Clinical and epidemiological characteristics of infective endocarditis

Enfektif endokarditli olguların klinik ve epidemiyolojik özellikleri

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Objectives: We evaluated the clinical and laboratory characteristics of patients with infective endocarditis (IE).

Study Design: During a five-year period (January 2002-December 2006), 96 patients (56 men, 40 women, mean age 47±15 years; range 16 to 81 years) were treated and followed for IE. All the patients underwent transthoracic and transesophageal echocardiography. Clinical and laboratory characteristics of the patients were reviewed. All cases of prosthetic valve endocarditis were late-onset IE. Blood samples were cultured in both aerobic and anaerobic media and incubated for 21 days. The diagnosis of IE was made according to the Duke criteria.

Results: Male-to-female ratio was 1.4. The most common complaint on presentation was dyspnea (n=58, 60.4%), followed by fever (n=20, 20.8%), and fatigue (n=16, 16.7%). The mean follow-up period was 21±12 days (range 2 to 52 days). While transthoracic echocardiography was sufficient to detect vegetations in 69 patients (71.9%), IE lesions could be demonstrated by transesophageal echocardiography in 27 patients (28.1%). The most common involvement was seen in the mitral valve (54.2%), and the incidence of native valve involvement (79.2%) was greater than that of prosthetic valve involvement. Forty-nine patients (51%) were submitted to surgery. In-hospital mortality occurred in 12 patients (12.5%). The prevalence of IE among all patients hospitalized in the cardiology department was 0.13%. The culprit microorganism was isolated in only 36 patients (37.5%) being staphylococci (33.3%), enterococci (27.8%), brucellae (22.2%), and streptococci (11.1%).

Conclusion: The diagnosis and treatment of IE should be designed taking into consideration that epidemiologic and clinical features of IE may differ from those of individual countries.

Key words: Endocarditis, bacterial/etiology/therapy; heart valve diseases; prosthesis-related infections.

Amaç: Enfektif endokarditli (EE) olguların klinik ve laboratuvar özellikleri değerlendirildi.

Çalışma planı: Kliniğimizde beş yıllık süre içinde (Ocak 2002-Aralık 2006) 96 hasta (56 erkek, 40 kadın; ort. yaş 47±15; dağılım 16-81) EE tanısıyla tedavi edildi ve izlendi. Tüm hastalar transtorasik ekokardiyografi ve transözofageal ekokardiyografi ile değerlendirildi. Hastaların klinik özellikleri, laboratuvar bulguları belirlendi. Protez kapak endokarditlerinin tümü geç dönem EE idi. Kültürler aerob ve anaerob ortamlara ekilerek 21 güne kadar inkübasyon sağlandı. Enfektif endokardit tanısı Duke ölçütlerine göre kondu.

Bulgular: Erkek/kadın oranı 1.4 bulundu. Başvuru sırasında en sık yakınma (n=58, %60.4) nefes darlığı idi; bunu ateş (n=20, %20.8) ve halsizlik (n=16, %16.7) izlemekteydi. Ortalama izlem süresi 21±12 gün (dağılım 2-52 gün) idi. Transtorasik ekokardiyografi 69 hastada (%71.9) vejetasyon saptanmasında yeterli olurken, EE'ye ait kitle lezyonları 27 hastada (%28.1) transözofageal ekokardiyografi ile saptanabildi. En sık mitral kapak tutulumu (%54.2) izlendi; doğal kapak tutulumu (%79.2) protez kapak tutulumundan fazlaydı. Kırk dokuz hastada (%51) cerrahi endikasyonu kondu. Hastane içi mortalite 12 hastada (%12.5) görüldü. Enfektif endokardit tanısı konan hastaların kardiyoloji servislerine yatan tüm hastalara oranı %0.13 bulundu. Hastaların yalnızca 36'sında (%37.5) sorumlu mikroorganizma kültürde gösterilebildi. En sık etken stafilokoklar (%33.3) idi, bunu enterokoklar (%27.8), brusella (%22.2) ve streptokoklar (%11.1) izlemekteydi.

Sonuç: Enfektif endokarditin tanı ve tedavisinin planlanmasında, ülkemizdeki epidemiyolojik ve klinik verilerin diğer ülkelerdekinden farklılıklar gösterdiği dikkate alınmalıdır.

Anahtar sözcükler: Endokardit, bakteriyel/etyoloji/tedavi; kalp kapak hastalığı; protez ilişkili enfeksiyon.

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Infective endocarditis (IE) is an inflammation of the heart valves and/or the endocardium due to bacteria or fungi leading to formation of vegetation.[1] There has been a recent rise in the incidence of the disease with increasing age. Age at presentation was found to be 36-69 in several studies.[2-4] The disease is more prevalent in men. The male-to-female ratio is 1.5 to 2.5.[5] The annual prevalence has been reported to be 2.4-11.6/100.000 persons.[2,6,7] This rate is particularly higher in patients >50 years old and reaches 14.5/100.000 -persons in 60-70-year-old patients.[8] The annual overall mortality rate is 1.4/100.000 persons and the in-hospital mortality rate is about 16-25%.[2,5,8,9] Despite technological developments in medicinal and surgical treatments, the importance of IE is becoming more prominent.[1] Streptococci are the most common culprit organisms, followed by Staphylococcus aureus. Enterococci and gram-negative baccili are also among the most commonly encountered organisms. However, S. aureus has recently become more common.[10-12] Fever is the most common complaint at presentation with the rate of %80-85. 5-30% of the patients with endocarditis may not develop blood culture growth. In addition, 10-30% of the patients with infective endocarditis have prosthetic valve endocarditis.[8,13] A limited number of studies has been conducted on IE in Turkey. In this study we aimed to determine clinical and laboratory characteristics of patients with IE and to compare their common characteristics.

PATIENTS AND METHODS

Patient group: Within a five-year period (January 2002-December 2006), 96 patients (56 men, 40 women, mean age 47±15 years; range 16 to 81 years) were admitted in our clinic with the preliminary diagnosis of IE and were followed up with a definite diagnosis of IE. All patients underwent transthoracic echocardiography, followed by transesophageal echocardiography to detect pathologies such as fistula, abscess and smaller vegetations. Clinical (age, sex, complaints at presentation, hemodynamic characteristics, follow-up period and mortality rate) and laboratory characteristics (complete blood count, biochemical and microbiological parameters and echocardiographic findings) of the patients were determined. All patients with prosthetic valve endocarditis visited the clinic a minimum of 2 months after the valve replacement surgery.

Diagnosis of infective endocarditis. The diagnosis of IE was made according to the Duke Criteria.[14] Pathologic or clinical criteria were used for definitive diagnosis. Modified Duke Criteria were used to diagnose IE as of June 2005.[15]

Blood cultures. Three blood samples in two sets were collected from sites cleaned with appropriate antiseptics in each patient, a minimum of one hour apart, and cultured in both aerobic and anaerobic media and incubated for up to 21 days. On the other hand, blood samples were cultured in specific media for patients who had predisposing factors and were clinically suspected.

Laboratory. Urea, creatinine, hemoglobin, hematocrit, white blood cell count, erythrocyte sedimentation rate, rheumatoid factor and serological markers were analyzed from peripheral venous blood samples.

RESULTS

The male-to-female ratio was 1.4 in our study. The most common complaint at presentation was dyspnea (n=58, 60.4%), followed by fever (n=20, 20.8%), fatigue (n=16, 16.7%) and other reasons (n=2, 2.1%).

While transthoracic echocardiography was sufficient to detect vegetations in 69 patients (71.9%), IE mass lesions could be demonstrated by transesophageal echocardiography in 27 patients (28.1%).

Hemodynamic, laboratory and echocardiographic characteristics of the patients are shown in Table 1. Signs of tachycardia and anemia were present on clini-

Table 1. Hemodynamic, laboratory and echocardiographic characteristics of the patients

	Mean±SD	Range
Systolic blood pressure (mmHg)	117±25	80-200
Diastolic blood pressure (mmHg)	70±13	40-110
Pulse (beat/min)	91±18	60-150
Hemoglobin (g/dL)	11.1±1.9	6.9-14.8
Hematocrit (%)	33.3±5.6	20.7-44.4
Erythrocyte sedimentation rate (mm/h)	50±33	1-120
White blood cell (/mm^3)	10595±4794	3700-25210
Urea (mg/dL)	55±32	19-135
Creatinine (mg/dL)	1.4±1.9	0.4-11.0
End-diastolic diameter (cm)	5.8±0.9	4.6-8.0
End-systolic diameter (cm)	4.1±0.9	3.0-5.5
Ejection fraction (%)	58±11	29-75

Table 2. Distribution of cardiac structures with mass lesions of infective endocarditis

	Number	Percentage
Native mitral valve	40	41.7
Native aortic valve	22	22.9
Mechanical prosthetic mitral valve	8	8.3
Native mitral + aortic valve	4	4.2
Mechanical prosthetic aortic valve	4	4.2
Bioprosthetic aortic valve	4	4.2
Native tricuspid valve	4	4.2
Bioprosthetic mitral valve	2	2.1
Native pulmonary valve	2	2.1
Native aortic + pulmonary valve	2	2.1
Native aortic + tricuspid valve	2	2.1
Pacemaker lead	2	2.1

cal presentation. There was no patient with severe left ventricular systolic insufficiency. Erythrocyte sedimentation rate was found to be high due to the underlying active infection. The most common involvement was seen with the mitral valve; the incidence of native valve involvement was greater than that of prosthetic valve involvement (Table 2). Furthermore, 51% of the patients received indication for surgery.

The mean follow-up period was 21±12 days (range 2 to 52 days). In-hospital mortality occurred in 12 patients (12.5%). The prevalence of IE among all patients hospitalized in the cardiology department was 0.13%. The distribution of this rate according to years was as follows: 0.20% in 2002, 0.19% in 2003, 0.09% in 2004, 0.07 in 2005 and 0.09% in 2006.

The culprit microorganism was isolated in only 36 of the patients (37.5%) being staphylococci, enterococci, brucellae, and streptococci (Table 3). Interestingly, steptococci were the forth most common culprit microorganisms. An antimicrobial combination therapy of penicillin and aminoglycoside was instituted for the majority of the patients, which was followed by addition of rifampicin to this combination (Table 4).

DISCUSSION

Currently, the prevalence of IE is on the increase in the elderly. This is associated with the decreased prevalence of rheumatic diseases and increased health problems in aging population.[6,7] However, this condition seems to be a problem of developed countries. Besides, a retrospective study conducted in Turkey reported a lower mean age.[16] Mean age at presentation was also found to be lower (mean age 47) in our study. This may be associated with the shorter life expectancy in Turkey, since the risk of IE development increases with increase in life expectancy. The high prevalence of rheumatic heart disease in our country, poor oral hygiene and ineffective prophylaxis may also be considered as underlying factors. The male-to-female ratio was also found to be 1.4/1 in our study, which was lower than the ratio in other studies.[5]

Dyspnea which was the most common complaint on presentation was significantly higher compared to fever. Although fever was reported in 80-85% of the patients,[17] this rate was found to be 20.8% in our study. This may be due to use of antimicrobial agents before diagnosis; it may also explain the significantly high culture-negative IE in these patients. Additionally, 56 of 96 patients (58.3%) in our study were referred to our hospital from other centers with the preliminary diagnosis of IE. Others were admitted to our hospital with the preliminary diagnosis of IE. Considering the high number of patients who were referred to our hospital, the prevalence of fever may be misleading.

With regard to laboratory parameters, mild anemia, erythrocyte sedimentation rate and high white blood cell count, which were considered as chronic anemia, were consistent with common knowledge. The rate of native valve endocarditis was high in our study (n=76, 79.2%). Cetinkaya et al.[16] also reported native valve involvement to be 80%.

Table 3. Comparison of clinical risk factors in patients receiving and not receiving oral anticoagulant treatment

	Native valve		Bioprosthetic valve		Mechanical valve		Other*	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Viridans streptococcus	2	2.1	-		2	2.1	-	
Staphylococci	6	6.3	2	2.1	2	2.1	2	2.1
S. aureus	2	2.1	-		-		2	2.1
S. epidermidis	4	4.2	2	2.1	2	2.1	-	
Enterococci	8	8.3	-		2	2.1	-	
Brucellae	8	8.3	-		-		-	
HACEK	2	2.1	-		-		-	
Culture negative	50	52.1	4	4.2	6	6.3	-	
Total	76	79.2	6	6.3	12	12.5	2	2.1

HACEK: *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella and Kingella species.* *Infection of pacemaker lead

Table 4. Antimicrobial therapies for infective endocarditis

	Number	Percentage
Penicillin and aminoglycoside	64	66.7
Penicillin, aminoglycoside and rifampicin	12	12.5
Vancomycin	4	4.2
Cephalosporin and aminoglycoside	4	4.2
Aminoglycoside, rifampicin and tetramicin	4	4.2
Cephalosporin, rifampicin and tetramicin	4	4.2
Cephalosporin	2	2.1
Penicillin	2	2.1

Microorganisms were cultured in only 37.5% of the patients. In addition, 62.5% were found to be culture-negative. Regardless of native or prosthetic valve, culture negative IE is most commonly seen. Infections caused by enterococci, brucellae and staphylococci, are more common in native wall IE, unlike streptococci. On the other hand, infections due to staphylococci are more frequently seen in prosthetic valve IE, than streptococci. Antibiotic use before the blood culture, culprit microorganisms which are difficult and slow to culture and inadequate technical and laboratory conditions (ranging from blood sample collection to incubation) are among factors for culture-negativity. Antibiotic use before the blood culture was the most common. Due to low sociocultural level of patients in Turkey, accurate information could not be obtained regarding antibiotic use. Nevertheless, it would not be inaccurate to establish an association between high prevalent culture-negativity of 62.5% and antibiotic use before the blood culture. In addition, insufficient level of healthcare services compared to developed countries is also a factor affecting for the results.

The prevalence of IE is also high in areas where brucellosis is endemic.[18] Brucellae should be taken into consideration particularly in areas in Turkey where the agent is endemic, in the evaluation of IE. We instituted two combination therapies including cephalosporin or aminoglycoside plus rifampicin and tetramicin for the treatment of IE due to brucellae.

Unlike it is generally known, the prevalence of streptococci was lower in both native and prosthetic valve IE compared to other agents.

Furthermore, the mortality rate was found to be lower, while prevalence of IE was similar. Low prevalence of fever is also an indicator suggesting antibiotic use before diagnosis for some of the patients and as a consequence low mortality rate. Therefore, the prevalence of fever may be misleading in IE.

The prevalence of IE among all patients hospitalized in the cardiology department was observed to decline according to years. This may be explained by more effective prophylactic treatment. However, a long-term observation is required to conclude that the rate of IE decreased, despite a decline in the prevalence according to years.

In conclusion, diagnosis and treatment of IE should be planned considering epidemiological and clinical data in our country, noting that they are different from those in other countries.

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