ภาวะทางหัวใจของผู้ป่วยโรคไข้รูมาติกเมื่อติดตามผู้ป่วยในเวลา 5 ปี ที่มารับการรักษาในโรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น

Cardiac Sequelae of Patients with Rheumatic Fever during a Five-year Follow-up in Srinagarind Hospital of Khon Kaen University

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บทคัดย่อ

การติดตามภาวะความผิดปกติทางหัวใจในผู้ป่วยโรคไข้รูมาติก ด้วยการตรวจ echocardiography ยังมีข้อมูลไม่มาก คณะผู้วิจัยได้ทำการศึกษาเปรียบเทียบผลการตรวจ echocardiography ในผู้ป่วยโรคไข้รูมาติกที่เป็นครั้งแรกและ 5 ปีหลังจากนั้น โดยทำการศึกษาในผู้ป่วยโรคไข้รูมาติกในโรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ตั้งแต่ มกราคม 2535-ธันวาคม 2546 การศึกษาพบว่าในจำนวนผู้ป่วย 110 คน มี 75 คน (ร้อยละ 68) มีภาวะหัวใจอักเสบจากการตรวจเมื่อเป็นครั้งแรก ผู้ป่วยทั้ง 75 คนที่มีภาวะหัวใจอักเสบ ทุกรายมีความผิดปกติทางหัวใจจากการตรวจ echocardiography สำหรับผู้ป่วยที่ไม่มีหัวใจอักเสบ มี 35 คน (ร้อยละ 32) ไม่มีภาวะหัวใจอักเสบแต่มีความผิดปกติทางหัวใจจากการตรวจ echocardiography เป็นจำนวน 7 คน(ร้อยละ 20) ในผู้ป่วยที่มีหัวใจอักเสบแต่เริ่มแรก 75 คน เมื่อติดตามไป 5 ปีพบว่ายังมีลิ้นหัวใจรั่วจากการฟัง 29 คน (ร้อยละ 39) แต่ยังมีความผิดปกติจาก echocardiograms 38 คน (ร้อยละ 51) จากการศึกษานี้พบว่าการตรวจ echocardiography มีประโยชน์ในการช่วยวินิจฉัยภาวะหัวใจอักเสบในผู้ป่วยที่เป็นครั้งแรก และมีประโยชน์ในการช่วยติดตามภาวะทางหัวใจในระยะ 5 ปีหลังการเกิดโรคครั้งแรก

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Abstract

The natural history of valvular regurgitation detected by echocardiography in acute rheumatic fever has been lacking. Clinical assessment and transthoracic color Doppler echocardiography were performed for each patient with an initial attack of acute rheumatic fever (Khon Kaen University, Thailand; 1992-2003) at the time of their presentation. Clinical examinations and echocardiography were done for each at five-year follow-up. Of 110 patients, 75 (68%) had carditis (valvulitis) evident by auscultation at the time of the initial attack. Seven (20%) of the 35 patients with no clinical evidence of carditis had echocardiographic evidence of acute valvular regurgitation (subclinical valvulitis). All 75 patients with carditis had echocardiographic evidence of acute mitral regurgitation. Of the 75 patients with carditis regularly followed, the persistence of a heart murmur and significant valvular regurgitation by echocardiography were 39% (29/75) and 51% (38/75) at five-year follow-up. This suggests that an echocardiographic examination in the patients with initial attack of acute rheumatic fever has more benefit than the usual auscultatory method in the early diagnosis of rheumatic carditis (valvulitis) and also beneficial is at five-year follow-up of rheumatic valvular heart disease.

คำสำคัญ: โรคไข้รูมาติก คลื่นเสียงสะท้อนหัวใจ หัวใจอักเสบ

Keywords: Acute rheumatic fever, Echocardiography, Rheumatic carditis

Introduction

Acute rheumatic fever is common and remains the leading cause of heart disease among children and adolescents in many developing countries (Kaplan, 1993). However, the resurgence of acute rheumatic fever documented in the United States beginning in the mid-1980s and continuing through 1999, has re-emphasized the need for better understanding of its natural history (Veasy et al., 1987; Kaplan, 1993; Veasy et al., 1994).

There are reports of subclinical mitral regurgitation demonstrated by color Doppler echocardiography in small numbers of patients with acute rheumatic fever (Folger et al., 1992; Swedo, 1994; Elevli et al., 1999; Figueroa et al., 2001). However, echocardiographic follow-up studies of patients with acute rheumatic fever have been reported with few patients (Figueroa et al., 2001) and with short durations of follow-up (Folger et al., 1992; Vasan et al., 1996). To date, however, the natural history of valvular regurgitation detected by echocardiography in acute rheumatic fever has been lacking.

We therefore conducted clinical examinations and color Doppler echocardiography in a cohort of patients who had an apparent initial attack of acute rheumatic fever to clarify the natural history of valvular involvement over time in those with carditis and those without carditis.

Methods

Patients

Between January 1992 and December 2003, consecutive patients having a first recognized episode of acute rheumatic fever fulfilling the revised Jones' criteria (American Heart Association, 1984), who presented to the Pediatric Department, were included in this study. Written informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the

1975 Declaration of Helsinki. This paper reports only data related to the patients with an initial attack of acute rheumatic fever.

Diagnosis of carditis was based on auscultatory finding of either mitral regurgitation or aortic regurgitation or both. The patient was considered to have mitral regurgitation if there was a characteristic pansystolic murmur maximal at the apex with radiation to left axilla. Aortic regurgitation was considered to be present if an early diastolic murmur was detected along the left sternal border. All systolic murmurs were graded on the scale of six described by Levine (Levine, 1993). Two qualified pediatric cardiologists independently categorized the patients according to murmur types, location, intensity and transmission; the auscultatory diagnosis was based on the agreement of both. A prolonged P-R interval alone was not considered an indication of carditis because its presence was not significantly related to the existence, severity, or outcome of cardiac damage (Feinstein, 1964).

A detailed history was obtained for each patient to determine the exact time of onset of illness, its chronological development, the presenting complaints, treatment received, and other pertinent clinical features. A routine complete blood count, erythrocyte sedimentation rate, C-reactive protein test, throat swab culture for group A streptococci, antistreptolysin O titer, antideoxyribonuclease B titer, chest roentgenogram, electrocardiogram, and color Doppler echocardiography were performed in each patient at enrollment.

Study Protocol

Patients with mild carditis were treated with aspirin (Panamonta, 1993). Patients with carditis and with cardiomegaly but without congestive heart failure (moderate carditis) were treated with corticosteroids (Panamonta, 1993). Injectable benzathine penicillin (1.2 million units) was initiated and continued every four weeks for secondary prophylaxis regardless of the patients' age or weight.

All 110 patients had a complete color Doppler echocardiographic evaluation at the time of enrollment. Each patient was examined in the Rheumatic Fever Clinic by two pediatric cardiologists every four weeks for the first six months and then every 3 months. At each visit, thorough histories including checks for sore throat, fever, arthralgia, arthritis, nocturnal cough, orthopnea, ease of fatigue, abnormal movement, subcutaneous nodules, and erythematous skin rash were taken. The documentation of auscultatory change was based on the agreement of these two pediatric cardiologists. Each patient was re-evaluated by color Doppler echocardiography at five years after the initial attack of rheumatic fever.

Echocardiographic Examination

Transthoracic color Doppler echocardio graphy was performed within three days of establishment of the diagnosis of acute rheumatic fever or Sydenham's chorea and before starting anti-inflammatory treatment. The echocardiographic operator was not informed of the severity of the acute rheumatic fever or the cardiac findings of the patients. The echocardiographic study was performed with a Hewlett-Packard Sonos 1000 or 5500 machine equipped with 2.5-, 3.5-, and 5-MHz transducers (Hewlett-Packard Inc, Andover, Massachusetts, USA).

A standardized M-mode, cross-sectional, color-flow-mapping and Doppler echocardiographic

examination was performed with multiple orthogonal parasternal, apical, and subcostal views. Two-dimensionally guided M-mode and two-dimensional echocardiographic tracings were analyzed for chamber enlargement, fractional shortening, valve morphology and pericardial effusion (Sahn, et al., 1978). Doppler color-flow-imaging was performed with the use of a standard velocity color map. Flow directed toward the transducer was conventionally coded in yellow-red and flow away from the transducer was coded in blue (Folger et al., 1992; Veasy et al., 1994).

Mitral regurgitation was assessed in both the two-chamber (long axis) and four-chamber views. For differentiation from physiologic regurgitation, mitral regurgitation was defined by the following three criteria:

1. Presence of a mosaic color regurgitation jet in at least two planes (Folger et al., 1992; Veasy et al., 1994; Elevli et al., 1999; Figueroa et al., 2001).

2. Regurgitating flow sample covering almost the entire systole by pulsed or continuous wave Doppler (Folger et al., 1992; Veasy et al., 1994; Elevli et al., 1999; Figueroa et al., 2001).

3. Doppler velocity regurgitation signals with pulsed or continuous waves close to that expected for the Bernoulli-predicted pressure gradient between left ventricle and left atrium (Sahn and Maciel., 1988; Elevli et al., 1999).

For aortic regurgitation, the apical five and the parasternal long axis views were used and only a high velocity diastolic mosaic color jet in at least two planes was accepted (Sahn and Maciel., 1988; Veasy et al., 1994). Regurgitation in the immediate vicinity of the valve leaflets was considered physiological.

Tricuspid regurgitation was evaluated in the apical four-chamber view and parasternal-short/long-axis-tricuspid-views. Tricuspid regurgitation was defined as systolic flow following tricuspid valve closure for almost the entire systole (Sahn and Maciel., 1988). Mosaic color flow jets in at least two planes fulfilled this criterion (Sahn and Maciel., 1988). The Doppler velocity regurgitation signals with pulsed or continuous wave should be close to those expected for the Bernoulli-predicted pressure gradient between right ventricle and right atrium (Sahn and Maciel., 1988).

All examinations were recorded on half-inch videotape for reviewing and analysis. Two of the authors (M.P. and A.C.) who were not aware of the clinical findings interpreted the echocardiographic data. The documentation of echocardiographic change was based on the agreement of the two authors.

Statistical Analysis

The data were analyzed with a computer using the SPSS program for Windows version 9 (SPSS Inc, Chicago).

Results

All 110 patients included in this study had their first attack of acute rheumatic fever without any previous history of acute rheumatic fever. The average age at enrollment of the 61 boys and 49 girls was 9.0+2.5 years (range, 4 to 15 years). Thirty-five patients (32%) had neither the murmur of mitral regurgitation nor aortic regurgitation with the initial attack of acute rheumatic fever. Of these 35, seven (20%) had evidence of significant acute valvular regurgitation by color Doppler echocardiography: mitral regurgitation in 3 cases,

mitral and aortic regurgitations in 2 cases, and mitral and tricuspid regurgitations in 2 cases. Seventy-five patients (68%) had auscultatory findings of valvular regurgitation. Of these 75, 42 (56%) were considered to have mild carditis and only three (4%) was considered to have severe carditis. All of the 75 patients had echocardiographic evidence of pathologically significant valvular regurgitation: mitral regurgitation in 41 cases, aortic regurgitation in 3 cases, mitral and aortic regurgitations in 9 cases, mitral and tricuspid regurgitations in 20 cases, and mitral, tricuspid and pulmonic regurgitations in 2 cases (Table 1).

Of the 75 patients with carditis regularly followed, the persistence of a heart murmur and of pathologically significant valvular regurgitation by echocardiography were 39% (29/75) and 51% (38/75) respectively at the duration of the 5 + 1.2 years follow-up (Table 2).

Of the 35 patients without carditis regularly followed, there was no heart murmur but pathologically significant valvular regurgitation by echocardiography was seen in 2.8% (1/35) at the duration of the 5 +1.2 years follow-up (Table 3).

Discussion

Although Doppler echocardiographic evidence of carditis in patients having acute rheumatic fever has been observed since 1987 (Veasy et al., 1987; Folger et al., 1992; Swedo, 1994; Veasy et al., 1994; Elevli et al., 1999; Figueroa et al., 2001), long-term follow up of these patients has never been attempted to our knowledge. Many observers contend that pathological subclinical mitral regurgitation can be differentiated from nonpathological mitral regurgitation when the regurgitant flow is holosystolic and accompanied by a mosaic pattern on color-flow Doppler studies (Folger et al., 1992; Veasy et al., 1994; Figueroa et al., 2001). Some authors recommend that the criteria should include the length of mosaic color jet > 1 cm (Folger et al., 1992; Veasy et al., 1994) while some others do not agree with these criteria (Elevli et al., 1999; Figueroa et al., 2001). The length of the mosaic color jet > 1 cm was not included in our color Doppler criteria for mitral regurgitation but in retrospect, all our patients having mitral regurgitation by the above criteria also had color jet length more than of 1 cm. We do not include systolic pulmonary venous flow reversal in our color Doppler echocardiographic criteria for mitral regurgitation although it is a useful method for the evaluation of the severity of mitral regurgitation (Eren et al., 2001). We had echocardiographic evidence of acute pathological valvular regurgitation in seven patients (20%) who initially had no carditis. Furthermore, an echocardiographic follow-up of 75 patients with carditis had a minimal incremental superiority in detection of valvular regurgitation over the usual auscultatory method (51% versus 39%) at five-year follow-up.

The course of rheumatic carditis is an important aspect of acute rheumatic fever (Taranta and Stollerman, 1956; Taranta, 1959; Aron et al., 1965; Swedo, 1994; Special writing group of the committee on rheumatic fever, endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association, 1992). The present study confirms the previous findings that all patients who are initially free of rheumatic carditis during acute rheumatic fever will be free of heart disease if there is no recurrence (Majeed et al., 1965; Tompkins et al., 1972).

In conclusion, where color Doppler echocardiography is available, it should be used in all patients with acute rheumatic fever, regardless of their presentation. This suggests that an echocardiographic examination in patients with an initial attack of acute rheumatic fever has more benefit than the usual auscultatory method in the early diagnosis of rheumatic carditis (valvulitis) and also benefits at five-year follow-up of rheumatic valvular heart disease (Panamonta et al., 2004).

Acknowledgements

This work is supported by a grant from Khon Kaen University.

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Table 1 Clinical characteristics of acute rheumatic fever patients with and without carditis at the time of the initial diagnosis.

Clinical characteristics of acute rheumatic fever	Carditis (75 cases)	Without carditis (35 cases)	Probability value
Age (yrs) (mean ± SD)	8.5 ± 2.4	10.3 ± 2.6	NS
Male	43	22	NS
Female	32	13	NS
Cardiomegaly	45	0	< 0.05
Prolonged PR interval	19	5	< 0.05
Echocardiographic abnormalities	MR 41	MR 3	< 0.05
	AR 3	AR 0	NS
	MR+AR 9	MR+AR 2	NS
	MR+TR 20	MR+TR 2	NS
	MR+TR +PR 2	MR+TR +PR 0	NS
Echocardiographic LV Fractional shortening	37.0 ± 2.0	38.1 ± 2.1	NS

Table 2 Follow-up of the patients with carditis (75 cases).

Clinical characteristic of acute rheumatic fever	Numbers of patients with initial abnormalities (cases)	Numbers of patients with follow-up abnormalities (cases)
Heart murmurs	75	29
Echocardiographic abnormalities	75	38
MR	41	15
AR	3	3
MR+AR	9	6
MR+TR	20	13
MR+TR+PR	2	1

Table 3 Follow-up of the patients without carditis (35 cases).

Clinical characteristic of acute rheumatic fever	Numbers of patients with initial abnormalities (cases)	Numbers of patients with follow-up abnormalities (cases)
No heart murmurs	35	0
Echocardiographic abnormalities	7	1
MR	3	0
MR+AR	2	1
MR+TR	2	0