Dicle Tıp Dergisi /
Dicle Medical Journal

2014; 41 (1): 54-58
doi: 10.5798/diclemedj.0921.2014.01.0372

ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Echocardiographic evaluation of patients with subacute sclerosing panencephalitis

Subakut sklerozan panensefalitli hastaların ekokardiyografik değerlendirilmesi

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ABSTRACT

Objective: Subacute sclerosing panencephalitis is a slowly progressive, inflammatory and neurodegenerative disease caused by virus infection in the central nervous system. Since there are a limited number of studies in the literature evaluating the cardiovascular functions of patients with SSPE, the present study evaluates the patients with SSPE using tissue Doppler echocardiography and compares them between the control group in order to shed some light on the subject.

Methods: The study is a prospective observational study. 49 patients (17 female, 32 male) with SSPE were included in the study. Patients were divided into two groups: Stage 2 (n=29) and Stage 3 (n=20). Echocardiographic data were compared with a control group of 26 which is the same average age. All children underwent a detailed echocardiography, which contained an M-mode, pulse Doppler and tissue Doppler imaging.

Results: Sinus tachycardia (>100 beats/min in children) was detected in nineteen (38.7%) patients. There were not significant differences between parameters of systolic and diastolic function of the heart. Stage 2 group, EF: 69.9±6.4; SF: 39.2±5.58; and MPI (mitral): 0.38±0.03 and MPI (tricuspid): 0.39±0.10. And in the Stage 3 group, EF: 68.5±7.0, SF: 37.8±5.34, MPI (mitral): 0.37±0.09 and MPI (tricuspid): 0.38±0.12. In the control group EF:70.96±5.54; SF:39.96±5.05 and MPI(mitral): 0.35±0.06 MPI (tricuspid):0.36±0.04 and statistically meaningful differences were not found between patients and control groups (p >0.05).

Conclusion: Cardiac functions may be preserved and cardiac functions constitute no significant risks of mortality in the advanced stages of patients with Subacute sclerosing panencephalitis, which is a group of chronic and bedridden patients.

Key words: Subacute Sclerosing Panencephalitis, echocardiography, cardiac function

ÖZET

Amaç: Subakut sklerozan panensefalit (SSPE), santral sinir sisteminin yavaş virüs enfeksiyonu sonucu ortaya çıkan kronik, progressif dejeneratif bir hastalığıdır. Bu hasta grubunun kalp fonksiyonları ile ilgili çalışmalar kısıtlı olduğu için bu konuya ışık tutmak amacıyla farklı evrelerdeki hastaların kalp fonksiyonları değerlendirilmiştir.

Yöntemler: Çalışma prospektif bir çalışma şeklinde olup, Çocuk Nörolojisi polikliniğinde takip edilen 49 SSPE olgusu (17 kız, 32 erkek) çalışmaya alındı. Hastalar evre 2(n=29) ve evre 3(n=20) olarak iki gruba ayrıldı. Ekokardiyografik veriler yaş ortalaması aynı olan 26 kontrol grubu ile karşılaştırıldı. M- mode, pulse Doppler ve doku Doppler ekokardiyografik incelemeler ve gruplara uygulandı.

Bulgular: Sinüs taşikardisi (100 atım/dak üzeri)19 hastada (%37,8) mevcuttu. Kalbin sistolik ve diyastolik fonksiyon parametreleri arasında anlamlı farklılık yoktu. Evre 2 SSPE grubunda, EF: 69.9±6.4, FS: 39.2±5.58, MPI(mitral):0.38±0.03, MPI(triküspid): 0.39±0.10, Evre 3 grubunda, EF: 68.5±7.00, FS: 37.8±5.34, MPI(mitral):0.37±0.09, MPI(triküspid):0.38±0.12, Kontrol grubunda EF:70.96±5.54, FS:39.96±5.05, MPI(mitral):0.35±0.06, MPI (triküspid):0,36±0,04 olarak bulundu. Farklı evrelerde bakılan hastaların ekokardiyografik verileri kontrol grubu ile karşılaştırıldığında istatistiki olarak anlamlı farklılık bulunmamıştır (p > 0,05).

Sonuç: Bu çalışma kalp fonksiyonlarının ileriki dönemlere kadar korunabileceğini, kronik ve yatağa bağımlı bir hastalık olan SSPE de bu durumun mortalite açısından önemli bir risk oluşturmayacağını göstermektedir.

Anahtar kelimeler: Subakut sklerozan panensefalit, ekokardiyografi, kardiyak fonksiyon

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Geliş Tarihi / Received: 13.12.2013, Kabul Tarihi / Accepted: 11.01.2014

INTRODUCTION

A progressive and inflammatory slow virus disease caused by the persistent measles infection of the central nervous system, subacute sclerosing panencephalitis (SSPE) is a fatal neurodegenerative disease typically observed during childhood and young adolescence [1]. SSPE is characteristically accompanied by personality changes and mental corruption. These are followed by myoclonies, atony, dementia, pyramidal system findings, autonomic disorders, and extrapyramidal system findings [2]. The progression speed of the disease varies, and the patients are typically lost 1-3 years after disease onset [3,4]. The early stage of the disease has an insidious onset and slow progression. Aphasic, apractic, and agnostic symptoms along with intellectual impairment and personality changes. Myoclonic and atonic seizures, decerebrate rigidity, increased hypotonia as well as and difficulty in breathing and swallowing occur in advanced stage. [5,6]. SSPE has no known definitive cure. However, antiviral and immunomodulator drugs are used either alone or in a variety of combinations. Acute cerebrovascular disease may change cardiovascular and autonomic function. Clinical studies have shown that it may result in cardiac function changes including acute cerebral lesions (stroke, hemorrhage, convulsion, etc.), hypertension, arrhythmia, myocardial necrosis, and sudden death. Damage in the cortex, amygdala, lateral hypothalamus and brain cells result in either sympathetic or parasympathetic autonomic dysfunction [7].In neurological disorders including cerebral palsy, epilepsy, stroke, and Wilson's disease, autonomic dysfunction was identified by analysis of heart rate variability.

Depressed heart rate variability showing decreased vagal activity directly affects the heart. Thus, it causes the sympathetic mechanism to become dominant and causes cardiac electrical imbalance, life-threatening arrhythmias and sudden death [8]. Previous studies demonstrate that autonomic dysfunction shows progress in SSPE. Increased epileptic activity and intracranial pressure in patients with SSPE result in autonomic imbalance. Decreased heart rate variability can be the harbinger of arrhythmia and sudden death [9].Cardiac arrhythmias developing as a result of autonomic dysfunction may cause sudden death by impairing cardiac functions.

Used to evaluate cardiac functions, telecardiography and electrocardiography are now replaced by conventional echocardiography and tissue Doppler echocardiographic methods. Ejection fraction (EF) and myocardial performance index (MPI), which can be measured by traditional methods of echocardiography, are quite valuable in demonstrating the functions of ventricles [10]. In recent years, MPI has been measured with this technique upon widespread use of tissue Doppler echocardiography technique in children [11] and [12]. In earlier studies, heart rate variability has been identified in patients with SSPE. Heart rate variability depends on the effects of the sympathetic and parasympathetic activity in the sinus node. Sympathetic and parasympathetic imbalance may change the cardiac rate and cause cardiac arrhythmia [8] Autonomic dysfunction has been shown to evolve in cerebral palsy, epilepsy, stroke, and Wilson's disease [13]. Based on these studies, low heart rate variability has been found in patients with SSPE as a result of autonomic dysfunction, with no meaningful difference were detected between the stages [9]. There are a limited number of studies focusing on the cardiac functions of these patients. This study evaluates the phenomenon of cardiac functions in 49 patients with SSPE using pulsed (PD) and tissue Doppler echocardiography (TDE).

METHODS

The study is a prospective observational study, and 49 patients (17 female, 32 male) with SSPE at the Pediatric Neurology Clinic were included in the study. Patients were classified by Risk staging system as follows: Stage 1: Psycho-intellectual symptoms. Stage 2A: Stereotypical episodes, but able towalk unassisted. Stage 2B: Stereotypical episodes, unable to walk unassisted. Stage 2C: Bedridden due to attacks. Stage 3A: Small number of spontaneous movements; responds to stimuli. Stage 3B: Vegetative responses to noxious stimuli there. Stage 3C: A deep coma, and death [6].

Patients were divided into two groups: Stage 2 (n=29) and Stage 3 (n=20). The mean age was 10.7±2.3 years in Stage 2, 10.9±1.97 years in Stage 3, 10.8±1.8 in control group. Systolic and diastolic cardiac functions were examined by echocardiography. Ejection Fraction (EF) and SF (Shortening Fraction) and the E/A ratio (the ratio of early dia-

stolic myocardial velocity to late diastolic myocardial velocity) for left and right ventricles were evaluated using left ventricular M-mode measurements, and MPI (Myocardial Performance Index) was evaluated by TDI (Tissue Doppler Imaging).

The study was commenced after their families were duly informed.

Echocardiographic evaluations

Right and left ventricular functions of patients were examined using Pulsed (PD) and Tissue Doppler Imaging (TDI) methods at the Pediatric Cardiology and Echocardiography Clinics. Echocardiographic examinations were performed using a GE Vivid 4 echocardiography device and 3S (2-4 MHz) probes. Echocardiographic examinations were performed as per the standard imaging techniques recommended by the American Society of Echocardiography [12]. Measurements for each patient were made three times on the by an experienced children's cardiologist and their averages were taken. Shortening Fraction (SF) and Ejection Fraction (EF) that reflect systolic cardiac functions were calculated from M-mode measurements of the left ventricular. PD echocardiographic examinations were performed with a Pulsed Doppler from the apical four-chamber position. A sample volume (2-5 mm) was placed at the tip of the mitral and tricuspid valve and flows were taken by Pulsed Doppler. Tissue Doppler Echocardiographic examinations were performed from the apical four-chamber position. The sample volume was placed on the lateral edges of the mitral and tricuspid annulus and the Doppler beams were aligned as parallel as possible to the corresponding myocardial wall segment in order to enhance the quality of signals. We tried to keep the angle between the Doppler beams and the longitudinal movement of the ventricle as small as possible. The synchronous recordings of Doppler velocity were obtained at a time resolution of 50 mm/s and 5 ms. Doppler signal quality was obtained by reducing the Nyquist limit to 10-30 cm/s, and the scan speed to a minimum of 100 mm/s.

Calculation of the Myocardial Performance Index (Tei Index)

Myocardial Performance Index was calculated by Tissue Doppler echocardiography technique using the formula MPI=(a-b)/b, where a is the time between the beginning and the end of peak atrial systolic velocity (Am) and the start of peak early myocardial velocity (Em), and b as the time between the start and end of the myocardial systolic wave velocity (Sm) [12].

Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 13.0 (Shareware, USA) was used for statistical analysis purposes. The results were given as mean±standard deviation (SD). Kolmogorov-Smirnov and parametric "t" test was used to compare the data of patients between the group. $p \leq 0.05$ was taken as the statistical significance value.

RESULTS

49 SSPE patients (17 female, 32 male) were included in the study. Patients were divided into two groups as Stage 2 (n = 29) and Stage 3 (n = 20) using a risk-based staging system. The mean age was found 10.7±2.3, 10.9±1.97, 10.8±1.8 years in Stage 2, Stage 3 and control group, respectively. Electrocardiogram was performed in all patients. No electrocardiographic changes such as bradycardia, ST-T alteration, premature contraction, bundle branch block, atrioventricular block, atrial and ventricular arrhythmias were detected in the patients. The mean heart rate was100±17 beats/min. in stage 2 SSPE, 104 ±19 beats/min. in stage 3 SSPE, 85±13 beats/min in control group ($p<0.001$). Sinus tachycardia (>100 beats/min in children) was detected in19 (38.7%) patients (Evre 2 and 3 SSPE). The chest roentgenograms were normal in all patients on admission. Echocardiography was performed in all patients. In the Stage 2 group, EF:69.9±6.4 ; SF:39.2±5.58; E/A(mitral):1.5± 0.21, E/A (tricuspid):1.37±0.26 ; and MPI (mitral):0.38±0.03 and MPI (tricuspid): 0.39±0.10. And in the Stage 3 group, EF:68.5±7.0, SF:37.8±5.34, E/A(mitral):1.5±0.15, E/A (tricuspid):1.36±0.30, MPI(mitral):0.37±0.09 and MPI (tricuspid):0.38±0.12. In the control group EF:70.96±5.54; SF:39.96±5.05. E/A(mitral):1.53±0.16, E/A (tricuspid):1.39±0.20 and MPI(mitral):0.35±0.06 MPI(tricuspid):0.36±0.04 ($P>0.05$). Conventional echocardiographic systolic function and diastolic function parameters, such as EF and FS, mitral and tricuspid E and A wave ratios, did not differ significantly. There were not statistically significant differences regarding parameters such as MPI ob-

served by tissue Doppler methods for right and left ventricles. Results of conventional and tissue Doppler imaging systolic and diastolic parameters are shown in Table 1.

Table 1. Demographic and echocardiographic characteristics of patients and the controls

	Stage 2 SSPE n= 29	Stage 3 SSPE n= 20	Control n=26	p	p'
Age(years)	10.7±2.3	10.9±1.97	10.8±1.8	NS	NS
Gender(male/female)	19/10	13/7	17/9	NS	NS
Heart rate(beat/min)	100± 17	104± 19	85± 13	<0.001	<0.001
EF (%)	69.9±6.40	68.5±70	70.96±5.54	NS	NS
SF (%)	39.2±5.58	37.8±5.34	39.96±5.05	NS	NS
Mitral E/A ratio	1.5±0.21	1.5±0.15	1.53±0.16	NS	NS
Tricuspid E/A ratio	1.37±0.26	1.36±0.30	1.39±0.20	NS	NS
MPI (mitral)	0.38±0.03	0.37±0.09	0.35 ± 0.6	NS	NS
MPI(tricuspid)	0.39±0.10	0.38±0.12	0.36 ±0.04	NS	NS

EF: Ejection Fraction, SF: Shortening Fraction, E: Early diastolic myocardial velocity, A:Late diastolic myocardial velocity, MPI: myocardial performance index observed by tissue Doppler method.

P: Stage 2 SSPE group compared with the control group. P': Stage 3 SSPE group compared with the control group. NS: no significant

DISCUSSION

A progressive and inflammatory viral disease of the central nervous system caused by progressive measles infection, SSPE is typically a fatal neurodegenerative disease. The disease has a variable progression speed and the patient is usually lost in 1-3 years. Many systems suffer dysfunction with increased disease stage [1]. Particularly as a result of autonomous system disorder, patients face difficulties in urination and defecation. Although there are limited cardiovascular system evaluations in this patient group, studies show heart rate variation and laziness as a result of autonomous dysfunction, however its direct relationship with mortality was not shown. [9]. In our study, we evaluated the cardiac functions of the same group of patients and investigated whether they had any cardiac function abnormalities in the advanced stage. Autonomic dysfunction present in this patient group was found to make functional changes that could result in sudden death [9]. Cardiac function can be noninvasively assessed by echocardiography. Clinical trials demonstrate that acute cerebral lesions (stroke, hemorrhage, seizure) resulted in cardiac function changes including hypertension, arrhythmia, myocardial necrosis, and sudden death. Damage to the brain cells cause either sympathetic or parasympathetic autonomic dysfunctions [7].

In patients with brain damage, high intracranial pressure and low brain flow pressure were found to be associated with low cardiac rate variability and this association was found to correlate with increased mortality. Aydin ÖF et al. found reduced heart rate variability in patients with SSPE, suggesting that this could be a predicting factor for arrhythmia and sudden death [9].Again, in that study, they found reduced heart rate variability in patients even before the onset of arrhythmia. In our study, we investigated whether or not there were any statistically meaningful differences between cardiac functions between patients and control groups.

The functions of the heart were echocardiographically examined to assess systolic and diastolic functions. Echocardiography, which can show cardiac response, is a non-invasive method assessing cardiac hemodynamic and ventricular functions. MPI (Tei index) is a parameter that can be detected by tissue Doppler echocardiography, showing both the systolic and diastolic functions of both the left and right ventricular [14]. In our study, cardiac dysfunction was not detected in both groups. Ejection Fraction (EF) and Fractional Shortening (FS) are

currently the most commonly used methods to measure myocardium contractility and myocardial systolic functions [15]. EF is known to be affected from heart rate, contractility, and preload and afterload. In our study, M-mode echocardiographic examination found the systolic functions of the left ventricular of Stage 2 and 3 measured by EF and FS to be in the normal range and no meaningful differences were found between the groups in terms of EF and FS ($p>0.05$). From a hemodynamic point of view, diastole is divided into four phases: isovolumic relaxation, rapid filling, diastasis, and atrial contraction [16]. The most common assessment is that the peak E velocity is primarily determined by ventricle relaxation and ventricle compliance of peak A velocity. The E/A ratio shows diastolic dysfunction. In our study, this ratio was found over 1, meaning that it is normal. Tei index, or, in other words, the myocardial performance index is a parameter noninvasively showing both the systolic and diastolic functions of the left and right ventricles [17]. Myocardial Performance Index was calculated by Tissue Doppler echocardiography technique using the formula MPI=(a-b)/b, where a is the time between the beginning and the end of peak atrial systolic velocity (Am) and the start of peak early myocardial velocity (Em), and b as the time between the start and end of the myocardial systolic wave velocity (Sm) [18,19].

In conclucion, we did not detect any considerable cardiac dysfunction in patients with SSPE except for sinus tachycardia.This shows that cardiac functions can be improved during the terminal periods of patients with SSPE, which is group of chronic and bedridden patients and that cardiac functions constitute no significant risks of mortality.

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