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Pediatric Endocarditis and Stroke: A Single Center Retrospective Review of Seven Cases

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Abstract

The approach to the acute management of stroke in children with infective endocarditis is limited by the paucity of published data on their clinical course and outcome. We conducted a retrospective study at an urban tertiary care academic center to characterize the clinical course of seven pediatric patients with endocarditis and subsequent cerebral infarct. Among 115 patients with endocarditis, a stroke occurred in seven. Four patients had congenital heart disease. In 6 patients, the stroke was in the distribution of the middle cerebral artery and there was no preference for left or right hemisphere. The most common presenting symptom was focal weakness. Three patients had mycotic aneurysms, all of which were successfully repaired. Two patients were placed on aspirin therapy with no adverse effects. All patients survived but neurological recovery was variable. The two youngest patients (3 and 14 weeks of age) had the longest periods of hospitalization and had the most severe neurologic impairment. These findings suggest that children may have better outcome than adults after stroke secondary to bacterial endocarditis. Routine surveillance for mycotic aneurysms in patients with new neurological deficits and the use of aspirin should be considered in the medical management.

Introduction

The incidence of infective endocarditis in adults is approximately 1.5 cases /100000/year [1]. It occurs less frequently in children, with an incidence of approximately 0.6/100 000/year but carries a mortality of 11 – 20% [2]. Predisposing factors are also different in the pediatric population. Congenital heart disease (CHD) accounts for the majority of cases (50-75%) and the remainder involves rheumatic heart disease (12%) or structurally normal heart (14-40%) [3].

In adults with infective endocarditis, neurological complications develop in 20 – 40% of patients [4]. The most frequent neurological complications include cerebral infarction, bacterial meningitis, intracerebral hemorrhage and mycotic aneurysms [5,6]. Neurological complications after infective endocarditis in children have been less well characterized. Among all children with stroke, up to 60% may have permanent neurologic deficits and stroke may recur in up to 50% [7].

Previous retrospective studies have analyzed children and adults as a single group and it is difficult to distinguish clinical variables that are specific to children [8,9]. In order to optimize medical and surgical management in children with endocarditis and stroke, it is important to

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identify factors correlated with poor or improved outcome. As a first step, this study describes the clinical course of seven pediatric patients with endocarditis and subsequent stroke.

Methods

A retrospective study was conducted at Childrens Memorial Hospital, an urban tertiary care academic medical center. The study was approved by the hospital Institutional Review Board. Medical records were searched using the International Classification of Diseases (ICD-9) codes to identify all patients less than 18 years of age admitted between 1990 and 2007 with diagnoses linked to endocarditis and stroke. Both ischemic and hemorrhagic strokes were included in this study. Comprehensive demographic and clinical details were recorded of their hospitalization. Long-term neurological recovery was evaluated when such information was available.

Results

One hundred and fifteen patients with endocarditis were identified with a computerized search using ICD-9 codes. Medical charts were comprehensively reviewed of patients with endocarditis and subsequent stroke. Seven children (6%) were identified as having the neurological complication of stroke after infective endocarditis (Table 1). There were 4 female and 3 male patients ranging in age from 3 weeks to 16 years. Four patients had some form of CHD. A pathogen was identified in 6 patients; four patients were infected with either *Streptococcus* or *Staphylococcus aureus*. All patients were placed on prolonged intravenous antibiotic therapy (4–8 weeks in duration), which included gentamycin and either vancomycin, ampicillin or penicillin. The mitral valve (4 patients) was the most frequently involved. Documentation of vegetation size was available for five patients; vegetation size was greater than 10 mm in four of these patients. Six of the patients (87%) underwent corrective cardiac surgery which was performed 1 day to 1 year after the diagnosis of stroke. There was no mortality associated with these surgical procedures.

In 6 patients, the initial stroke occurred in the distribution of the middle cerebral artery (Table 2) but there was no preference for left or right hemisphere. Two patients (28%) sustained only an ischemic stroke; 3 patients (42%) sustained both ischemic and hemorrhagic strokes and 2 patients (28%) had only hemorrhagic infarcts.

Most (86%) of these patients had clinical neurologic deficits at the time of stroke (Table 3). Strokes occurred between 0 and 27 days after the diagnosis of endocarditis. The most common presenting symptom (86%) was focal weakness. Other symptoms included seizures and headaches.

Notably, three patients developed mycotic aneurysms. Two patients underwent endovascular embolization by an Interventional Radiologist. One patient underwent neurosurgical coil embolization of the mycotic aneurysm and placement of an external ventricular drain for intraventricular hemorrhage. One patient with intracranial hematoma and no evidence of mycotic aneurysm had evacuation of the hematoma. In all but one of these patients, the surgical intervention was performed within 3 days of identifying the lesion.

Two patients were treated with aspirin [7]. Patient # 5 did not undergo corrective surgery as her cardiac function remained stable and the size of the vegetation decreased over time. She was placed on long term aspirin therapy at a dose of approximately 3 mg/kg/day. She had close neurological follow-up and periodic MRI scans to evaluate for silent ischemic lesions. She had no further thrombo-embolic events. Patient #6 was placed on high dose aspirin (5mg/kg/day) after diagnosis of embolic stroke. She continued on aspirin until she underwent valve replacement and she was then switched to maintenance therapy with coumadin.

Neurological outcome was also variable. Data were available for 6 patients. Patient #6 complained of headache and had a normal neurological exam even though CT scan detected intracranial hemorrhage. Patient #4 had transient left hemiparesis on presentation that subsequently resolved. The remaining four patients had residual neurological deficits of varying severity. The two youngest patients had the most severe deficits. Patient #1 was 3.5 months at the time of presentation and had CHD. She had a 4 month period of hospitalization and her course was complicated by sepsis. She continued to receive ancillary therapies in the form of speech, physical and occupational therapies 3 years after her initial presentation. She was globally delayed at age 3. Patient #4 had no significant cardiac history and was 3 weeks of age at the time of initial presentation. She too had a prolonged hospital course and was discharged after a 3 month hospitalization. Four months following her initial presentation, her neurological status was remarkable for dysphagia and significant axial hypotonia.

Discussion

This retrospective evaluation over 17 years at a single medical center identified 115 pediatric cases of endocarditis of which six percent developed cerebral infarction. The small number of patients prevents any statistical analyses. Nevertheless, these data add to the limited pediatric experience on management and outcome of stroke due to infective endocarditis [8,9].

Risk factors associated with cerebral embolic events in infective endocarditis are comparable to previously published reports [10]. These include size of vegetation >10 mm and lesions localized to the mitral valve. Higher risk of embolism has also been found with Staphylococcal and fungal infections [10]. With respect to congenital heart disease, data are lacking to allow us to predict which lesion type is associated with an increased frequency of cerebro-embolic events after infective endocarditis. In adult patients with neurological complications due to endocarditis, there is no consensus on the optimal time for cardiac surgery [11,12]. One study found the risk of neurological deterioration was highest if cardiac surgery was performed within the first 2 weeks after cerebral infarction [12]. There are no published data to assess such risk for children. In our series, six patients underwent cardiac surgery. The interval between diagnosis of stroke and cardiac surgery varied from 1 day to 1 year. There appeared to be no correlation between timing of surgery and clinical outcome.

Mycotic aneurysms were detected in 2% of cases of endocarditis in our series, comparable to rates reported in other series that have incorporated both adult and pediatric patients [13]. Of the 7 patients with strokes, 43% had a mycotic aneurysm, all of which were successfully repaired. This repair was done using endovascular techniques by an Interventional Radiologist in 2 out of 3 patients. These data suggest that surveillance for such aneurysms with Magnetic Resonance Angiography (MRA) or Computed Tomography Angiography (CTA) should be performed routinely in children with endocarditis and stroke or new neurological deficit.

Aspirin therapy at a dose of 5mg/kg/day acutely and maintenance therapy at a dose of 1-5mg/kg/day has been recommended by the UK guidelines after childhood arterial ischemic stroke due to vasculopathy [7]. There are no guidelines with regards to anti-coagulation in pediatric patients with endocarditis and stroke. Prospective and retrospective studies of adult patients report conflicting results on the role of aspirin therapy in preventing cerebral embolic events. These may reflect differences in dosing and duration of therapy [14,15]. Two patients in our series were placed on aspirin therapy at doses of 3-5 mg/kg/day with no adverse cerebral events. This suggests that there may be a benefit to aspirin therapy in the pediatric population and should be considered as part of medical management in children with endocarditis and stroke.

Evaluation of factors affecting outcome is limited by the small number of patients and limited long-term follow-up data. There are no data on long-term neurological outcome in children

with endocarditis and stroke. Previous studies of adult patients with endocarditis have found a higher mortality rate in those with neurological complications [8]. All the patients in our series survived but neurological recovery was variable. The two youngest patients (3 and 14 weeks) had the longest periods of hospitalization and were the most debilitated neurologically. However, long term follow-up on one of these patients is unavailable. The other patient is currently being followed in our institution and her long-term neurological outcome will be of interest. Of the 3 patients who did not have CHD, all have persistent neurologic deficits. Interestingly, 2 of the 4 patients with CHD are neurologically normal. Both of these latter cases were older (9 and 15 years) and involved the aortic valve, rather than the mitral valve which was affected in 4 of the 5 other patients. The contribution of age, valve injury and other medical history to outcome will require larger studies.

The findings of this study suggest that pediatric patients with stroke associated with infective endocarditis may have better outcome than adults. Aspirin therapy at doses of 3-5mg/kg/day should be considered as part of routine medical management in patients with endocarditis and stroke. Given that stroke occurred in only 6% of all children with endocarditis, we cannot advocate routine surveillance screening with CT or MRI in all children with endocarditis. Similarly, screening all such patients for genetic and biochemical risk factors associated with pediatric strokes cannot be justified. However, surveillance for mycotic aneurysms using MRA or CTA should also be considered in children with neurological deficits.

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Table 1
Demographic and clinical features of children with endocarditis and stroke

	Patients						
	1	2	3	4	5	6	7
Sex	Female	Male	Male	Female	Female	Female	Male
Age (years)	0.3	9	15	11	16	0.08	1.3
Organism	Enterococcus faecalis	Granulicatella elegans	Staphylococcus aureus	Alphahemolytic Streptococcus	Group B Streptococcus	Staphylococcus aureus	Culture negative
Cardiac history	TGA, VSD s/p repair	Bicuspid AV, coarctation of aorta s/p repair	TGA, s/p repair	Redundant MV; cleft in anterior leaflet	None	None	None
Size of vegetation	No size recorded	5.5 × 4.8 mm	No size recorded	3 masses; 1.7 × 0.8 cm 0.5 × 0.5 cm 0.5 × 0.5 cm	10-11 mm	8 × 16 mm	2.5-3 cm
Location of vegetation	SVC/RA junction	Aortic root	AV	Left Atrium	MV	MV	MV
Cardiac surgery	arterial switch	Aortic root replacement	AV replacement	MV repair	None	MV replacement	MV replacement
Interval bet. stroke and surgery (D)	75	21	1	3	N/A	45	1

Abbreviations: AV = aortic valve SVC = superior vena cava D = days S/P = status post MV = mitral valve TGV = transposition of great vessels RA = right atrium VSD = ventricular septal defect

Table 2

Stroke characteristics and therapeutic intervention

Patient	Type of stroke	Blood vessel involved	Mycotic aneurysm	Intracranial surgical intervention	Timing of surgery after diagnosis of intracranial lesion (days)
1	Ischemic	Right MCA	No	No	N/A
2	Ischemic/hemorrhagic	Right MCA	Yes	NS: coil embolization of aneurysm; VPS for intraventricular hemorrhage	Embolization: 2 days
3	Hemorrhagic	Left MCA	No	No	N/A
4	Hemorrhagic	Right MCA	No	NS: Evacuation of intracranial hematoma	1
5	Ischemic/hemorrhagic	Left MCA	Yes	IR: endovascular repair of aneurysm	1
6	Ischemic/hemorrhagic	Multiple	Yes	IR: endovascular repair of aneurysm	7
7	Ischemic	Left MCA	No	No	N/A

Abbreviations: IR = intervention radiology NS = neurosurgery MCA = middle cerebral artery VPS = ventriculo-peritoneal shunt

Table 3

Neurological outcome in children with endocarditis and stroke

Patient	Neurological exam/findings at time of stroke	Neurological exam 4 -6 months after stroke	Neurological status approx. 1 year after stroke
1	Decreased spontaneous movements on left side	Unavailable	Global delay
2	Left hemiparesis; visual field cut on left	Normal neurological exam	Normal neurological exam
3	Headache; normal neurological exam	Normal neurological exam	Normal neurological exam
4	Left hemiparesis; visual field cut on left	Unknown	Unknown
5	Right hemiparesis; expressive aphasia; later dysarthria	Resolved dysarthria; improved right hemiplegia	Stable right hemiplegia
6	Right hemi-paresis seizure	Dysphagia; axial hypotonia; resolved hemi-paresis	Pending
7	Right hemiparesis	Persistent right hemiparesis	Persistent right hemiparesis