patients referred to Kasr Al-Aini IEP between February 2005 till December 2008 with a suspicion or diagnosis of IE was analyzed. Patients were divided according to modified Duke criteria into definite endocarditis (IE group; n = 160) and rejected endocarditis (non-IE group; n = 31). Case report forms were analyzed to collect various clinical, laboratory, microbiologic and echocardiographic features. Inhospital course was recorded. Long term Follow up was conducted to identify the clinical outcome of both groups and to ascertain the original rejection of IE in the non-IE group.

Results and conclusion:

Among patients referred to Kasr Al-Aini IEP, patients with endocarditis-like diseases represented one sixth of all enrolled patients, Chest infection, acute rheumatic activity, genitourinary tract infection and autoimmune diseases represent the commonest endocarditis mimics. Almost half of patients presented with major complications and one sixth developed new major complications during hospitalization, patients with endocarditis-like diseases had better response to medical therapy, less need to early cardiac surgery during hospitalization and a trend towards higher need for late cardiac surgery.. Patients with and without endocarditis had similar long term composite outcome in term of hospitalization, cardiac surgery and total mortality.

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List of abbreviations

CKD, Chronic Kidney Disease

CNE, Culture Negative Endocarditis

CRP, C-Reactive Protein

ESR, Erythrocyte Sedimentation Rate

HAI, Health Care Associated Infection

IVDU, Intravenous Drug User

ICE, International Collaboration on Endocarditis

ICMA, Intracranial Mycotic Aneurysms

IE, Infective Endocarditis

IEP, Infective Endocarditis Project

MAC, Mitral Annular Calcification

MKV, Mitral Kissing Vegetation

NBC, Negative Blood Culture

PAPS, Primary Anti Phospholipid Syndrome

PVE, Prosthetic Valve Endocariditis

RF, Rheumatoid Factor

SLE, Systemic Lupus Erythematosus

TIA, Transient Ischemic Attack

TEE, Trans Esophageal Echocardiography

TTE, Trans Thoracic Echocardiography

VRC, Von Reyn Criteria

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Background

Infective endocarditis (IE) poses a difficult diagnostic dilemma when it generates constellation of findings that are classic for other disorders. The diagnostic challenge of IE arises from the various non-specific clinical features often found on presentation in addition to the presence of culture negative endocarditis (CNE). Moreover, various clinical syndromes present with valvular and non valvular masses that could mimic IE vegetations. If untreated IE is always fatal.

Despite this, there is little data in the current literature regarding the contemporary profile of endocarditis-like diseases. In addition the spectrum of these mimics is supposed to vary between different populations according to their defining characteristics (e.g. age, underlying valvular heart disease, level of awareness of both the patients and their treating physicians). This is further confounded by the fact that IE has changed its face with loss of its classic clinical features; which in turn is associated with a changing profile of IE-like disease.

Reaching a swift and accurate diagnosis has a great impact on both treatment and prognosis. On the other hand, late diagnosis often leads to mismanagement and early antibiotic administration which in turn leads to negative results of blood cultures.

The Kasr Al-Aini Infective Endocarditis Project started in 2005 aiming at providing a better service for patients with suspected or definite IE by reaching an early diagnosis and hence proper management. Also through creating an electronic database for these patients it is hoping to provide a tool for follow up of these patients and to provide effective methods of tackling IE.

Aim of the work

Through analyzing the database of Kasr Al-Aini infective endocarditis project, (IEP) the main aim of this work was to:

1-Identify the spectrum of diseases that could mimic IE

2-Detect clinical, laboratory and echocardiographic features that may aid in differentiating infective endocarditis from other mimicking diagnoses.

3-Determine the inhospital and long term outcome of endocarditis-like diseases.

Chapter I

IE Overview

Infective endocarditis (IE) is an endovascular microbial infection of the cardiovascular structures (e.g. native valves, ventricular or atrial endocardium) including endarteritis of the large intrathoracic vessels (e.g. in a patent ductus arteriosus, arterio-venous shunts, coarctation of the aorta) or of intracardiac foreign bodies (e.g. prosthetic valves, pacemaker or ICD leads, surgically created conduits) facing the blood stream.[1] Despite the major advances in diagnostic technology and improvements in antimicrobial selection and monitoring, accompanied by parallel advances in surgical techniques, the morbidity and mortality remain high.[2] The in-hospital mortality rates in the contemporary era approaches 20-25%.[3, 69] Infective endocarditis now represents the fourth leading cause of life-threatening infectious disease syndromes.[2] Rapid diagnosis, effective treatment, and prompt recognition of complications are essential to good patient outcome.[4]

Epidemiology:

IE is a rare condition.[5] The incidence of community acquired native-valve endocarditis in most recent studies is 1.7 to 6.2 cases per 100,000 person-years.[6] In adults, IE disease affects males more than females, with a ratio of 2.5:1.[7] The median age of patients has gradually increased; it was 30 to 40 years during the preantibiotic era and 47 to 69 years more recently.[8] The incidence of infective mitral valve endocarditis on the native valve exceeds that of the aortic valve.[9] In contrast, the incidence of endocarditis on aortic valve prosthesis far exceeds that associated with mitral valve prosthesis.[10]

While in developing countries rheumatic heart disease remains the most frequent underlying cardiac condition predisposing patients to infective endocarditis[11], in developed countries mitral valve prolapse, prosthetic heart valves infection, nosocomial infection and intravenous drug misuse have a greater impact.

Despite this change in predisposing factors, the potentially serious impact of IE on the individual has not changed.18

Recent series found S. aureus as the main microorganism[;12,13,33,87] however in the previous decennia and also in a few recent studies, S. viridians was still the prevailing aetiological agent.[14,15,16,17,67] Notable trends include a rising prevalence of staphylococcal skin flora caused by iatrogenic nosocomial infection, Staphylococcus aureus affecting intravenous drug users, and Streptococcus bovis in the elderly, often connected to underlying gastrointestinal neoplasia.[18]

IE risk factors can be classified as either host related or procedure related. [19] Cardiac valvular abnormalities are well recognized as host-related risk factors.[20,21] Other previously cited host-related risk factors include chronic alcoholism,[22,23] meningitis,[24,25] and diseases with accompanying disorders of immunity, such as systemic lupus erythematosus, diabetes, and inflammatory bowel disease.[26,27] Contradictory reports exist for leukemia.21

Bacterial infection is a well-described complication of chronic liver disease and is a major cause of death.[28] However, infective endocarditis complicating chronic liver disease has been reported infrequently.[29] Denton et al. identified 2 (0.58%) of 342 patients with liver cirrhosis having bacterial endocarditis.[30] Chronic liver disease leads to multiple invasive procedures that may result in higher rates of bacteremia and infective endocarditis.[31]

Nosocomial infection

Nosocomial IE is defined as an infection occurring > 72 h after admission to the hospital or IE acquired in association with a significant invasive procedure performed during a recent hospitalization $\leq$ 8 weeks before the onset of symptoms.[32,33]

Nosocomial infection accounted for endocarditis in 22% of cases in one recent series with mortality greater than 50%.[34] Predominant pathogens were staphylococci and enterococci, often related to intravenous catheters or surgical

procedures. Particular risk groups in this category include the immunosuppressed with central venous catheters and those undergoing haemodialysis.18

Prosthetic valve endocarditis

Prosthetic valve endocarditis (PVE) is classified as early or late, depending on when infection was diagnosed; some authors define early PVE within 12 months after surgery and late PVE after 12 months.1 Others define early PVE as those occurring within 2 months after surgery and late PVE as that occurring after 2 months.[35] The rates of early and late infections are about 20% and 80%, respectively[36,37] regardless which definition is used.

Prosthetic valve endocarditis accounts for 10–15% of most series with an overall incidence of 0.1–2.3% / patient year.[38] Both mechanical valves and bioprostheses appear equally susceptible. Early infection peaks two months after surgery and is often caused by S. epidermidis or S. aureus, whereas the spectrum of late infection mirrors that of native valve disease.18

Intravenous drug users (IVDU)

The incidence of IE in IVDU tends to be 100-1000 times higher than in the general population.[39] The overall incidence of IE in this group is 1–5% / year.[40] The tricuspid valve is infected in over 50% of patients and the majority has no known pre-existing cardiac disease. Repeated injections of impure material could encourage cytokine production, valvar inflammation, and fibronectin deposition on previously healthy valve tissue, thereby predisposing to infection. S aureus species predominate, although unusual infections including Pseudomonas aeruginosa, fungi, bartonella, salmonella, and listeria may also be encountered.18

Pacemaker Endocarditis

Endocarditis related to PM-lead infection is a rare but serious complication of permanent transvenous pacing.[41] The reported incidence varies in the literature from 0.13% to 7%[42,43] with a mortality rate of 33%.41 Staphylococci are responsible for the vast majority of these infections. It is considered to be due to an infection during the pacemaker implantation period or the subcutaneous

implantation of the battery and not due to transient bacteremia, as the wire becomes covered by fibrous tissue rendering the attachment of microbes during transient bacteremia difficult.[44,45,46,47,48]

Medical treatment alone is rarely successful, and several studies have suggested that the material should be removed quickly for optimal management.[49,50]

Non-valvular mural endocarditis

Is an extremely uncommon condition and may be seen in all cardiac chambers.[206] Only 62 cases have been previously reported on MEDLINE between 1970 and 2005.[57] It develops secondary to several predisposing conditions like high velocity intracardiac regurgitant jets, congenital shunts, ventricular aneurysms or pseudoaneurysms, idiopathic hypertrophic subaortic stenosis, systemic immunosuppression, and pacemakers.[51] Alternatively, mural endocarditis may result as an extension of infection from underlying myocardial abscesses in critically ill patients.[52] Hematogenous infection of normal mural endocardium without an anatomic substrate or systemic immunosuppression has been reported to be exceptional.[206]

The most common pathogens associated with mural endocarditis are staphylococci and streptococci, although fungal infection has been well described.[53,54,55] Overwhelming sepsis is generally cited as the most common cause of death.[55,56] Prognosis in mural endocarditis has been reported to be dismal.[206]

Koray et al,[206] described a case of Right ventricular mural endocarditis presenting as an isolated apical mass in a non-addict patient with congenital deafness and aphasia. The mass measured 32x27 mm, was slightly mobile, solid and attached to the apical part of the right ventricular septum with a short stalk. Tricuspid and pulmonary valves were morphologically normal. There was no evidence of a congenital defect or other cardiac pathology. For apical endocarditic masses, TTE is regarded to be superior to transesophageal echocardiography (TEE). This is because apical regions of both ventricles are often foreshortened on TEE.[57]