Cardiovascular changes in children with pneumonia

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Pneumonia is an important cause of death in childhood, especially in the infancy period. Since the respiratory and cardiovascular systems cannot be thought of independently, it is important to detect cardiovascular changes during pneumonia. We prospectively studied 50 children aged 2-24 months admitted to the hospital because of pneumonia in order to evaluate their cardiovascular findings with noninvasive methods. Patients were classified according to the World Health Organization (WHO) criteria of pneumonia, and evaluated by obtaining complete blood counts, serum electrolytes, renal and liver function tests, blood gases, creatinine kinase MB fraction (CK-MB), chest X-ray, electrocardiography (ECG) and echocardiography at the admission and after clinical recovery. Right ventricular systolic pressure (RVSP) was found to be high in 70% of patients and there was a correlation between the severity of the pneumonia and RVSP. All patients had normal left ventricular dimensions and functions, but in 68% of them CK-MB was elevated. In these infants, T voltages in D_1 derivation showed a significant rise with clinical recovery. Seven cases developed congestive heart failure, and three died. CK-MB was found to be high in all patients who died and in six of seven patients with congestive heart failure.

Our findings suggest that myocarditis incidence in children with pneumonia may be higher than previously known. Since myocarditis can be a fatal disease, its detection is important by noninvasive techniques like ECG, echocardiography and cardiac enzyme measurements.

Key words: children, pneumonia, cardiovascular changes, myocarditis.

Pneumonia is an important cause of death in childhood. According to the World Health Organization (WHO) data, 3-5 million children under five years die each year from this disease[1]. Also, in Turkey, pneumonia is the commonest cause of death in children under one year of age[2].

Cardiac failure is a serious complication of pneumonia and may also contribute to mortality[3]. Acute lower respiratory tract infections could alter the cardiovascular performance in several ways, including hypoxia and invasion of micro-organisms, resulting in myocarditis[4,5].

We prospectively studied 50 children aged 2-24 months without preexisting cardiovascular diseases admitted to the hospital because of acute pneumonia in order to evaluate cardiovascular changes with noninvasive methods.

Material and Methods

The study population comprised 50 children admitted to the hospital because of acute pneumonia. Their ages ranged between 2-24 months. We recorded the age and gender of the patients, and classified them according to the WHO definitions as pneumonia, severe pneumonia and very severe pneumonia[6]. Patients with other preexisting diseases like congenital heart anomalies, malnutrition and chromosomal syndromes were excluded from the study.

All patients received antimicrobial therapy, and digoxin was used in cases with heart failure. Blood samples were taken at the admission for complete blood count, serum sodium, potassium, calcium, magnesium, urea, creatinine, glucose, alanine transaminase, aspartate transaminase, C-reactive protein (CRP), arterial blood gas profile, blood culture and creatinine kinase MB fraction (CK-MB).

A second test for CK-MB was done approximately six weeks after the first analysis for those with high values. Viral cultures could not be obtained for economical reasons.

Complete blood counts were done with Max-M (Coulter Maxiss, U.S.A.) device, CRP was calculated with Behring nephelometric method (Dade-Behring, Germany), and hepatic and renal

function tests and serum electrolytes were analyzed with a Hitachi 911 (Boehringer Manheim, Germany) device and Rondox kite. Blood cultures were taken prior to any antimcrobial therapy and inoculated into BacT/Alert (Organnon Technica, U.S.A) at the bedside. Arterial blood gases were investigated with Radiometer ABL-5 (Dade-Behring, Germany) device. CK-MB levels were calculated with I. Lab 900 (Unstrumentuons Laboratory, Italy) autoanalyzer within six hours at room temperature and values higher than 25 u/L were considered high.

Each child had a chest X-ray and 12-lead electrocardiogram which was taken with a Hewlett Packard Page Writer 100 (Andover, Massachusetts); QRS and T voltages and QT interval were measured. Correted QT (QTc) interval was calculated with Bazzett formula ($QTc=QT/\sqrt{214RR}$).

After the normalization of the body temperature and sedation with intravenous midazolam (0.2 mg/kg), an echocardiogram was performed on each patient with a Hewlett Packard Sonos 1000 (Andover, Massachusetts) device using 5.5 and 3.5 MHz transducers in order to measure heart rate, left and right ventricular dimensions and left ventricular functions. Continuous wave Doppler technique was used to measure tricuspid regurgitation at apical four chamber position. Systolic transtricuspid gradient was measured using modified Bernouilli formula ($\Delta P=4V^2$) and right ventricular systolic (RVSP) was calculated adding estimated mean right atrial pressure to the transtricuspid gradient. Values higher than 30 mm Hg were considered high. Repeat electrocardiographies (ECGs) and echocardiograms were performed for each child after clinical recovery.

Statistical analyses were performed using chi-square and Wilcoxon signed ranks tests with the Statistical Package for the Social Science Program (SPSS). P values under 0.05 were considered statistically significant. Results are expressed as mean values ± SD.

Results

Of 50 patients, 36 (72%) were male, and 14 (28%) were female. Mean age was 9.4±6.2 months. Thirteen (26%) had pneumonia, 15 (30%) had severe, and 22 (44%) had very severe pneumonia.

Mean heart rates at admission and after recovery were 156.78±23.4 and 148±25.6 bpm, respectively (p=0.027).

All patients had normal serum electrolytes, and hepatic and renal function test results. Mean levels of blood gases at the admission were as follows: PO_2=89.5±45 mm Hg, PCO_2=34.6±8.2 mm Hg and PH=7.37±2.03. The mean level of CRP was 44 mg/L (normal value <5 mg/L). All but one of the blood cultures were negative; in one child, blood culture revealed coagulase negative staphylococci.

Thirty-four (68%) of the patients had high values of CK-MB. The mean values of CK- MB at admission and at the 6th week were 43.4±5.2 u/L and 22.6±4.3 u/L, respectively (p=0.000).

The mean values of the ECGs taken at the admission and after clinical recovery can be seen in Table I. The comparison of D_1R and D_1T voltages and QRS axis were statistically significant (p=0.022, 0.048 and 0.039, respectively).

Table I. Mean Values of ECGs Taken at Admission and After Clinical Recovery

ECG	At admission	After clinical recovery	P
QTc	0.39±2.8 s	0.39±3.1 s	0.627
PR	0.10±1.35 s	0.10±1.37 s	0.432
D_1R	2.9±3.80 mm	4.0±4.5 mm	0.022
V_1R	3.02±3.3 mm	2.5±3 mm	0.513
V_5R	9.6±5.5 mm	10.3±5.6 mm	0.194
D_1T	1.5±0.9 mm	2±1 mm	0.048
V_5T	2.4±1.7 mm	3.4±1.7 mm	0.067
QRS axis	+71±29°	+61.09±29°	0.039
ST deviation	None	None	–

ECG: electrocardiography.

The comparisons of the echocardiographic measurements obtained at the first hospitalization day and after clinical recovery are shown in Table II. The only statistically significant variation was the difference between RVSPs (p=0.002). Also, statistical analysis revealed a significant relation between the severity of pneumonia and initial RVSP values (p=0.02) (Table III). But no relation was found between the severity of pneumonia and high CK-MB (p=0.079).

Table III. Relation Between the Severity of Pneumonia and RVSP

	RVP		
Diagnosis	Normal	High	Number
Pneumonia	7	6	13
Severe pneumonia	6	9	15
Very severe pneumonia	2	20	22
Total	15	35	50

P=0.002, x^2=0.007, RVSP: right ventricular systolic pressure.

Table II. Echocardiographic Measurements Obtained at Admission and After Clinical Recovery

ECHO	At admission	After clinical recovery	P
LVEDD	23.5±3.8 mm	24.5±3.4 mm	0.274
LVEF	75.3%±7.8	74.2%±10.5	0.736
LVFS	42.8%±8.6	42.3%±9.7	0.647
RVEDD	11.4±3.1 mm	10.4±2.6 mm	0.580
RVSP	39.8±11.6 mm Hg	27.5±12.3 mm Hg	0.002

LVEDD: left ventricular end diastolic diameter, LVEF: left ventricular ejection fraction, LVFS: left ventricular fractional shortening, RVEDD: right ventricular end diastolic diameter, RVSP: right ventricular systolic pressure.

In patients with high CK-MB results, the initial and recovery values obtained from electrocardiographic and echocardiographic measurements showed significant differences in D_1R, D_1T and RVP levels (Table IV).

In seven patients (14%), congestive heart failure supervened, and three of them succumbed. Permission for autopsy could not be obtained. All children with congestive heart failure had high RVSP measurements (mean=45.2 mm Hg), and six of them had high CK-MB values (mean=102.1 u/L).

Left ventricular dimensions and functions were found to be normal in all cases and none of them showed ST segment or T wave alterations. Right ventricular dimensions were elevated four patients with high RVSP levels.

Discussion

The cardiovascular and respiratory systems function as a single unit and cannot be thought of independently. Alterations in cardiorespiratory interactions can cause significant changes in cardiac functions[4]. Pneumonia can cause myocarditis by

Table IV. Electrocardiographic (ECG) and Echocardiographic Measurements in Patients with High CK-MB Results

ECG and ECHO	At admission	Clinical recovery	P
QTC	0.39±3.1 s	0.40±3.2 s	0.920
PR	9.7±1.8 s	10.1±1.3 s	0.543
D_1R	3.18±3.5 mm	4.34±4.7 mm	0.040
V_1R	2.68±3.6 mm	2.39±3.05 mm	0.344
V_5R	9.79±5.4 mm	11.48±5.6 mm	0.247
D_1T	1.56±0.9 mm	2.06±0.74 mm	0.020
V_5T	2.62±10.8 mm	3.4±1.9 mm	0.277
QRS AXIS	+70.1±28.5°	+63.9±27.7°	0.130
LVEDD	23.4±3.9 mm	24.6±3.7 mm	0.536
LVEF	74.8%±8.2	74.72%±11.1	0.882
LVFS	42.7%±9.5	42.9%±10.4	0.767
RVEDD	12.6±3.0 mm	10.6±2.8 mm	0.097
RVSP	35.4±10.7 mm Hg	28.3±13.6 mm Hg	0.011
Pulse	157.9±24.5 bpm	149.25±26 bpm	0.071

n: 34; CK-MB: creatinine kinase MB fraction; LVEDD: left ventricular end diastolic diameter; LVEF. left ventricular ejection fraction; LVFS: left ventricular fractional shortening; RVEDD: right ventricular end diastolic diameter; RVP: right ventricular systolic pressure.

direct invasion of the microorganisms, can lead to cardiac failure by myocardial depressant effect of hypoxia, and may further deteriorate cardiac function by altering preload and afterleod[4,5,7].

In a study of 84 cases with clinical myocarditis, tachycardia was present in 26.1%[8]. Our patients' heart rates were significantly decreased after recovery, but in cases with high initial CK-MB values, there was no significant difference between pre- and post-therapy heart rates.

Electrocardiographic changes including right axis deviation, right bundle branch block, ventricular extrasystoles, atrial fibrillation and nodal rhythm can be seen in patients with pneumonia[7]. Our study showed lower R and T voltages and rightward deviation of the QRS axis in children with pneumonia compared with post infection values. No arrhythmia was detected. During the influenza epidemics in 1957, an increase of myocarditis cases was reported[9]. Also, Neubauer[10] claimed that acute infection was the most important cause of myocarditis, and that ECG changes were suggestive, especially in mild cases. In a study performed by Fine and Brainerd[8], they showed that T wave alteration was the most common sign of myocarditis. None of our cases had T wave alterations. But in infants with high CK-MB values, T voltages in D_1 derivation yielded a significant rise with clinical recovery.

Isolated tricuspid incompetence can be detected with Doppler echocardiographic study in children with normal cardiac anatomy and hemodynamics[11]. The estimated right atrial pressure added to transtricuspid gradient equals right ventricular and pulmonary artery systolic pressure[12]. Thirty-five (70%) of our patients had high RVSP prior to infection therapy, and there was a correlation between the severity of the pneumonia and RVSP ($p=0.002$). After the clinical recovery, RVSP values of all the patients returned to normal levels except in the three patients who died. This finding is similar to those found in other studies[3,13].

Echocardiographic studies revealed normal left ventricular dimensions and functions in all cases. Right ventricular dimensions were elevated in only four patients with high RVSPs. Except in one infant who died during the hospital stay, RVSP values of the remaining three cases returned to normal after clinical recovery.

Various studies have revealed that left ventricular functions and dimensions may be in normal ranges in patients with mild myocarditis[14,15]. Endomyocardial biopsy is the gold standard in the diagnosis of myocarditis[16]. But since it is an invasive procedure, cardiac enzyme measurements can be used in suspected cases[7,17]. A rise in CK-MB is highly specific for myocardial damage and may be the only sign of subclinical myocarditis[18]. Despite the lack of electrocardiographic and echocardiographic changes, high CK-MB levels were detected in 68% of our cases in the absence of severe hypoxia, acidosis and sepsis. Also, six of seven patients who developed congestive heart failure and all three patients who died had high initial CK-MB values.

Our findings suggest that the incidence of myocarditis in children with pneumonia may be higher than previously estimated, and since there may be no suggestive clinical, electrocardiographic or echocardiographic changes for myocarditis, cardiac enzyme measurements are useful in the detection of subclinical cases. Myocarditis can cause mortality not only by deteriorating ventricular pump function, leading to circulatory collapse, but may also be fatal by formation of severe arrhythmias[19]. It is therefore important to detect mild myocarditis by noninvasive methods like ECG, echocardiography and cardiac enzyme measurements in pneumonia cases.

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