CARDIOVASCULAR MANIFESTATIONS AND LEFT VENTRICULAR FUNCTIONS IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN INFANTS AND CHILDREN IN THAILAND

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Abstract. During January through December 1993, twelve symptomatic infants and children (6 females, 6 males) with human immunodeficiency virus infection were prospectively evaluated for their cardiovascular clinical manifestations and ventricular functions, using two-dimensional, M-mode and Doppler echocardiographic examination. From auscultation, the pulmonic component of the second heart sound was accentuated in 8 cases and the murmur of atrioventricula valve regurgitation and pericardial friction rub were audible in 7 and 6 patients, respectively. Cardiomegaly and venous congestion were present on chest roentgenogram in 6 cases and electrocardiogram was abnormal in 5. The echocardiogram demonstrated elevated pulmonary arterial pressure in 9 patients. There were 5 cases of non-tamponade pericardial effusion. Five patients had mitral and pulmonary insufficiency while six had tricuspid insufficiency. The ejection fraction and shortening fraction were increased in all. The incidence of pulmonary hypertension was more frequent than previously reported.

INTRODUCTION

Since the first case of an infant born to the infected mother of human immunodeficiency virus (HIV) was reported in Thailand in 1988 (Chumdermpadetsuk *et al*, 1989), the spread of HIV infection was progressed rapidly in all age groups. HIV infection in children causes a broad spectrum of disease manifestations, including pulmonary, gastrointestinal and neurological involvement. Recently cardiovascular abnormalities such as dysrythmias, myocardial dysfuntion, myocarditis, endocarditis, pericarditis or tumor in the myocardium have been documented (Bharati *et al*, 1989; Cammarosano and Lewis, 1985; Fink *et al*, 1984; Grody *et al*, 1990; Lipshultz *et al*, 1989; Rogers, 1985; Shannon and Ammann, 1985; Steinherz *et al*, 1986; Stewart *et al*, 1989). Since these abnormalities have not previously been described in Thailand, we performed cardiac evaluation prospectively in a group of infected children.

PATIENTS AND METHODS

Patients diagnosed as having AIDS according to the criteria of Centers for Disease Control, Atlanta USA (CDC, 1987) and World Health Organization (WHO, 1986), who were admitted to the Department of Pediatrics, Chulalongkorn University Hospital from January to December 1993, were studied at the time when the acute clinical manifestations had been treated and subsided. History taking and physical examination were performed by the same physician after informed consent had been granted. Chest roentgenogram and twelve lead electrocardiogram were examined. ALOKA SSP 860 M-Mode and two dimensional echocardiography with 3.5 and 5.5 mHz phase array doppler was used for investigation in which the standard views were explored (Feigenbaum, 1986) while the patients were completely sedated with chloral hydrate. The pulmonary pressure (Chotivitayatarakorn *et al*, 1992), the ejection fraction and fractional shortening were measured. The data were then analysed by Student's *t*-test.

RESULTS

There were 12 patients who completed the program. All cases were born to the mothers and fathers who were infected with HIV. Table 1 shows age, sex and clinical manifestations. Their ages

Table 1

Age, sex and clinical manifestations.

Case No.	Age(year)	Sex	RR	BP	S_2P	S_3	Pansystolic murmur LLSB	Pansystolic murmur apex	Pericardial friction rub
1	1yr1mo	F	36	76/37	1^+	-	-	-	-
2	1yr4mo	F	40	80/47	1^+	+	2^+	2^+	+
3	1yr10mo	M	32	100/60	N	-	-	-	-
4	1yr2mo	M	36	97/59	N	-	-	-	-
5	9mo	F	36	84/52	N	-	-	-	-
6	1yr11mo	M	36	100/60	2^+	+	1^+	1^+	+
7	1yr10mo	M	60	90/60	1^+	+	1^+	1^+	+
8	1yr1mo	F	36	76/40	N	-	-	-	-
9	1yr10mo	M	44	96/66	2^+	+	1^+	1^+	+
10	2yr2mo	F	36	100/60	2^+	+	2^+	2^+	+
11	1yr9mo	M	36	98/58	1^+	+	1^+	1^+	-
12	1yr3mo	F	40	90/60	1^+	+	1^+	1^+	+

ranged from 9 months to 2 years 2 months. There were 6 females and 6 males. All cases were recovered from active symptoms with normal heart rate and blood pressure. The respiratory rate were rapid in most cases. The cardiovascular examination revealed accentuated pulmonic component of the second heart sound in 8, atrioventricular and pulmonic valve regurgitation murmur in 7 and pericardial friction rub in 6.

The roentgenogram and electrocardiographic findings are shown in Table 2. There was cardiomegaly in 7, pulmonary venous congestion in 5.

All cases showed normal sinus rhythm without conduction disturbance. Right ventricular hypertrophy was present in 4, and 3 showed combined ventricular hypertrophy.

Echocardiographic findings are shown in Table 3A. The pericardial effusion was present in 5 without signs of cardiac tamponade. During the

Table 2

Roentgenographic findings and electrocardiographic findings.

Case No.	Cardiac enlargement	Roentgenographic		Electrocardiogram				
		Vasculature	Congestion	RAE	RVH	LAE	LVH	LVstrain
1	N	N	-	-	-	-	-	-
2	2^+	N	+	Y	-	-	-	-
3	N	N	-	-	-	-	-	-
4	N	N	-	-	-	-	-	-
5	N	N	-	-	-	-	-	-
6	1^+	N	+	-	Y	-	-	-
7	2^+	N	+	-	Y	-	Y	-
8	N	N	-	-	-	-	-	-
9	2^+	N	+	-	Y	-	Y	-
10	2^+	N	+	-	Y	-	Y	-
11	1^+	N	-	-	-	-	-	-
12	1^+	N	-	-	-	-	-	-

RAE = Right atrial enlargement; RVH= Right ventricular hypertrophy;
LAE = Left atrial enlargement; LVH=Left ventricular hypertrophy;
LV strain = Left ventricular strain

follow up period of 12 weeks, the effusion was still present in two.

The chamber enlargement most frequently seen was right ventricular hypertrophy (5) accompanied by regurgitation of the tricuspid and pulmonary valves. The estimated mean pulmonary arterial pressure was increased in the dilated right ventricle and tricuspid regurgitation cases. There was accompanying mitral regurgitation in 5 cases. The movement of ventricular septum and free wall were very active in most cases.

The diastolic inflow pattern were normal in all. The ejection fraction (EF, range 0.74-0.84, mean 0.79 normal 0.66 ± 0.04), and the fractional shortening (FS, range 37-50%, mean 42.4% normal 36±4), showed high value (Table 3B).

DISCUSSION

Our report describes cardiovascular manifestations in a series of 12 children infected with HIV. Cardiac abnormalities included pulmonary hyper-

Table 3 A

Echocardiographic findings.

Case No.	Effusion	Enlargement	MI	TI	AI	PI	Diastolic	IVS	MPA pressure(mmHg) DO
1	-	RV	-	-	-	-	E>A	N	60
2	Y	RV	2+	2+	-	1+	E>A	N	50
3	-	-	-	-	-	-	E>A	N	20
4	-	-	-	-	-	-	E>A	N	15
5	-	-	-	1+	-	-	E>A	N	43
6	Y	RV	2+	2+	-	2+	E>A	N	61
7	Y	RV,LV	1+	2+	-	1+	E>A	N	47
8	-	-	-	-	-	-	E>A	N	20
9	Y	RV,LV	2+	2+	-	2+	E>A	N	60
10	Y	RV,LV	1+	2+	-	1+	E>A	N	60
11	-	-	-	-	-	-	E>A	N	47
12	-	-	-	-	-	-	E>A	N	43

MI = Mitral insufficiency; TI = Tricuspid insufficiency; AI = Aortic insufficiency; PI = Pulmonic insufficiency
Diastolic flow = inflow across MV; E = Early peak; A = Atrial peak; IVS = Interventricular septum;
MPA = Mean pulmonary arterial pressure; N = Normal; Y = Yes

Table 3 B

Additional echocardiographic findings.

Case No.	Ejection fraction					% Fractional shortening
	D0	D7	D28	D56	D84	D0
1	0.78	0.76	0.77	0.74	0.76	41
2	0.78	0.74	0.76	0.78	0.77	40
3	0.75	0.74	0.76	0.75	0.74	37
4	0.77	0.76	0.77	0.74	0.78	40
5	0.85	0.84	0.84	0.86	0.84	50
6	0.83	0.82	0.81	0.83	0.82	48
7	0.83	0.81	0.80	0.85	0.84	51
8	0.78	0.76	0.75	0.78	0.77	41
9	0.78	0.74	0.76	0.77	0.76	42
10	0.82	0.84	0.82	0.84	0.80	41
11	0.76	0.80	0.79	0.71	0.72	40
12	0.75	0.74	0.76	0.77	0.74	38

tension, atrioventricular valve and pulmonic valve regurgitation, pericardial effusion without tamponade and increased left ventricular contractility. Those findings were observed in a majority of the patients. Previous reports described abnormal cardiac function as high as 72-93% of children with HIV infection, with enhanced left ventricular performance accompanied by reduced after-load and elevated contractility as the most common echocardiographic findings (Grody *et al*, 1990; Issenberg *et al*, 1985; Sherron *et al*, 1985). Only about 20% had diminished contractility. Other findings reported include mononuclear pericarditis, myocarditis, dilated myocardiopathy, inflammation of the intracardiac conduction tissue as well as in the peripheral nerve, fibrosis spongiosa of the tricuspid and mitral valves based on autopsy specimens, yet histologic or culture evidence of myocardial infection with opportunistic organisms was lacking. However, one autopsy report showed evidence of cytoplasmic tubuloreticular inclusions in endothelial cells of interstitial capillaries which may be a marker of HIV myocardial infection (Grody *et al*, 1990).

Pericardial effusion is relatively a common finding in HIV infection. It ranges between 18-25% from other report. From our data, the incidence was about 42% and none of the children studied had associated Karposi's sarcoma, vegetation, lymphoma, or tuberculosis which are often found in adult AIDS populations of which some terminate from cardiac tamponade.

Our findings demonstrate an increased percentage of fractional shortening, and elevated ejection fraction with increased contractility in all 12 patients. This may be because the group of children studied were in the younger age group and the number was too small, that none showed evidence of diminished contractility.

Interestingly enough, 9 of our 12 patients demonstrated increased pulmonary pressure detected clinically by the increased pulmonic component of the second heart sound and confirmed by echocardiography. There were only two patients in our series who previously had 3-4 episodes of lung infection, the rest being admitted following their first attack of pneumonia or diarrhea, when the cardiovascular investigations were performed when the patients were symptom-free. This is in contrast to other studies by which the incidence of pulmonalry hypertension was only seen in 9-13.4% and mostly following left ventricle dysfunction (Grody *et al*, 1990; Issenberg *et al*, 1985; Sherron *et al*, 1985). All in our series had a hyperdynamic left heart. The causes of pulmonary hypertension may follow the process of pneumonia (Coplan *et al*, 1990; Diaz and Clanton 1993; Himeiman *et al*, 1989; Kane, 1992;Legoux *et al*, 1990; Mani and Smith, 1994; Polos *et al*, 1992; Speich *et al*, 1991) or it may result from obstruction of pulmonary venous drainage, or due to high flow into the pulmonary bed with low cardiac output, which is severe enough to cause reduced mixed venous PO_2 (Mercy and Reynolds, 1989; Nunn, 1993). Recent attention has been focused upon the infected T-cells which can cause pulmonary arteriolar endothelial cell proliferation and proliferating abnormal vessels as an etiologic factor in pulmonary hypertension (Legoux *et al*, 1990; Mani and Smith, 1994). In such cases, therapeutic intervention such as vasodilators, ACE inhibitors or positive inotropic therapy in patients with HIV associated left ventricular dysfunction or with pulmonary hypertension may play an important role in preventing or delaying the changes that will subsequently occur in the microcirculation of the cardiac and pulmonary vessels. Early detection of abnormal cardiovascular manifestations is necessary to determine whether therapeutic intervention is mandatory.

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