Pediatric bacterial endocarditis

Long-term follow-up[1]

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The authors studied 18 cases of endocarditis. Thirteen of the patients (72%) had underlying congenital heart disease and 5 (28%) had rheumatic heart disease. Fifteen patients had positive blood cultures, most commonly caused by *Streptococcus viridans*, *Staphylococcus aureus*, and *Streptococcus mitis*. At diagnosis, 11 patients (group A) were in functional class I and 7 (group B) were in functional class II, based on the criteria of the New York Heart Association. Medical therapy alone was instituted in 11 (60%). Seventeen patients were followed up for one month to 27 years. All 11 patients in group A were still in class I. Three of the 7 patients in group B were still in class II, although 1 had been rehospitalized for recurrent endocarditis. Due to the uncorrected congenital lesion, 1 group B patient was categorized in functional class III at follow-up. Three patients in group B died of complications from endocarditis (2 within the year of initial diagnosis), and 1 was lost to follow-up. With medical and surgical treatment, most pediatric patients with endocarditis remain hemodynamically stable at long-term follow-up. The functional class prior to treatment appears to be predictive of long-term functional status.

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Children with congenital and rheumatic heart disease have an increased risk of life-threatening infective endocarditis. Blumenthal et al[1] reported 58 cases of infective endocarditis from 1930 through 1960, including 41 patients with congenital heart disease. Several other studies have mentioned this same association.[2–6] Before antibiotics, mortality from infective endocarditis was 100%.[1,3] Since then, early detection and appropriate antibiotic therapy

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Table 1. Incidence of heart lesions in patients with congenital heart disease

Lesion	No. of Cases
Bicuspid aortic valve	4 (30%)
Tetralogy of Fallot	2 (15%)
Ventricular septal defect with pulmonary stenosis	2 (15%)
Mitral regurgitation	2 (15%)
Isolated ventricular septal defect	1 (8%)
Ventricular septal defect with bicuspid aortic valve and coarctation of the aorta	1 (8%)
Subvalvular aortic stenosis and coarctation of the aorta	1 (8%)

Table 2. Symptoms

Symptoms	No. of Cases
Prolonged fever	16 (89%)
Malaise	15 (83%)
Splenomegaly	9 (50%)
Polyarthritis	6 (33%)
Petechiae	6 (33%)
Janeway lesions	4 (22%)
Roth spots	2 (11%)

Table 3. Laboratory findings

Laboratory Findings	No. of Cases
Borderline anemia (hemoglobin <11.0)	8 (44%)
Elevated sedimentation rate	3 (17%)
Pyuria	2 (11%)
Leukocytosis (>12,000)	1 (5.6%)
Hematuria	1 (5.6%)

have improved survival to 76% at the time of hospital discharge.[3]

No clinical studies to date report the long-term follow-up of children treated medically (with or without surgery) for infective endocarditis. Johnson and Rhodes[6] followed up only 18 of their 50 patients for one year. We present our findings involving 18 pediatric patients with infective endocarditis who underwent long-term follow-up and consider prognostic factors present at the initial examination.

Materials and methods

Eighteen patients, ranging in age from 6 months to 20 years (mean, 13 years), were seen at the Cleveland Clinic from 1956 to 1983. A diagnosis of infective endocarditis was confirmed by positive blood cultures or classic symptoms in the appropriate clinical setting. Chart analysis and follow-up questionnaires were the primary means of obtaining information on diagnosis, therapy, and response.

Chart analysis

The chart on each patient was obtained from central files and specifically analyzed for demographic variables such as age, sex, and ethnic background. There were 11 males and 7 females; 16 (89%) were white. The underlying or preexisting cardiac disease was assessed and recorded in all cases (*Table 1*). Thirteen of our patients (72%) had congenital heart disease; a bicuspid aortic valve was the most common abnormality. For 10 patients, catheterization data led to the diagnosis of congenital heart disease. Rheumatic heart disease was present in 5 patients (28%), involving the mitral valve in two cases and the aortic valve in three cases. Only 1 patient was documented to have undergone dental work within three months of presenting with endocarditis. One patient had severe dental disease, but no associated dental procedure. Endocarditis was found to have involved natural valves or endocardium in all but a 12-year-old boy, who had a right-ventricle-to-pulmonary-artery conduit. No patients contracted endocarditis immediately following cardiac surgery.

The most common clinical manifestations were prolonged fever, malaise, splenomegaly, and migratory arthralgias (*Table 2*). The laboratory findings were nonspecific (*Table 3*). Borderline anemia was the most common abnormality.

The initial electrocardiogram was obtained in 72% and was abnormal in all. A prolonged PR interval was seen in 2 patients. No patient, however, demonstrated complete heart block. A right bundle branch block was seen in 2 patients, and left ventricular hypertrophy was seen in 6 (33%).

Chest radiographs of all patients were obtained and revealed cardiomegaly in 8 (44%) and an infiltrate in 1. Three of six echocardiograms obtained on admission revealed abnormalities. Two patients had aortic valve dysfunction with vegetations. One patient had fluttering of the anterior leaflet of the mitral valve suggestive of aortic regurgitation.

Bacteriology

Blood cultures were obtained in all patients on admission for suspected endocarditis or unex-

plained fever and constitutional symptoms. Fifteen patients (83%) had positive blood cultures. Seven different organisms were recovered (*Table 4*). Three patients had negative cultures, but had classic clinical stigmata of endocarditis, including prolonged fever, malaise, a new heart murmur, and in 1 patient, Janeway lesions and splenomegaly. Two of these 3 patients received antibiotics prior to their admission and the acquisition of blood cultures. *Pseudomonas aeruginosa* was cultured from 1 patient who later died of complications during a recurrent episode of endocarditis. His initial episode was due to *Streptococcus viridans.*

After their initial hospitalization and therapy, all patients were discharged with instructions for appropriate antibiotic prophylaxis and follow-up. Of the 18 patients admitted, 17 (94%) survived their initial hospitalization.

Cardiac status

Functional cardiac status at diagnosis, discharge, and long-term follow-up was determined for each patient, excluding those patients who died during their initial hospitalization or within one year of discharge. Cardiac status was determined by a critical review of symptoms and by criteria based on New York Heart Association (NYHA) standards. Patients were further assigned to groups based on their NYHA class at diagnosis, and subsequent comparisons of outcomes were based on these groups. Group A consisted of patients who, at initial diagnosis of endocarditis, were NYHA class I. Group B consisted of patients who, at diagnosis, were NYHA class II. There were 11 patients (6 males and 5 females) in group A, and 7 patients (5 males and 2 females) in group B.

Cases were followed up for one to 27 years (mean, 10 years), with ages at follow-up ranging from 11 to 39 years (mean, 23 years). One case involving a child with *Staphylococcus aureus* endocarditis of the aortic valve and subsequent aortic valve replacement for insufficiency was lost to follow-up.

Therapy

Medical therapy alone was given at diagnosis to 64% of group A patients and 57% of group B patients (total, 7 patients [39%]). Medical and surgical therapy was received by 36% of group A and 43% of group B patients (*Table 5*).

Table 4. Bacteriological findings

Bacteriological Findings	No. of Cases
Streptococcus viridans	5 (27%)
Staphylococcus aureus	5 (27%)
Culture-negative	3 (17%)
Streptococcus mitis	2 (11%)
Streptococcus bovis	1 (5.6%)
Erysipelothrix insidiosa	1 (5.6%)
Candida albicans	1 (5.6%)

Table 5. Antibiotic therapy

Antibiotic Therapy	No. of Cases
Penicillin alone	6 (33%)
Penicillin and streptomycin	5 (27%)
Erythromycin	2 (11%)
Penicillin and chloramphenicol	1 (5.6%)
Oxacillin	1 (5.6%)
Penicillin and cephalosporin*	1 (5.6%)
Cephalosporin alone	1 (5.6%)
Penicillin and tetracycline	1 (5.6%)

* Keflin was given intravenously for four weeks, followed by penicillin given orally.

Table 6. Long-term follow-up

		No. of Cases
Group A		
NYHA class at diagnosis	F.C. I	—11 (100%)
NYHA class at follow-up	F.C. I	—11 (100%)
Died		0
Group B		
NYHA class at diagnosis	F.C. II	— 7 (100%)
NYHA class at follow-up	F.C. II	— 3 (43%)
	F.C.III	— 1 (14%)
Died		3 (43%)

F.C. = functional class.

Surgical therapy was required in 5 patients, all of whom required an aortic valve replacement. In addition, 1 patient with subvalvular aortic stenosis and coarctation of the aorta underwent excision of the fibrous ring after 28 days of medical therapy, resulting in a good clinical response. A ventricular septal defect was closed in one case of recurrent *Streptococcus viridans* endocarditis with an underlying ventricular septal defect and pulmonic stenosis. Late surgical correction was performed 10 years later in a patient with tetralogy of Fallot. No patient required emergency surgical intervention for acute decompensation.

Results

The 11 group A patients who were initially in NYHA class I remained in class I (*Table 6*). None have been rehospitalized for recurrent endocarditis. Most of these patients are gainfully employed.

Group B patients who were NYHA class II at the initial diagnosis of endocarditis experienced different outcomes as compared to those in group A. Three patients remained in class II, but 1 with a sedentary occupation was rehospitalized with amaurosis fugax several years after her medical therapy and aortic valve replacement, and another patient, who received antibiotics alone, was rehospitalized for recurrent endocarditis at another hospital. Three patients died of the suppurative complications and valvular insufficiency associated with their endocarditis. One died of septic embolic phenomenon during her initial hospitalization with *Candida albicans* endocarditis, and 1 died of septic and congestive sequelae four to five months after diagnosis. The third patient had recurrent *Streptococcus viridans* endocarditis after closure of a ventricular septal defect and died of the suppurative and congestive complications of *Pseudomonas aeruginosa* endocarditis four years later. The mortality rate was 11% one year after diagnosis and 17% at five years; thus, the mean survival rate was 86%. Follow-up of a six-month-old infant with Down's syndrome showed that he was in class III with cardiac symptoms attributable to his uncorrected congenital heart lesion.

Discussion

In the literature, McNeill et al[7] reported 102 adult patients with endocarditis; the mortality rate was 56% at one year as the result of embolic complications and congestive heart failure. Jackson and Allison[8] reported a mortality rate of 50% at one year compared to 10% in a series by Weinstein and Rubin.[9] Pre-existing cardiac disease was identified in 97 of 102 adult patients in the study by McNeill et al,[7] with rheumatic heart disease accounting for 75%. In comparison, congenital heart lesions have been more frequently associated with subsequent endocarditis in pediatric reports. In our group of patients, 72% had pre-existing congenital heart disease and 28% had pre-existing rheumatic heart disease.

Blumenthal et al[1] reported several prognostic indicators in their early study of infective endocarditis. They found a high mortality in younger patients. Four of 5 patients between the ages of three months and four years died. Seven of 8 patients with culture-negative endocarditis died, as did all patients with congestive heart failure. In a study by Zakrzewski and Keith,[2] 5 of 8 children with culture-negative endocarditis died. This high mortality may be due to a delay in either diagnosis or adequate antimicrobial therapy. *Staphylococcus aureus* has been found with increasing frequency in several studies.[3,4] Mills et al[10] reported a 35% incidence of severe heart failure within six months of discharge in adult patients with *Staphylococcus aureus* endocarditis.

Clinical manifestations involving the 18 patients reported here were similar to those reported in previous adult and pediatric series.[1,2,4,11,12] The bacteriology, as in other reports,[1,2,12] showed a predominance of *Staphylococcus aureus* and *Streptococcus viridans* as the commonly infecting organisms. *Streptococcus mitis* was found in 2 patients in our series.

In our patients, the long-term clinical outcome could not be related to the age at presentation. Our patients were somewhat older than those reported previously, with only 1 patient less than five years of age at presentation. We failed to demonstrate an increased mortality or morbidity in patients with *Staphylococcus aureus* or culture-negative endocarditis. The initial functional status of the patient was the only factor that significantly affected long-term prognosis.

Conclusion

Infective endocarditis affects children with congenital or rheumatic heart disease. Prolonged fever and malaise were the most common symptoms at initial presentation. There was no difference in long-term prognosis based on the mode of therapy (medical versus medical and surgical) in our group of patients. Functional cardiac status prior to treatment appears to be predictive of long-term survival and functional class. Morbidity and mortality were increased in those patients who were more symptomatic and disabled early in their disease.

Although this study presents a small group of patients, we believe that this data will enable us to better understand the natural history of infective endocarditis in the pediatric population.

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