ORIGINAL ARTICLE

Infective endocarditis in children without underlying heart disease

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Background/Purpose: Although pre-existing heart disease is the main predisposing factor for pediatric infective endocarditis (IE), cases of IE in children without underlying heart disease have been increasingly reported. This study reviews the clinical and laboratory characteristics of pediatric IE patients with and without underlying heart disease, and presents the unique features of patients with no apparent pre-existing heart disease.
Methods: Children who were admitted to our hospital from January 1991 to April 2011 and met the Modified Duke criteria for definite or possible IE were retrospectively analyzed. Clinical characteristics and laboratory data were collected by chart review.
Results: Forty-seven patients with a total of 48 episodes of IE were enrolled. Of these patients, 31 children (64.6%) had congenital heart disease (CHD), six (12.5%) had non-CHD chronic disease, and eleven (22.9%) were previously healthy adolescents. Five patients with non-CHD chronic conditions acquired infection from central catheter: two methicillin-resistant *Staphylococcus aureus* (MRSA), two *Candida albicans* and one coagulase-negative *Staphylococcus* (CoNS). The microbial pathogens in 11 previously healthy individuals were *Streptococcus viridans* ($n = 3$), methicillin-sensitive *S. aureus* (MSSA, $n = 2$), *Haemophilus parainfluenzae* ($n = 2$), *Staphylococcus lugdunensis* ($n = 1$), *Enterococcus* ($n = 1$), and Diphtheroid ($n = 1$). In total, five of 17 non-CHD patients were infected with *S. aureus* (two MRSA and three MSSA) and the vegetations in these five patients were detected in the right side of the heart (tricuspid valve or right atrium). The average interval between onset of symptoms and diagnosis of IE in the CHD and previously healthy groups was 18 and 31 days, respectively. Patients in the previously healthy group were older and more often required surgical interventions for removal of vegetation.

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Conclusion: Over one-third (35.4%) of cases of IE in children occurred in patients without pre-existing cardiac disease. Early identification of these patients is critical and requires a high index of suspicion. The pathogenesis of IE in previously healthy individuals is still uncertain, but previous skin infection or dental problems may contribute to potential risk.

Introduction

The risk factors for infective endocarditis (IE) include cardiac valvular abnormalities, rheumatic heart disease, prosthetic valves, prior history of endocarditis, and healthcare-associated bacteremia. Endocarditis is uncommon in individuals with healthy hearts. Although IE occurs less commonly in children than in adults, the incidence of IE in children appears to have increased in recent years, especially among those with predisposing risk factors.[1–5]

Recent reports have shown a continuing shift in the epidemiology of pediatric IE toward a higher proportion of children without pre-existing heart disease. Such a shift is mostly related to the growing numbers of premature infants and chronically ill children requiring indwelling central venous catheters (CVCs) for the management of their illness.[3–5] Many studies including those reported from Taiwan[6–10] have increased our understanding of IE in children; however, information concerning patients without underlying heart disease is limited.[11,12] This paper presents the demographic, diagnostic, clinical, and microbiological features of IE in children with and without underlying heart disease, and offers further information on IE in previously healthy individuals.

Patients and methods

Patient selection

This retrospective, descriptive study was performed in Kaohsiung Veterans General Hospital (KVGH), a tertiary referral hospital in Southern Taiwan. All consecutive pediatric patients (age ≤18 years) with a diagnosis of definite or possible IE in KVGH from January 1991 to April 2011 were enrolled in the study. Patients were identified from our hospital database using discharge diagnosis codes. Data were collected from the patients' medical, laboratory, and imaging records. All interventions and echocardiography were performed by the same medical team.

The Modified Duke criteria, which are used to evaluate our patients, involve two major criteria: (1) the presence of at least two positive blood cultures with typical organisms consistent with IE, and (2) evidence of endocardial involvement, primarily diagnosed using echocardiography; and several minor criteria such as predisposing cardiac condition or injection drug abuse, fever >38°C, vascular phenomena (arterial embolism, septic pulmonary infarction, intracranial hemorrhage, Janeway lesions) or immunologic phenomena (Osler nodes, Roth spots, glomerulonephritis), and serological evidence of organisms consistent with IE. To be enrolled in this study as definite IE, patients had to meet one of the following criteria: (1) the major two criteria; (2) one major and three minor criteria; (3) five minor criteria; or (4) histopathologic evidence obtained surgically. Patients were enrolled as possible IE if fulfilling one major and one minor criterion.

Data collection

The following data were recorded: age, gender, underlying diseases (including pre-existing cardiac disease or noncardiac disease), intravenous (IV) insertion or parenteral antibiotic usage within 8 weeks before the onset of endocarditis, previous cardiac procedures (surgery or catheterization within 8 weeks prior admission), IV drug addiction, dental condition and interventions, presence of an indwelling CVC at the time of diagnosis of IE, length of hospitalization, clinical, laboratory and microbiological data, vegetation location, complications of IE (defined as embolic phenomena, heart failure, other organs failure), treatment (included antibiotics and surgical intervention), and outcome. Echocardiography and other imaging reports were also collected. Microbiological data included blood and intraoperative specimen cultures.

Definitions

Patients were categorized into congenital heart disease (CHD) group (patients with pre-existing heart disease) and non-CHD group. The non-CHD group consisted of two subgroups: patients having underlying chronic conditions other than CHD, and previously healthy individuals. CHD was defined as "valvular" when defect involved only valves; as "simple" when a single defect not in a valve was found, including mainly ventricular or atrial septal defect, aortic or pulmonary stenosis and coarctation of the aorta; or as "complex" when more than a single defect was found, mainly including tetralogy of Fallot, transposition of the great vessels, total anomalous pulmonary venous return, and double outlet of right ventricle, with other multiple defects. An infection was defined as healthcare-associated infective endocarditis (HAIE) when it occurred more than 48 hours after admission or within 8 weeks after cardiac surgery or catheterization. All children who did not meet the criteria for HAIE were classified as community-acquired infective endocarditis (CAIE). Predisposing risk factors for IE were defined as having underlying diseases (included pre-existing cardiac disease or non-cardiac conditions), previous cardiac procedures (surgery or catheterization) within 8 weeks prior admission, indwelling CVC, or IV drug abuser. Dental problems and interventions, and skin

wounds or infectious episodes were particularly recorded to evaluate if they could be associated with predisposing risk factors for IE in non-CHD patients.

Statistical analysis

Data analysis was performed using SPSS version 17.0 for Windows. Categorical variables were compared using Pearson Chi-square (χ^2) test or Fisher's exact test in univariate analysis. A two-tailed p-value <0.05 was considered statistically significant.

Results

Patient characteristics and diagnostic features

During the study period, 48 episodes of IE were observed in 47 patients, including one premature infant who had IE twice at 2.7 years interval. The majority (31/48, 64.6%) of our patients had CHD. Six patients (12.5%) had non-CHD underlying chronic conditions, and 11 (22.9%) were previously healthy (Table 1). There was a male preponderance with male to female ratio of 2:1.

Fig. 1 depicts age distribution in patients with different underlying conditions. The mean age for all patients was 9.2 years (range 3 days to 18.7 years). Cases of IE occurred throughout the age spectrum in patients with congenital heart conditions, especially those aged <4 years. In contrast, IE cases in previously healthy children were seen primarily in patients and aged >14 years. There was no obvious age disparity observed among the few patients with underlying chronic illnesses.

Based on the Modified Duke criteria, 34 patients (70.8%) fulfilled the diagnosis of definite IE, and 14 (29.2%) possible IE. Whereas all 11 patients who were previously healthy met the definite IE criteria, only 19 of 31 (61%) children with CHD met such criteria (Table 2). Blood cultures were positive in 45 of 48 episodes (93.8 %) and only three patients (6.2%) had negative blood cultures. The three culture-negative patients, two with CHD and one previously healthy, were diagnosed as definite IE by the following criteria: two patients had positive echocardiographic findings plus three minor criteria, and one patient was proven by positive histopathological findings.

Thirty-two (66.7%) patients had documented vegetations via transthoracic or transesophageal echocardiography. Vegetations could not be determined by echocardiography in 16 (33.3%) events; among these, 14 (87.5%) patients were with CHD ($p = 0.026$). Children with a structurally normal heart or with isolated valvular defects were more likely to have detectable vegetations in echocardiography (Fig. 2).

Clinical characteristics of IE patients with and without congenital heart disease

The comparative clinical characteristics of patients with CHD and non-CHD are shown in Table 2. Overall, the differences between the two groups are limited. However, when comparing the patients in the CHD and the previously healthy groups, there were significant differences in

Table 1 Underlying conditions among 47 patients (48 episodes) of infective endocarditis admitted to Kaohsiung Veterans General Hospital from January 1991 to April 2011

Underlying condition	Number of episodes
Congenital heart disease (CHD)	31
Valvular	4
MVP	3[b]
Valvular AS	1
Simple	15
VSD (unrepaired/repaired)	12 (9/3)
ASD	1
CoA	1
Coronary AV fistula	1
Complex	12
TOF	5
DORV with other defect	3
TGA	2
TAPVR	1
TA	1
Without-congenital heart disease	17
Chronic disease	6
Prematurity[a]	1
H-F-M disease in vegetative state	1
Acute lymphoblastic leukemia	1
Corrosive injury with malnutrition	1
Hodgkin's lymphoma	1
Intravenous drug abuser	1
Previously healthy	11

[a] The premature infant had two episodes of IE. The first episode was associated with central catheter line infection and resulted in a complication of mitral valve prolapse; the second episode occurred 2 years later, but is not listed here.
[b] One of the three episodes was contributed by the premature infant with MVP.
AS = aortic stenosis; ASD = atrial septal defect; CoA = aortic coarctation; DORV = double outlet right ventricle; H-F-M disease = hand-foot-mouth disease; MVP = mitral valve prolapse; TA = truncus arteriosus; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries; TOF = Tetralogy of Fallot; VSD = ventricular septal defect.

Figure 1. Age distribution in three groups of patients with different underlying conditions.

Table 2 Characteristics of infective endocarditis (IE) patients with and without congenital heart disease (CHD)

Characteristics	CHD, $n = 31$	Non-CHD, $n = 17$		$p*$
		Chronic disease, $n = 6$	Previously healthy, $n = 11$	
Diagnostic				
Definite/possible IE	19/12	4/2	11/0	0.095[a]
Positive/negative blood culture	29/2	6/0	10/1	1.000
Presence of vegetations	17	4	11	0.026[b]
Clinical				
Age (y): mean $\pm$ SD (range)	6.8 $\pm$ 5.2 (0-18)	6.9 $\pm$ 8.9 (0-18)	17.3 $\pm$ 6.8 (14-18)	0.002[c]
Illness prior to diagnosis (days)	18 $\pm$ 22	10 $\pm$ 8	31 $\pm$ 22	0.390
Fever over 2 weeks (n)	12	1	8	0.342
Embolic events (n)	5	2	4	0.131
CRP (mg/dl): mean $\pm$ SD (range)	9.1 $\pm$ 8.2 (0.8-30.6)	16.6 $\pm$ 16.2 (1.0-37.6)	16.4 $\pm$ 8.5 (4.9-28.5)	0.077
Hb: mean $\pm$ SD (range)	11.4 $\pm$ 2.7 (6.4-18.4)	10.5 $\pm$ 3.1 (5.7-15.3)	9.2 $\pm$ 1.6 (6.6-11.6)	0.023
History of dental problems (n)	7	0	2	0.460
History of infected skin/soft tissues (n)	0	0	3	0.005
Surgical intervention (n)	9	0	8	0.212[d]
Fatality during hospitalization (n)	6	1	0	0.396

CRP = C-reactive protein; Hb = hemoglobin; SD = standard deviation.
*p value is between CHD vs. non-CHD, $p < 0.05$ is significant. Significant p value between CHD vs. healthy group included:
[a] $p = 0.018$.
[b] $p = 0.007$.
[c] $p < 0.001$.
[d] $p = 0.029$.

several respects. The average duration between onset of symptoms and diagnosis of IE in CHD patients and healthy group was 18 and 31 days, respectively. The previously healthy patients were older (age 17 vs. 6.8 years) and more often required surgical interventions (73% vs. 29%). Overall,

Figure 2. Cardiac anatomy correlated with echocardiographic findings. [a]The number under each bar represents numbers of patients for each heart condition, and the fraction indicates patients with/without vegetation; [b]valvular defect: defect involved only valve; [c]simple defect: a single defect not of the valve.

the most common presenting symptom was fever (39/48, 81.3%). Over half (54%) of all febrile patients had prolonged fever (>2 weeks) prior to the diagnosis. Prolonged fever occurred in 73% of patients who were previously healthy. Other nonspecific symptoms included respiratory illnesses (cough, hemoptysis, chest pain), gastrointestinal discomfort, CNS symptoms (headache, consciousness disturbance), malaise, body weight loss, and myalgia.

Eleven (22.9%) patients experienced systemic (including brain, lung, kidney, or conjunctiva) embolism, and it occurred twice more often in non-CHD than in CHD patients, although this was not statistically significant. Fifty-three percent (9/17) of non-CHD patients had "new" murmurs at the time of diagnosis. The classic signs of IE, such as Osler nodes, Janeway lesions, and Roth spots were noted in only 2 (4.2%) of our patients.

Clinical characteristics and infections in 17 patients without CHD are summarized in Table 3. Possible risk factors for IE were identified in 5 of 11 (45%) patients, including three with skin and soft tissue infections and two with dental problems. Medical history revealed that one child suffered cellulitis on the left thigh one week earlier and received oral cephalexin therapy; two patients had wound infections from skin abrasions in automobile accidents one month previously and did not receive any antibiotics. Of the two children with dental caries, one underwent dental extraction two months prior to becoming ill with IE.

Four of the 5 patients infected with *S. aureus* in the non-CHD group had vegetations in the right heart (including tricuspid valve or right atrium); one patient with *Candida albicans* IE had bilateral vegetations (left ventricle and

Table 3 Clinical summary of 17 patients with infective endocarditis without underlying heart disease

Patient	Gender	Age	Underlying condition	Initial presentation	Past history[a]				Acquisition of infection	Side of IE	Blood culture	Diagnostic IE criteria
					D	T	C	A				
1	M	3m	Prematurity (GA 30 weeks)	Fever and heart murmur			CVC	(+)	HAIE	L	*Candida albicans*	Definite
2	M	7m	Hand-foot-mouth disease in vegetative state	Fever and conscious drowsy			CVC	(+)	HAIE	N	CoNS	Possible
3	M	1y3m	Leukemia	Neutropenic fever			Port-A		HAIE	R	MRSA	Definite
4	M	2y5m	Corrosive injury	SOB, diarrhea			CVC	(+)	HAIE	N	MRSA	Possible
5	F	17y11m	Hodgkin's lymphoma	Neutropenic fever			Port-A	(+)	HAIE	R,L	*Candida albicans*	Definite
6	M	18y10m	IV drug abuser	Fever, SOB, hemoptysis					CAIE	R	MSSA	Definite
7	M	14y9m	Healthy	Fever and left thigh pain		Cellulitis one week ago		(+)	CAIE	R	MSSA	Definite
8	F	15y4m	Healthy	Fever, abdominal pain		Skin abrasion one month ago			CAIE	L	*S. lugdunensis*	Definite
9	M	16y4m	Healthy	Fever, malaise					CAIE	L	Enterococcus	Definite
10	M	16y5m	Healthy	SOB, chest pain, headache					CAIE	L	Diphtheroid	Definite
11	F	17y11m	Healthy	Fever	(+)				CAIE	L	*H. parainfluenzae*	Definite
12	M	17y11m	Healthy	Fever, conscious change	(+)				CAIE	L	*H. parainfluenzae*	Definite
13	F	17y11m	Healthy	Fever, SOB, headache					CAIE	L	Viridans streptotoccus	Definite
14	M	18y1m	Healthy	Fever, SOB, hypotension					CAIE	L	negative	Definite
15	M	18y2m	Healthy	Fever, SOB, headache					CAIE	L	Viridans streptotoccus	Definite
16	M	18y6m	Healthy	Fever, SOB		Skin abrasion one weeks ago			CAIE	R	MSSA	Definite
17	M	18y6m	healthy	Fever, SOB, chest tightness					CAIE	L	Viridans streptotoccus	Definite

CAIE = community associated infective endocarditis; CoNS = coagulase negative *Staphylococcus*; CVC = central venous catheter; HAIE = hospital associated infective endocarditis; L = left side vegetation; MRSA = methicillin resistant *Staphylococcus aureus*; MSSA = methicillin sensitive *Staphylococcus aureus*; N = no vegetation; R = right side vegetation; SOB = shortness of breath.

[a] Within two months prior to admission: dental problem or intervention (D), external trauma or skin infection history (T), usage of central catheter (C), prescription of antibiotic before IE episode (A).

superior *vena cava—right atrium* junction) as well as septic emboli in the brain. Vegetations in other non-CHD patients were discovered in the left side of the hearts (including mitral valve, aortic valve, or both).

Microbial pathogens

Microbial pathogens isolated from blood cultures are shown in Table 4. The most common bacterial isolates were S*treptococcus viridans* (33%) and *S. aureus* (27%). Together they accounted for 60.4% (29/48) of all blood culture isolates. Of the 16 *Streptococcus viridans*, 13 (81%) were from patients with CHD and 3 (19%) from non-CHD patients. Among 13 *S. aureus* isolates, 8 were from CHD and 5 from non-CHD patients. MRSA and MSSA were evenly distributed among patients with CHD and non-CHD. All *Candida albicans* were from patients with CHD ($n = 3$) and chronic conditions ($n = 2$) associated with HAIE, and none in the healthy group. Other causative pathogens in patients with CHD included *Enterococci* ($n = 2$), coagulase-negative *Staphylococci* (CoNS, $n = 1$), *Klebsiella pneumoniae* ($n = 1$), and *Pseudomonas aeruginosa* ($n = 1$).

Various pathogens were isolated from 9 patients with dental conditions, these included five viridians group streptococci, one each of MSSA and *Candida albicans* in the CHD group, and two β-lactamase negative *H. parainfluenzae* in previously healthy patients.

Management and outcome

Antimicrobials were administrated to all patients. The mean duration of parenteral antibiotic administration was 41 days (range 14—60 days). In addition, 17 patients also underwent surgical interventions. The need for surgical interventions varied greatly among the groups: it was highest in previously healthy patients (8/11, 72.7%), followed by CHD (9/31, 29%) and non-CHD with chronic conditions (0%). All 8 patients who had surgical interventions in the previously healthy group underwent valve replacement. The indications for surgery included large vegetation (>10 mm) or abscess, destructive lesion of the valve (perforation, chordae rupture, fistula), severe aortic

or mitral regurgitation with heart failure. In the CHD group, only 3 underwent valve replacement, and the other 6 had surgery for vegetectomy and repair of CHD. Seven (14.6%) patients died during hospitalization: six in the CHD group and one in the non-CHD group. The only patient who died in the non-CHD group was a 7-month-old infant who had a severe hand-foot-mouth disease with rhombencephalitis in a vegetative state. He died of CoNS sepsis and multiple organ failure probably resulting from healthcare-associated infection. Pathogens isolated in these seven fatal cases were the usual pathogens including viridians group *streptococci* ($n = 3$), CoNS ($n = 2$), MRSA ($n = 1$), and *Candida albicans* ($n = 1$).

Discussion

The diagnostic criteria and epidemiologic features of infective endocarditis have continued to evolve in recent years. The Duke criteria, introduced in 1994, have been widely used as a sensitive tool for the clinical diagnosis of IE. However, some uncertainty remains and modifications of the Duke criteria have emerged.[13] In our series, 71% of our patients met the Modified Duke criteria as definite IE and 29% possible IE. This is comparable to 34% (37/109) of possible IE previously reported in Taiwan.[6]

In recent decades, IE in children has had significant demographic and epidemiological changes: a decreasing incidence of rheumatic heart disease, an increasing number of children without pre-existing heart disease, and the ever-changing infecting pathogens.[2,3,5] In an earlier study from Taiwan,[7] 11% of the IE children were found to have rheumatic heart disase. In contrast, our current series along with another report[8] found no cases of underlying rheumatic heart disease. Recent observations on pediatric IE indicated that approximately 12% to 26% of the cases were patients without pre-existing heart disease,[2,3,8] and most of these patients were premature neonate or chronically ill who acquired IE from indwelling central catheters. During our 20-year study period, we found that over one-third (35.4%) of our IE cases were patients without pre-existing heart disease. We had only one premature infant with the diagnosis of IE in the first

Table 4 Microbial pathogens isolated from blood cultures in infective endocarditis patents with and without congenital heart disease (CHD)

Pathogens	CHD, $n = 31$	Non-CHD, $n = 17$	
		Chronic disease, $n = 6$	Healthy, $n = 11$
Streptococcus viridans	13	0	3
Staphylococcus aureus	8	3	2
Candida albicans	3	2	0
Enterococci	2	0	1
CoNS	1	1	1
Haemophilus parainfluenzae	0	0	2
Klebsiella pneumoniae	1	0	0
Pseudomonas aeruginosa	1	0	0
Diphtheroid	0	0	1
Negative	2	0	1

CoNS = coagulase-negative staphylococci.

decade, and four patients with other chronic underlying conditions had IE in the second decade. All five patients acquired IE from the indwelling central catheters (MRSA, Candida, CoNS). In our series, the number of IE cases related to prematurity and chronic underlying conditions was smaller when compared with some other reports. A possible explanation for this difference might be related to the selective referral of patients to the medical centers, namely expertise of the medical staff and facility of the hospitals (such as neonatal ICU, oncology—hematology center). Our hospital, which lacks a large neonatal ICU and pediatric oncology unit, has been known as one of the referral centers for the care of cardiac diseases , including congenital heart disease and infective endocarditis.

It was unexpected that 11 (22.9%) previously healthy adolescents would become IE victims. They were evenly distributed in the first and second decades, with five and six patients respectively. Literature information on IE in previously healthy children is relatively sparse, and the pathogenesis and underlying risk factors remain largely unknown. In a recent study, Marom et al[14] reported nine (18%) IE patients who were previously healthy. In a cohort of randomly selected healthy junior high school children, by echocardiography and Doppler studies, Steinberger et al[15] found that 3.6% (13/357) had asymptomatic but significant cardiac abnormalities. In a most recent study, Castillo et al[16] also described an increased proportion of cases (from 25% to 67%) without predisposing heart disease, and a high percentage (79%) of patients who were unaware of their predisposing heart condition. It remains to be determined whether some of these apparently healthy adolescents with asymptomatic and undetected cardiac abnormalities pose an increased risk for IE. Among our 11 previously healthy children (all met the Modified Duke criteria) five (45%) had potential risk factors for IE, including three with history of infected skin/soft tissue and two with dental health conditions. Blood cultures were positive from all five patients: two S. aureus and one S. lugdunensis from children with skin and soft tissues infections, and H. parainfluenzae from both children with dental problems.

H. parainfluenzae, one of the oral and upper respiratory tract flora, is part of HACEK group (Haemophilus spp., Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae) of Gram-negative bacteria that are responsible for a small percentage of endocarditis cases. Risk factors for developing H. parainfluenzae endocarditis include dental work, cleaning of teeth, nasopharyngeal infection, tongue piercing, and the use of tongue scrapers.[17—20] H. parainfluenzae is the most common (31%) pathogen in HACEK endocarditis in pediatrics,[21] and more than half (7/13) of cases were without prior cardiac abnormality; the age of patients was distributed mainly in the late teenage years. Among all age groups, the average age of patients with H. parainfluenzae endocarditis was 27 years,[22] and over 60% of the patients had no identible predisposing illness. Strom et al[23] conducted a large-scale, case-control study to identify the risk factors for IE and also reported that cases infected with dental flora were more likely to have teeth than not, and to have poorer dental hygiene.

Earlier studies indicated that S. aureus bacteremia was considered to be at low risk (about 2—13%) to develop into S. aureus endocarditis.[24—26] However, S. aureus is now one of the most common pathogens of IE in the developed world,[27,28] and the proportion of IE due to S. aureus seems to be increasing in both community-acquired and healthcare-associated modalities.[23—28] From these reports, CAIE were often associated with skin infection or pneumonia,[27,28] whereas HAIE with intravascular devices. In these studies, S. aureus bacteremia or endocarditis often occurred in the elderly and in patients with chronic underlying disease (such as chronic lung disease, hemodialysis, diabetes mellitus) or with long periods of intravascular device. Others have also described that community-associated MRSA (CA-MRSA) has became an emerging pathogen in IE.[28] Furthermore, MSSA native IE and CA-MRSA native IE have been associated with young healhy individuals,[28] and a large proportion of cases have had documented history of skin lesions or IV drug use. Our findings support the observations of others that our five patients in the non-CHD group had infection with S. aureus: two MRSA with HAIE and three MSSA were community associated (one IV drug abuser and two skin infection); and four of them had vegetations in the tricuspid valve or right atrium (vegetation was undetectable in one patient).

Our echocardiographic studies indicated that vegetations were more common in patients who were previously healthy than those with underlying cyanotic complex heart disease. It is likely that a low index of suspicion and a delay in diagnosis (31 days of illness) of IE among previously healthy patients might have contributed to a higher proportion of patients with vegetations. Diagnosis of IE in a previously healthy child, although rare, remains a challenge to clinicians. Nevertheless, prolonged fever, anemia, and heart murmur in a previously healthy child, with or without history of skin infection or oral health problem, should raise the index of suspicion and deserve an IE work-up.

Prevention of IE has continued to be problematic and challenging. The newest guidelines from AHA (American Heart Association, 2007, USA)[29] and NICE (National Institute for Health and Clinical Excellence, 2008, UK)[30] have suggested that the IE prophylaxis should be restricted to those with underlying cardiac conditions associated with the highest risk of acquisition of IE or of adverse outcome from IE, such as patients with a prosthetic cardiac valve, previous or relapsing IE episodes, and some types of CHD. Improving dental health and maintaining good habits of dental hygiene are more crucial to reduce transient bacteremia, which is one of the factors for IE.

As in other retrospective studies, there are several limitations in our report. Although we were able to identify IE in previously healthy adolescents, but few data were available to help understand the pathogensis. In addition, the information on risk factors was not fully assessed in each patient. Our data on clinical course and follow-up (such as duration of becoming afebrile, clearance of pathogens in blood culture, or vegetation become undetectable after prescription of antibiotic) were not complete. Our diagnostic blood cultures were obtained on the day of admission (or of raised suspicion of IE for long-term hospitalized patients), prior to administration of antibiotics;

however, the precise timing between two sets of blood sampling was not recorded. In spite of these limitations, we have added useful information on IE in children without underlying heart condition, and provided new information on this serious infection in previously healthy adolescents. Our report also suggests the need for further studies on the pathogenesis and prevention of IE in previously healthy individuals.

Acknowledgments

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