

A Retrospective Study of Infective Endocarditis at Changhua Christian Hospital during the years 1989-1999

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Abstract

Objective : The purpose of this study was to describe clinical manifestations and microbiological characteristics of infective endocarditis.

Study design : This study analyzed the data on patients with infective endocarditis treated at Changhua Christian Hospital who were diagnosed based on Duke's criteria performed during the period from January 1, 1989 to September 30, 1998.

Results : A total of 58 patients were included, with a male to female ratio of 3.8 and a mean age of 40.6 years old (range, 3 to 71 year-old). Predisposing factors were identified in 28 (48.3%) patients. Thirty (51.7%) of the patients had no identified underlying cardiac lesion. Fifty (86.2%) patients had fever, 19 (32.8%) had new cardiac murmur, and 11 (19.0%) had peripheral embolic phenomenon. Vegetation was found in 49 (84.5%) patients who underwent echocardiography. Pathogens were isolated by blood culture in 55 (94.8%) patients. The most common pathogens were viridans streptococcus (32/58) and Staphylococcus aureus (12/58). All patients received antimicrobial agents initially. Cardiovascular surgery was performed in 8 (13.8%) patients. A total of 17 (29.3%) patients died. Complications occurred in 40 (69.0%) patients, including 16 (27.6%) patients with neurological complications, and 24 (41.4%) patients with cardiovascular complications. Neurological complications (OR=9.034, 95% CI= 1.651-49.428, p=0.01) and heart complications (OR=7.920, 95% CI= 1.487-42.177, p=0.02) were most frequently associated with mortality.

Conclusion : The leading two causes of death were neurological complications (27.6%), and cardiovascular complications (41.4%). To reduce the associated complications as far as possible is the most critical point in improving the survival rate. (J Intern Med Taiwan 2001;12:177-183)

Key Words : Infective endocarditis

Introduction

Infective endocarditis is an inflammation of the endocardium caused by microorganisms including bacteria, fungi, viruses, and parasites. Infective endocarditis involves infection of the endothelial surfaces of the valves and chambers of the heart. The spectrum of clinical presentation ranges from rapidly progressive and destructive disease to more indolent or chronic infections. Infective endocarditis has catastrophic complications in some patients with severe infection. Risk factors for endocarditis have been well-studied 1. Degenerative valvular lesions, cyanotic congenital heart disease, rheumatic heart disease, prosthetic heart valve, and mitral valve prolapse are well-documented preexisting cardiac risk factors for endocarditis. Although many community hospitals still report viridans streptococci as the most common isolates among patients with infective endocarditis 2, staphylococci have assumed increasing importance among isolates in community hospitals in recent years 3. The incidence of infective endocarditis is difficult to determine because the criteria for diagnosis and the methods for reporting vary with different series 4. Although infective endocarditis is a rare infectious disease in Taiwan, there were some literatures about infective endocarditis in Taiwan 5,6. In this study, we report the clinical and microbiological characteristics of patients with infectious endocarditis treated during the recent 10 years at Changhua Christian Hospital. And, we accessed the relationship between the mortality and endocarditis induced complications.

Materials and Methods

1. Selection of Study Participants

The medical records of patients with infective endocarditis treated at Changhua Christian Hospital from January 1, 1989 to September 30, 1998 were obtained by searching the computerized medical records database. To be included in the study, subjects had to meet at least one of the following criteria 7 : a) demonstration of bacterial endocarditis at surgery; b) typical positive blood culture for infective endocarditis from two separate blood cultures and typical positive echocardiography for infective endocarditis; c) one or more otherwise unexplained positive blood cultures in a patient with three of the following: predisposition to the development of endocarditis, fever (body temperature $>38^{\circ}\text{C}$), vascular embolic phenomena (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctiva hemorrhage, Janeway's lesion), evidence of immune system disease (glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor),

echocardiography consistent with infective endocarditis .

2. Microbiological Investigation

Blood culture was performed for every patient who was suspected to have infectious endocarditis. The BACTEC NR-860 system (Beckton Dickinson Diagnostic Instrument Systems, USA) was used for detecting pathogens. Gram positive, catalase positive pathogens were identified by conventional biochemical tests including a latex agglutination kit (Latex test, Pastorex Staph-Plus, Tokyo, Japan), coagulase tubing test (Coagulase plasma edta, Difco, USA), 1% glucose fermentation test and 5- μ g novobiocin disk (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD). Gram positive, catalase-negative pathogens were identified by conventional biochemical tests, including a sensitized latex agglutination kit for grouping beta-hemolysis Streptococci (Slide Strepto-Kit, bio Merieux Vitek, Hazelwood, MO), the API-20 Strp kit (bio Merieux Vitek, Hazelwood, MO), and the optochin test (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD). Gram negative pathogens were identified by conventional biochemical tests, including the API-20E kit (bio Merieux Vitek, Hazelwood, MO) and the API-20NE kit (bio Merieux Vitek, Hazelwood, MO). Routine antibiotic sensitivity testing was done by the disk diffusion method (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD) according to guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) 8. The findings of echocardiography were recorded including cardiac performance, appearance of cardiac valves, chordae tendineae, and presence of perivalvular lesions. The involved cardiac valve was recorded as the valve exhibiting the most damage if more than one valve was involved. Histological evidence of infective endocarditis was available from all operated patients. Valvular replacement, when necessary, was performed with standard cardiopulmonary bypass techniques. The annular areas were inspected for abscess. Any complications associated with infective endocarditis were recorded, including neurological complications (such as cerebral embolism, mycotic aneurysm, intracranial hemorrhage, subarachnoid hemorrhage, brain abscess, optic nerve atrophy, and meningitis) and cardiovascular complications (such as congestive heart failure , rupture of chordae tendineae, coronary artery embolism, perivalvular abscess, cardiac arrhythmia).

3. Statistical Analysis:

The Chi-square test was used to analyze categorical data. A p value < 0.05 was considered statistically significant. Further testing was done by multiple logistic analysis. Odd ratios of potential risk factors were obtained by logistic regression analysis. All data were analyzed on a personal computer using SAS v6.12 software.

Results

A total of 114 episodes of clinically diagnosed infective endocarditis among 112 patients were treated during the study period. Fifty-six of those patients were excluded due to either incomplete medical records or failure to meet Duke's criteria. The remaining 58 patients, including 46 males (80%) and 12 females (20%) (M/F ratio 4:1), fulfilled the definitive Duke's criteria and were included in the study. The age of these 58 patients ranged from 3 to 71 years with a mean of 40.6 years. Predisposing heart diseases were found in 28 (48.3%) of these 58 patients. Risk factors showed at Table 1. Fifty (86.2%) of the 58 patients had fever. Nineteen (32.8%) patients had new cardiac murmur. Peripheral vascular phenomenon was observed in 11 patients, including Janeway lesion in 2, Osler node in 2, petechiae in 2, subconjunctival hemorrhage in 2, splinter hemorrhage of the nail bed in 2, and Roth spot in 1. Leukocytosis was found in 47 (81.0%) of the 58 patients, and 45 patients had anemia. At initial examination, ESR was elevated in 56 (96.6%) patients and CRP (98.3%) was elevated in 57 patients. Of the 36 patients who underwent urinalysis, 13 (36.1%) had hematuria. Echocardiographic findings listed at Table 2.

The following pathogens of infective endocarditis were isolated by blood culture in 55 (94.8%) of 58 patients: viridans streptococcus in 32, methicillin-sensitive *Staphylococcus aureus* in 11, *Staphylococcus epidermidis* in 5, *Enterococcus* sp. in 2, *Pseudomonas aeruginosa* in 2, nutritional variants streptococcus in 1, methicillin-resistant *Staphylococcus aureus* in 1, and fungus [unidentified genus in 1991] in 1. The two most common pathogens were viridans streptococcus and *Staphylococcus aureus*. A similar mortality rate was found in patients with *Staphylococcal aureus* endocarditis and those with infective endocarditis caused by viridans streptococcus (23% vs. 31%, $p=0.747$).

All 58 patients received antimicrobial therapy for 1~42 days (mean 19 days). Initially, all patients were treated with one beta-lactam and an aminoglycoside. Eight (13.8%) patients received surgical valvular replacement due to medical treatment failure. Overall, 17 (29.3%) of the 58 patients died. The crude morbidity rate was 17/58 (29.3%). The major causes of mortality included neurological complications in 16 (27.6%) and cardiovascular complications in 24 (41.4%). The neurological complications included cerebral embolism (n=8), intracranial hemorrhage including subarachnoid hemorrhage (n=6), and meningitis (n=2). The cardiovascular complications included congestive heart failure (n=16), rupture of the chordae tendineae (n=5), myocardial infarction (n=1), perivalvular abscess (n=1), and cardiac arrhythmia (n=1). Cardiovascular complications (41.4%) were the most

common complications associated with infective endocarditis. Neurological complications (27.6%) were the most serious complications associated with infective endocarditis Neurological complications (OR=9.034, 95% CI=1.651-49.428, p=0.01) and heart complications (OR=7.920, 95% CI=1.487-42.177, p=0.02) were the most likely causes of mortality.

Table-1 Demography and risk factors in 58 infective endocarditis patients

	N	%
Sex		
Female	12	20.7
Male	46	79.3
Total	58	100
Risk factor		
Prior endocarditis	2	3.4
Rheumatic heart disease	13	22.4
Congenital heart disease	6	10.3
Drug abuse	7	12.1

Table-2 Echocardiographic findings in 58 infective endocarditis patients

	N	%
Echo Positive	49	84.5
Mitral Valve	31	53.4
Aortic Valve	10	17.2
Tricuspid Valve	7	12.1
Pulmonary Valve	1	1.7
Echo Negative	9	15.5
Total	58	100

Discussion

Estimates of the relative risks for infective endocarditis associated with various cardiac lesions. Rheumatic heart disease (22.4%) and congenital heart disease (10.3%) were the most common underlying diseases in this series. Patients who were intravenous drug users (12.1%) and patients who had prior endocarditis (3.4%) had increased. In this study, 51.7% (30/58) of patients had no identifiable cardiac lesions. The result is different from previous studies 9,10. In Mouldsdale's study 9, degenerative heart disease (22/93) was the most common underlying cardiac status in endocarditis. Mckinsey 11 described that the spectrum of recognized cardiac lesions underlying infective endocarditis has been changing as a result of the decline in incidence of

rheumatic heart disease, the recognition of the entity of mitral valve prolapse, and the improvement in cardiac diagnostic technique. In their study, only 31.0% of patients had either rheumatic heart disease or congenital heart disease. In contrast, 32.7% of patients in this study had either rheumatic heart disease or congenital heart disease, and 30 (51.7%) had no evidence of underlying cardiac lesions. Although techniques for the diagnosis of heart disease has improved, the high ratio (51.7%) of no identified cardiac lesion in our

study may have resulted from that some cardiac lesions may have been difficult to recognize in the early stages while others may have been overlooked due to degenerative change. We realized that the risk of infective endocarditis has increased both in patients with degenerative change of the cardiac valve and in patients with normal cardiac valves. Seven (12.1%) of the 58 patients in this series had a history of intravenous drug use. All 7 of those patients had right-sided infective endocarditis. *Staphylococcus aureus*

(n=5) and *Pseudomonas aeruginosa* (n=1) were the most common pathogens among those patients with a history of intravenous drug use. The other one patient had culture-negative endocarditis. Three (42.9%) of these 7 patients died.

Fever was present initially in 50 (86.2%) patients. Change in the status of cardiac murmur was noted initially in 19 patients (32.8%), and peripheral embolism phenomena were initially found in 11 patients (19.0%). It is very likely that the ratio of patients with both changing cardiac murmur and peripheral embolism phenomena were underestimated in this study due to the lack of detailed physical examination data for every new patient. Such detailed exams need to be performed to improve diagnostic rates. Vegetation over the cardiac valve was noted on echocardiography in 49 (84.51%) of 58 patients, and 9 (15.5%) of 58 patients showed no vegetation. With improvement in the resolution of echocardiography, its use has become increasingly important for early diagnosis.

In the present study, pathogens of infective endocarditis were identified by blood culture in 55 of 58 patients. Overall, the two leading pathogens were viridans streptococcus and *S. aureus*. The ratio of culture-negative infective endocarditis was 5.2%. The possible reasons for culture negative findings include previous antibiotic usage, incorrect specimen collection, and failure to identify organisms from the HACEK (*H. parainfluenzae*, *H. aphrophilus*, *Actinobacillus* sp., *Cardiobacterium* sp., *Eikenella* sp., *Kingella* sp.) group. Viridans streptococcus was still the most important causative pathogen. This finding is different from some previous reports¹² which found that *S. aureus* was the most important pathogen. *S. aureus* was the second most common pathogen responsible for infective endocarditis. The Karchmer's study¹² found that *S. aureus* infective endocarditis had a higher mortality rate than

streptococcus infective endocarditis. However, no significant difference in mortality between *S. aureus* infective endocarditis and streptococcus infective endocarditis was found in the present study. *P. aeruginosa* comprised two (4%) of the 55 pathogens isolated and one (50%) of the two patients died. The ratio of Gram negative pathogens was higher in the present study than Pelletier's series (4/112) 10. Culture negative endocarditis was found in 3 (5.2%) of 58 patients, which is similar to Pelletier's series. However, the rate of microbiological diagnosis is obtained might have been decreased in this study due to antimicrobial treatment before blood culture, incorrect specimen collection, and HACEK group organisms. The complications associated with infective endocarditis are variable and difficult to predict. Infective endocarditis has catastrophic complications in some patients with severe infection. The overall crude mortality rate in this study was 29.3% (17/58). That is similar previous study 13. Neurological complications (27.6%, OR=9.034, 95% CI=1.651-49.428, p=0.01) and heart complications (41.4%, OR=7.920, 95% CI= 1.487-42.177, p=0.02) were the leading two causes of mortality. In Chao's study, in-hospital mortality was associated with noncardiac shock, neurological complications, cardiac complications, and older age 14. However, to reduce the associated complications as far as possible is the most critical point in improving the survival rate.

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彰化基督教醫院 1989 到 1999 年間 感染性心內膜炎回顧性分析

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摘 要

本研究主要是描述感染性心內膜炎的臨床與微生物學的特徵。分析自 1989 年 1 月 1 日到 1998 年 9 月 30 日止的感染性心內膜炎個案。共 58 例，男女比例為 3.8，平均年紀分別為 40.6 歲。28 例找到。40 例 (69.0%) 發生併發症，16 例 (27.6%) 是神經系統併發症，24 例 (41.4%) 是心臟血管系統併發症。全部有 8 例 (13.8%) 接受外科手術。19 例死亡。死亡率是 29.3%。死亡與神經系統併發症 (OR=9.034, 95% CI= 1.651-49.428, p=0.01) 及心臟血管系統併發症危

險因素，其中風濕性心臟病 13 例、先天性心臟病 6 例，此外有 7 例是藥物濫用。30 例 (51.7%) 沒有明顯的危險因素。15 例 (86.2%) 病患有發燒、19 例 (32.8%) 有新的心臟雜音、11 例 (19.0%) 有周邊血管貯塞現象。10 例 (17.2%) 是右側感染性心內膜炎。最常見的致病菌是草綠色鏈球菌 (*viridans streptococcus*) (32/55) 與金黃色葡萄球菌 (*Staphylococcus aureus*) (12/55)。40 例 (69.0%) 發生併發症，16 例 (27.6%) 是神經系統併發症，24 例 (41.4%) 是心臟血管系統併發症。全部有 8 例 (13.8%) 接受外科手術。19 例死亡。死亡率是 29.3%。死亡與神經系統併發症 (OR=9.034, 95% CI= 1.651-49.428, p=0.01) 及心臟血管系統併發症 (OR=7.920, 95% CI= 1.487-42.177, p=0.02) 最有關係。