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Pneumococcal endocarditis in children: A nationwide survey in Japan ☆

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Abstract

Background: Infective endocarditis (IE) due to *Streptococcus pneumoniae* (*S. pneumoniae*) carries a high mortality rate. However, little is known about pneumococcal IE in children and no optimal therapy has been established. Thus, we attempted to identify the clinical features of this disorder through a Japanese nationwide survey.
Methods: Members of the Japanese Society of Pediatrics Cardiology and Cardiac Surgery registered 170 pediatric patients with IE diagnosed during a 5-year period (1997–2001). Nine of these patients (5.3%) had pneumococcal IE. The clinical course, treatment and outcome of these 9 patients, aged 7 months to 4 years, were analyzed.
Results: Pneumococcal IE was associated with congenital heart disease in 7 patients and accompanied by other systemic infections including meningitis, pneumonia and otitis media, in 4 patients. Five of the 9 (55.6%) strains isolated by blood culture were penicillin-resistant *S. pneumoniae* strains. Seven patients were treated with carbapenem. Three underwent cardiac surgery due to cardiac failure and/or vegetation. One died due to septic shock on the first day of hospitalization.
Conclusions: In children, pneumococcal endocarditis is often accompanied by severe systemic infections. The majority of pediatric cases are caused by penicillin-resistant *S. pneumoniae* strains. Carbapenem is an effective for IE caused by penicillin-resistant *S. pneumoniae*. This survey might be helpful to establish proper management strategies for pediatric pneumococcal IE.

Keywords: Infective endocarditis; *Streptococcus pneumoniae*; Penicillin-resistant; Congenital heart disease; Carbapenem

1. Introduction

Infective endocarditis (IE) is one of the most severe systemic infectious diseases in children. The main causative microorganisms of pediatric IE are viridans streptococci and *Staphylococcus* species [1]. To date, *Streptococcus pneumoniae* (*S. pneumoniae*) has been considered an uncommon cause of IE, however, pneumococcal endocarditis is a rapidly destructive infection, with a high mortality rate [2,3]. An increasing number of pneumococcus strains worldwide are becoming resistant to penicillin, raising the concern that the number of cases of antibiotic-resistant pneumococcal endocarditis will increase in the near future. However, no optimal therapy has been established for pneumococcal endocarditis and there is consequently little information on pediatric pneumococcal IE. Thus, the clinical features and

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therapeutic aspects of 9 cases of pediatric pneumococcal IE in Japan during a 5-year period through a nationwide survey were analyzed for future establishment of proper management of this situation.

2. Materials and methods

Members of the Japanese Society of Pediatrics Cardiology and Cardiac Surgery registered 170 pediatric patients with IE diagnosed according to the Duke criteria [4] during a 5-year period (1997–2001) [5,6]. There were 147 patients with congenital heart disease (CHD) and 23 patients with no apparent cardiac disease. In 9 of the 170 (5.3%) patients, *S. pneumoniae* strains were identified by blood culture. In these 9 patients, clinical course, treatment and outcome were analyzed from their clinical records.

3. Results

Clinical and microbiological features of the 9 cases of pneumococcal endocarditis are shown in Table 1. Patients' age ranged from 7 months to 4 years 11 months, with a median age of 28 months. Five patients were less than 1 year of age. The male/female ratio was 4/5. In 2 patients, underlying cardiac disease was not identified. There were 4 patients with cyanotic CHD (tetralogy of Fallot 2; asplenia 2 (one with double outlet right ventricle and the other one with single ventricle)) and 3 patients with acyanotic CHD (ventricular septal defect 2; patent ductus arteriosus 1). Chromosomal abnormality was found in 2 patients, trisomy 21 in 1 and Noonan syndrome in the other. Among the 7 patients with CHD, 5 had a history of cardiac surgery: palliative (2 patients) and reparative (3 patients). One patient underwent cardiac surgery within 1 month before the onset of IE. By transthoracic echocardiography, vegetation was detected in 3 patients: aortic valve in 1 and mitral valve in the other 2. Blood culture was positive for *S. pneumoniae* in all 9 patients. Systemic infection was identified in 4 patients: meningitis in 2, pneumonia in 1 and otitis media in 1. Eight *S. pneumoniae* isolates were subjected to antimicrobial susceptibility testing. Isolates were classified according to the minimal inhibitory concentration of penicillin G. Of the 8 isolates, 1 was penicillin-susceptible *S. pneumoniae* (PSSP), 2 were penicillin-intermediate-resistant *S. pneumoniae* (PISP) and the remaining 5 were penicillin-resistant *S. pneumoniae* (PRSP). All patients were treated with intravenous antibiotics. Five patients received a combination of 2 antibiotics. In 6 patients, initial antibiotics were replaced by other alternate antibiotics according to susceptibility of the isolated *S. pneumoniae* strain. In total, 6 patients were treated with carbapenem. One patient died on the first day of hospitalization, the other 8 patients were given intravenous antibiotics for 13–64 days. Three patients developed cardiac complications followed by cardiac surgery during the active phase of infection. The overall mortality rate was 11.1% (1/9).

Table 1
Clinical and microbiological features of 9 cases of pediatric pneumococcal endocarditis in Japan (1997–2001)

Patients	1	2	3	4	5	6	7	8	9
Age	7 mo	1 y 2 mo	1 y 0 mo	3 y 9 mo	1 y 0 mo	1 y 3 mo	3 y 2 mo	4 y 0 mo	4 y 11 mo
Sex	Female	Female	Female	Female	Male	Male	Male	Male	Female
Underlying disease	SV asplenia	DORV asplenia	VSD+PDA	PDA Noonan syndrome	None	VSD 21 trisomy	None	TOF	TOF
Previous cardiac surgery	Palliative	Palliative	Reparative	−	−	−	−	Reparative	Reparative
Site of vegetation on TTE	−	−	AV	−	MV	−	MV	−	−
Concomitant infection	Pneumonia	−	Meningitis	−	Meningitis	−	OMA	−	−
Drug sensitivity of pneumococcus	Unknown	PSSP	PISP	PISP	PRSP	PRSP	PRSP	PRSP	PRSP
Initial antibiotic	SBT/ABPC +AMK	FMOX	ABPC +CTX	CTM	CTX +PAPM/BP	PAPM/BP	PAPM/BP +ABK	IPM/CS +VCM	ABPC
Alternative antibiotics	−	PAPM/BP	PAPM/BP	PcG	IPM/CS +GM	−	CPR +VCM	−	PAPM/BP
Duration of antibiotics (days)	1	15	54	13	64	28	35	42	26
Cardiac surgery	−	−	+	−	+	−	+	−	−
Complications	−	−	Valvular regurgitation	−	Cardiac failure	−	Cardiac failure	−	−
Outcome	Died	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived

SV: single ventricle, DORV: double-outlet right ventricle, VSD: ventricular septal defect, PDA: patent ductus arteriosus, TOF: tetralogy of Fallot, TTE: transthoratic echocardiography, AV: aortic valve, MV: mitral valve, OMA: acute otitis media, PSSP: penicillin-susceptible *Streptococcus pneumoniae*, PISP: penicillin-intermediate-resistant *Streptococcus pneumoniae*, PRSP: penicillin-resistant *Streptococcus pneumoniae*, SBT/ABPC: sulbactam/ampicillin, AMK: amikacin, FMOX: flomoxef, ABPC: ampicillin, CTX: cefotaxime, CTM: cefotiam, PAPM/BP: panipenem/betamipron, ABK: arbekacin, IPM/CS: imipenem/cilastatin, VCM: vancomycin, PcG: penicillin G, GM: gentamicin, CPR: cefpirome.