

Original Article

Clinical assessment and echocardiography follow-up results of the children with acute rheumatic fever

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Abstract. Acute rheumatic fever (ARF) is an inflammatory collagenous tissue disease which shows its cardinal signs in joints, heart, skin and nervous system while affecting whole connective tissue system more or less. This study was conducted in order to investigate the clinical pattern and severity of ARF, echocardiographic findings and the course of the patients with heart valve involvement by studying the clinical and laboratory aspects of the patients diagnosed with ARF according to updated Jones Criteria. The study included 214 patients diagnosed with ARF for the first time between January 2005 and May 2008. All patients were scanned with doppler echocardiography (ECHO) between certain intervals. Severity of carditis was grouped into 3 groups of mild, moderate and severe. The frequency of carditis was 57.9%, arthritis was 73.4%, chorea was 11.7% and erythema marginatum was 0.9% but no subcutaneous nodules. Recovery was observed in 22% of the cases of isolated aortic insufficiency (AI), 50% of the cases with isolated mitral insufficiency (MI) and 80% of the cases with mitral and aortic insufficiencies together (MI+AI). Recovery in isolated MI was significantly much more than recovery in isolated AI. However, recovery in AI was significantly much more than in MI in cases of mitral and aortic insufficiencies together. In conclusion, ARF is a cause of acquired and preventable heart disease and it can be reversed through right diagnosis and appropriate treatment. Isolated mitral insufficiency, isolated aortic insufficiency and both mitral and aortic insufficiency are observed during a valvular disease. Remission among valvular diseases are most commonly in those with mitral insufficiency and remissions in both mitral and aortic insufficiency occur most commonly in aortic ones. Regular prophylaxis is the key element for long term prevention of patients with ARF.

Keywords: Acute rheumatic fever, echocardiography, children, carditis, mitral insufficiency, aortic insufficiency

Introduction

Acute rheumatic fever (ARF) is a systemic inflammatory disease that can involve heart, joints, skin, subepidermal tissues and brain. It is a result of a delayed reaction to acute pharyngeal infections caused by Group A β -Hemolytic Streptococci. ARF can manifest with arthritis, carditis, subcutaneous nodules, and erythema marginatum and sydenham chorea in a certain amount of time (approx. 3 weeks) after the infection. ARF doesn't necessarily develop in every individual who had streptococcal pharyngitis. Probability of ARF developing is 0.5-3%. As the most important cause of mortality and morbidity of the disease is carditis, it can cause heart failure and death due to pancarditis during acute phase. However, most common result is development of permanent dysfunction of the affected heart valves like stenosis or insufficiency which happens years after the episode [1, 2].

Although incidence is getting low in developed countries during the century, it is still a significant public

health problem in developing countries [3].

T. Duckett Jones established criteria concerning ARF and recurrences in 1944. These criteria, which are used today, were reviewed preserving the core features in 1965 and 1984 and in 1992 they took their latest form [4].

This study was conducted in order to investigate the clinical pattern and severity of the disease, echocardiographic findings and the course of the patients with heart valve involvement by studying the clinical and laboratory aspects of the patients diagnosed with ARF according to updated Jones Criteria.

Materials and Methods

This study included 214 patients diagnosed with acute ARF for the first time between January 2005 and May 2008 at the Pediatric Clinic of Istanbul Bakırköy Obstetrics and Pediatrics Research and Training Hospital. Approval by the Ethics Committee of the Istanbul Bakırköy Obstetrics and Pediatrics Research and Training Hospital

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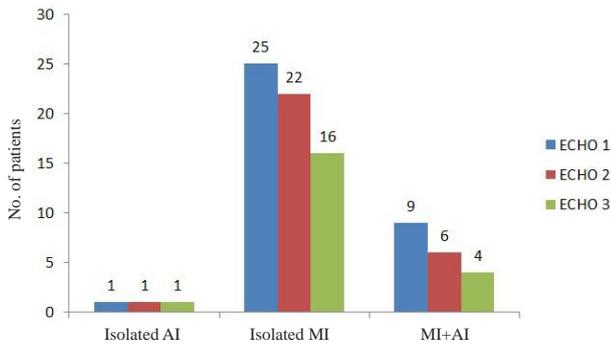


Figure 1 Echocardiography follow-up findings in patients with carditis.

(Ref. No. 131). Patients were diagnosed as ARF according to the Jones Criteria updated in 1992. Findings were recorded from the patient follow-up file. In all patients, complete blood count (CBC), erythrocyte sedimentation rate (ESR), Anti-streptolysin O (ASO), C-reactive protein (CRP) and throat swab cultures were studied. A 12-Lead electrocardiogram (ECG) and teleradiography (TELE) were done. Cardiomegaly was graded according to the cardiothoracic ratio in teleradiographic study. Cardiothoracic ratio over 0.5 was defined as cardiomegaly in older children. All patients were scanned with doppler echocardiography between certain intervals. ECHO at the time of the diagnosis was recorded as ECHO1, one after acute inflammation was recorded as ECHO2 and the last one done during follow-up was recorded as ECHO3. All echocardiographies were done by the same pediatric cardiology specialist.

Carditis was diagnosed according to physical examination and auscultatory findings. Any valve insufficiency detected by doppler ECHO but normal according to physical examination or auscultation was not used as a diagnostic criteria alone. Severity of carditis was grouped into 3 groups as mild, moderate and severe. Carditis without cardiomegaly was considered as mild carditis, carditis with cardiomegaly without heart failure was assigned as moderate carditis and carditis with advanced cardiomegaly and congestive heart failure and/or pericardial involvement was set as severe carditis [5, 6].

Grading of the valve insufficiency was done by measurement of the aortic and mitral jet length detected by Doppler ECHO. Grade 1 was ≤ 1.5 cm, Grade 2 was 1.5-2.9 cm, Grade 3 was 3-4.4 cm and Grade 4 was ≥ 4.5 cm [7]. Grade 1 was grouped as mild, Grade 2 as moderate and grade 3 and 4 as severe. Other factors were fever (axillary temperature of 38°C or above), CRP (≥ 5 g/L positive and < 5 g/L negative), prolonged PR interval (PR interval in ECG being longer than upper limit according to age and heart rate), prolonged QTc interval (QTc interval in ECG being longer than upper limit according to age and heart rate), elevation of ASO (above 250 Todd units), elevation of ESR (20 mm/h or above) and leukocytosis (white blood cell count over 10000/mm³).

Statistical analysis

The SPSS 15.0 statistical software (SPSS Inc.,

TABLE 1
DISTRIBUTION OF MAJOR CRITERIA

Major criteria	No. (%)
Isolated	
Carditis	31 (25.0)
Arthritis	75 (35.0)
Chorea	15 (7.0)
Erythema marginatum	1 (0.5)
Subcutaneous nodules	0 (0)
Combined	
Arthritis-carditis	82 (38.3)
Carditis-chorea	10 (4.7)
Carditis-erythema marginatum	1 (0.5)

TABLE 2
DISTRIBUTION OF MINOR CRITERIA AND SUPPORTING SIGNS

Minor criteria	No. (%)
Fever	140 (65.4)
Arthralgia	108 (50.5)
Prolonged PR interval	50 (23.4)
Acute phase reactants	
CRP positivity	63 (29.4)
Elevation of ESR	149 (69.6)
Leukocytosis	80 (37.4)
Supporting signs	
Elevation of ASO	199 (93.0)
Positive throat culture	23 (10.7)

Chicago, IL) was used to analyze the data. During the analysis of the data, Chi-Square and analysis of variance was used in comparison along with definitive statistical methods (average, standard deviation, frequency). Results were in 95% confidence interval and statistical significance was $p < 0.05$.

Results

Age at presentation of patients with ARF was between 5 and 15, average 11.09 \pm 2.61 and male to female ratio was 1/1. Season of the presentations was most often in spring (36.9%) and least often summer (10.7%). Family history of the disease was seen in 5.1% of cases and 94.9% of the cases had no family history.

As reviewing distribution of the cases according to the major Jones Criteria, we've seen carditis in 57.9%, arthritis in 73.4%, chorea in 11.7%, erythema marginatum in 0.9% but no subcutaneous nodules (Table 1).

As reviewing distribution of the cases according to the minor Jones Criteria, we've seen fever in 65.4%, arthralgia in 50.5%, prolonged PR interval in 23.4%, elevation of one and/or two acute phase reactants in 69.6. ASO elevation was seen in 93% of the patients, and throat cultures were

positive in 10.7% of the patients. Reviewing the distribution of the presenting symptoms, 86.9% of them had joint problems, 11.7% had involuntary movement, 9.3% had chest pain, 7.5% had trouble in breathing and 1.4% had racing heartbeat (Table 2).

We detected that carditis was accompanied by cardiomegaly in 30.6% of the patients, heart failure in 16.9% of them and pericardial effusion in 4% of the patients. Of the total of 124 cases who had carditis, 69.3% had mild, 12.1% had moderate and 18.5% had severe carditis.

As reviewing distribution according to ECHO1 findings in patients with carditis, 62.2% of them had isolated mitral insufficiency (MI), 32% had mitral and aortic insufficiencies together (MI+AI) and 5.7% had isolated aortic insufficiency (AI). While of the patients with aortic insufficiency, 90% had mild and 10% had moderate carditis, and of the patients with mitral insufficiency, 56.7% had mild, 24.7% had moderate and 18.6% had severe carditis.

As reviewing distribution according to ECHO2 findings after acute inflammation in patients with carditis, 4.4% of the patients had isolated aortic insufficiency, 62.3% had isolated mitral insufficiency, 24.5% had mitral and aortic insufficiencies together and 8.8% had recovered.

As reviewing distribution according to ECHO3 findings in patients with carditis, 4.4% of the patients had isolated aortic insufficiency, 62.9% had isolated mitral insufficiency, 19.5% had mitral and aortic insufficiencies together and 19.5% had recovered (Fig. 1).

We detected recurrences in 2 patients who had regular prophylaxis and 25 patients who had irregular prophylaxis. Rate of recurrence was above 90% in patients who had irregular prophylaxis ($p < 0.05$). One patient who had regular prophylaxis and 4 patients who had irregular prophylaxis were operated on. Incidence of recurrence and surgery was higher in patients who had irregular prophylaxis ($p < 0.05$).

Discussion

Acute rheumatic fever is responsible for many of the acquired heart diseases. Sequela seen in adults holds its significance among valvular heart diseases [3]. The disease is commonly seen in ages between 5 to 15 years old. However, attacks have been reported in ages between 2 and 65 years old [2, 8]. Different studies conducted in different times reported an incidence higher in males as though some studies reported an incidence higher in females [9]. In our study (108 females and 106 males) no significant difference between sexes were seen. ARF is seen more commonly in winter and spring seasons when streptococcal infections are more common [10]. In our study, we had 79 patients seen in spring and 78 patients seen in winter, comprising 73.3% of all patients.

Arthritis is the most common sign of ARF. Typically, it affects bigger joints like knee, elbow, wrist and ankle. More than one joint is affected and arthritis is migratory [11]. In our study, arthritis was the most common major sign. Arthritis was seen in 57.9% of the patients and affected different joints such as ankle in 80.3% of the

patients, knee in 55.4%, elbow in 10.2% and others (hip, shoulder, and wrist) in 26% of them.

Carditis is the major sign, which is seen in 45%-50% of the patients and defines the progress of the disease, it can affect all layers of the heart. Involvement is from endocardium to pericardium; without endocardial involvement, there cannot be pericardial or myocardial involvement [12]. Endocardial involvement is seen as valvular insufficiency. While insufficiency is seen during acute illness, stenosis occurs due to fibrosis after years. Most commonly affected valve is mitral valve. Mitral insufficiency murmur is heard due to mitral involvement. Second most commonly affected valve is aortic and insufficiency murmur is heard. Tricuspid and pulmonary valves are affected rarely [10].

In our study, the incidence of carditis was 57.9 % which is consistent with the literature [12]. We've seen isolated carditis in 25% ($n=31$) of the patients; together with arthritis in 38.3% ($n=82$) of the patients, with chorea in 4.7% ($n=10$) of them and with erythema marginatum in 0.5% ($n=1$) of the patients. While first symptom which patients with carditis presents with is shortness of breath and chest pain there was significant difference with those without carditis ($p < 0.05$). While cardiomegaly was detected by TELE during first presentation in 69.4% ($n=86$) of the patients with carditis heart failure was detected in 16.9% of the patients and it is seen more in those with carditis significantly ($p < 0.05$). There was no significant difference in prolonged PR interval in patients with carditis compared to those without.

Arthralgia and positive ASO incidence in patients with carditis was significantly much more than in those without ($p < 0.05$). ESR elevation was significantly much more in patients without carditis ($p < 0.05$).

In our study, most commonly seen valvular lesion in patients with carditis was isolated mitral insufficiency 62.2% (99). 5.7% ($n=9$) of the patients had isolated aortic insufficiency, 32% ($n=51$) of the patients had aortic and mitral insufficiencies together.

Valvular lesions, which were mild in the beginning, regress and disappear in time [13, 14]. Meira et al. [14] detected 61% regression in 6 month to 7 years old surveys among mild and moderate valvular lesions. Also in our study, recoveries in transitions from ECHO1 to ECHO2 and ECHO2 to ECHO3 in isolated aortic insufficiency were equal and 22%. Recoveries were seen 21% in transition from ECHO1 to ECHO2 and 50% from ECHO1 to ECHO3 in isolated mitral insufficiency.

Recoveries were seen 50% in transition from ECHO1 to ECHO2 and 80% from ECHO1 to ECHO3 in patients with both mitral and aortic insufficiency. All recoveries but one was seen in aortic insufficiency, one was for both.

Recovery in patients with isolated mitral insufficiency was significantly more than those with isolated aortic insufficiency during approx. 12-40 months follow-up, however, recovery in isolated aortic insufficiency was more than those with both mitral and aortic insufficiency.

Chorea is a late sign of ARF. We've seen chorea in 25 patients in our study of whom 4.7% (10 patients) had carditis. The incidence of chorea was significantly higher

in females than in males (18 female and 7 male) ($p < 0.05$).

Erythema marginatum is a big macular lesion that is located in trunk and proximal portions of the limbs during the progress of ARF. It's seen in 5% of the patients [15]. We've seen erythema marginatum in 0.9% ($n=2$) of our patients. We haven't come across any subcutaneous nodules.

Prednisolone is used in the treatment of carditis in ARF. Salicylates are added to the treatment while titrating down the steroids in the last week of treatment [16]. It's been suggested that the incidence of heart disease has not changed after steroid and aspirin treatment. However, steroid treatments achieved faster acute phase responses and decline of numbers of cases undergone surgery [17, 18].

All patients were treated with benzathine penicillin and administered secondary prophylaxis. All the patients who had arthritis and mild carditis was started aspirin treatment, those with moderate or severe carditis who were treated with steroids were given aspirin during titration.

Six patients who had congestive heart failure were treated with diuretics and 2 patients with heart failure was treated with digoxin. Haloperidol was used in patients who developed chorea.

Secondary prophylaxis is the only and the most important preventive intervention that affects the progression of the disease and has a proven effectiveness. The most effective way of prophylaxis is intramuscular injections of benzathine penicillin every three weeks. Prophylaxis is the most effective preventive method today. In our study, 27 patients presented with recurrence, 2 (7%) of them had regular prophylaxis but 25 (93%) of them had irregular prophylaxis. As seen in our study, most important factor in recurrence of ARF is irregular prophylaxis. Since there is a correlation between irregular prophylaxis and surgical intervention, 5 patients who had surgery were cases with recurrences. Four of them had irregular prophylaxis but 1 patient had recurrence despite of regular prophylaxis. Among patients who had surgery, 4 of them had severe mitral insufficiency and 1 had severe mitral insufficiency and mild aortic insufficiency. Mitral valves were repaired in all patients who had surgery.

Probability of having carditis during recurring attacks was higher among patients who had carditis during the initial ARF attack [10]. Attacks occurred most commonly in first 5 years of follow-ups. Most important factors in preventing valve replacement are patient's education and compliance of prophylactic treatment along with proper dosage and timing.

In conclusion, ARF is a cause of acquired and preventable heart disease and it can be reversed through right diagnosis and appropriate treatment. Prognosis of ARF is mostly defined by carditis. Mitral and aortic valves are most commonly affected during carditis. Most commonly seen valvular diseases are isolated mitral insufficiency, both mitral and aortic insufficiencies and isolated aortic sufficiency, respectively. Mitral and aortic insufficiencies can be fixed by appropriate treatment and regular prophylaxis. Especially, isolated mitral insufficiency instead of aortic and aortic component of

both mitral and aortic insufficiencies can recover. Patients who had carditis in their first episodes have significantly high risks of having a recurring episodes. Most important factor preventing recurrence of ARF carditis is regular prophylaxis. There is a significant association between irregular prophylaxis and surgical intervention. Most commonly valve replacement is performed during surgery. Therefore, the most important element in preventing valvular replacement is appropriate dosage and perfectly-timed prophylaxis accompanied by patient education.

Conflict of interest

The authors declare no conflicts of interest and no financial support.

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