

Childhood acute rheumatic fever in Ankara, Turkey

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SUMMARY: Özer S, Hallıoğlu O, Özkutlu S, Çeliker A, Alehan D, Karagöz T. Childhood acute rheumatic fever in Ankara, Turkey. Turk J Pediatr 2005; 47: 120-124.

Patients with acute rheumatic fever (ARF) admitted to a tertiary hospital in Ankara between January 1999 and July 2002 were studied cross-sectionally to verify the clinical profile and were followed during the acute period.

All patients were investigated for throat culture, streptococcal serologic study, C-reactive protein, and erythrocyte sedimentation rate, and telecardiograms, electrocardiograms and echocardiographic study were done.

During the study period, 129 attacks of ARF were observed: 118 were initial attacks and 11 were recurrences. Age on admission was 11.2 ± 2.73 years (mean \pm SD, range: 6-21 years). Polyarthritis alone was present in 42 cases (33%), carditis alone in 33 (25%), combined carditis and polyarthritis in 36 (28%), combined carditis and chorea in 15 (12%) and chorea alone in 3 (2%). Nineteen (14%) patients with isolated arthritis and pure chorea had silent mitral and/or aortic regurgitation. Carditis was a dominant presenting manifestation, but appeared to be mild or moderate.

The present study indicates that ARF is still a significant problem in Turkey. The observation that 8.5% of the attacks were recurrent reaffirms the need for more effective secondary prevention programs.

Key words: acute rheumatic fever, rheumatic heart disease, children.

Acute rheumatic fever (ARF) is the most serious nonsuppurative sequela of group A streptococcus infection. The incidence of ARF has declined in industrialized countries since the 1950's and now has an annual incidence of around 0.5 cases per 100,000 children of school age¹. In developing countries, however, it remains an endemic disease with annual incidences ranging from 100 to 200 per 100,000 school aged children, and is a major cause of cardiovascular mortality¹. Turkey is one of the countries in which the incidence of ARF and the prevalence of rheumatic heart disease are still high^{2,3}.

We studied cross-sectionally 129 children seen between January 1999 – July 2002 with an initial attack or recurrence of ARF to verify the clinical profile.

Material and Methods

During January 1999 to July 2002; all children with an initial attack of ARF were cross-sectionally studied and followed during the acute period (first two months) at the Pediatric Cardiology Section of Hacettepe University Faculty of Medicine. Two major criteria or one major and two minor criteria are required for the diagnosis of ARF according to the revised Jones criteria, 1992 update⁴. Patients were classified in the acute attack by major and minor manifestations according to the Jones criteria. The diagnosis of Sydenham's chorea was made by excluding other causes of pediatric chorea. Polyarthritis was defined as swelling, heat, redness and tenderness or pain and limitation of motion of two or more joints. The diagnosis of carditis was based on physical findings,

auscultation and echocardiography. Silent carditis was defined as having Doppler echocardiographic findings of valvular insufficiency without clinical evidence of carditis. The following Doppler echocardiographic guidelines were used to define pathological mitral and aortic insufficiency^{5,6}. Pathologic mitral regurgitation was defined as meeting the four criteria: 1) length of color jet >1 cm, 2) color jet identified in at least two planes, 3) mosaic color jet, and 4) persistence of the jet throughout systole⁵. Pathologic aortic regurgitation was defined as substantial color jet seen in two planes extending well beyond the valve leaflets and holodiastolic high velocity spectral envelope with pulsed Doppler echocardiography⁶. Severe carditis was defined as evidence of congestive heart failure in the presence of significant valvular regurgitation. Presence of congestive heart failure, pericarditis or both was noted during the clinical course.

Information on sex, age, preceding history of pharyngitis or scarlet fever, family history of rheumatic fever and current place of residence were collected from the parents. On admission of patients to the hospital, specimens for both throat culture and streptococcal serologic study (antistreptolysin O titers). C-reactive protein and erythrocyte sedimentation rate (ESR) (Westergen method) were routinely obtained. The ASO titer was considered to be elevated if it was >320 Todd u/ml⁴. Two-dimensional and Doppler echocardiography was performed routinely (GE Vingmed Ultrasound). Telecardiograms and electrocardiograms of all patients were also obtained. The patients with carditis were treated with prednisone (2 mg/kg/day) while the others were given acetyl salicylates (75-100 mg/kg/day). Benzathine penicillin (1.2 million units for patients weighing 27 kg or more and 600,000 units for those weighing less than 27 kg) was recommended every 21 days for the prophylaxis of streptococcus.

Results

Patients

Between January 1999 and July 2002, 129 attacks of ARF were observed: 118 were initial attack and 11 were recurrent. The patients' ages were 11.2 ± 2.73 years (mean \pm SD, range 6-21 years): 91.1% of the cases occurred between 6-14 years. Age of the patients with carditis (11.09 ± 2.7) and non carditis

involvement (10.7 ± 2.2) was not significantly different. There were 71 male and 58 female patients. There was a slight male predominance (55%). All patients were Turk and 62% of them were living in Ankara. There was positive family history of rheumatic fever in 10.8%.

Clinical Manifestations

Forty-two patients had arthritis only (33%), 33 carditis (25%), 36 arthritis and carditis (28%), 15 carditis and chorea (12%), and 3 chorea (2%). Erythema marginatum and subcutaneous nodules were not observed in our patients. Nineteen patients (14%) with arthritis (17 patients) or pure chorea (2 patients) had silent valvitis demonstrated only by echocardiographic investigation but without any significant murmur (mitral regurgitation in 14, aortic regurgitation in 1 and combination of mitral and aortic regurgitation in 4 cases). Mild to moderate carditis was present in 68 patients (80%). Mitral regurgitation in 44, aortic regurgitation in 2 and combination of mitral and aortic regurgitation in 22. The mitral valve was the most commonly affected valve (97%), followed by aortic valve (35%). Severe carditis as defined by valvulitis and congestive heart failure was diagnosed in 16 (19%); five of these patients also had pericardial effusion. In each of these cases, prednisone was administered. A mitral valve replacement was carried out in one patient with severe carditis.

Only 53 patients (41%) gave a history of pharyngitis. Two patients had a history of scarlet fever. In nine patients, positive throat culture with group A streptococcus that had been treated with antibiotics was documented. Elevated ASO levels were detected in 83 (64%) of the patients. C-reactive protein was high in 93 (72%) patients. Highly elevated ESR was detected (>100 mm/h) in 18 (14%) and moderately elevated ESR (30-100 mm/h) in 77 (59%) patients. Prolonged PR or first-degree block was noted in 18 (13%) patients (Table I). Only 23% of the patients required hospitalization. None of the patients died during the acute stage of illness.

Recurrences

Eleven of 129 patients (8.5%) had a recurrent attack; all of them were the second attack. The patient age at the time of recurrence ranged from 11-21 years (median: 14 years). The

Table I. Diagnostic Criteria for 129 Children with Attack of Acute Rheumatic Fever

	Males (n=71)	Females (n=58)	Total (%) (n=129)
Major criteria			
Arthritis	28	14	42 (33)
Carditis	19	14	33 (25)
Chorea	–	3	3 (2)
Arthritis and carditis	19	17	36 (28)
Carditis and chorea	5	10	15 (12)
Minor criteria			
Fever	40	29	69 (53)
Arthralgia	55	39	94 (72)
ESR (>30 mm/h)	50	45	95 (73)
Elevated C-reactive protein	49	44	93 (72)
Prolonged P-R interval	13	5	18 (13)
ASO titer (>320 Todd u/ml)	49	34	83 (64)
Positive throat culture (Group-A β -hemolytic streptococcus)	6	3	9 (6)

ESR: erythrocyte sedimentation rate.

interval between attacks varied from 7 months-13 years (median: 5 years). Carditis was detected in 65% of patients in the present study with a first episode of ARF and in 90.9% of patients with recurrences. Penicillin prophylaxis had been discontinued in 10 of 11 patients before recurrences.

Discussion

After four decades of continuous decline in the incidence of ARF in developed countries, a resurgence was reported from several regions of the USA in the 1980s.^{7,8} Some investigators reported a persistence of ARF in the USA in the 1990s^{9,10}. In contrast to the developed countries, this disease has remained a significant problem for years in developing countries decline¹¹. We know that rheumatic heart disease is one of the most common causes of cardiovascular morbidity and mortality in developing countries. Rheumatic fever incidence has been calculated to range from 20 to 100 cases per 100,000 population in these countries¹². Although knowledge of the incidence of ARF and the prevalence of rheumatic heart disease in Turkey is rather limited, ARF is still an important problem in our country. Saraçlar et al.¹³ found the incidence of ARF in Turkey to be 20 per 100,000 children in 1972-1976. On the other hand, Beyazova et al.¹⁴ estimated it at 56.6 per 100,000 children during 1970-1973 and 36.7 per 100,000 15 years later. İmamoğlu and Özen¹⁵ showed a decrease of 0.38% in the prevalence of rheumatic heart disease over a decade. But, similar to other countries, the ARF incidence

appears to have increased in recent years. Karademir et al.¹⁶ found this incidence to be 107.7 per 100,000 in 1990-1992.

Our patients were similar in age and sex distribution to those reported previously^{3,16-18}. Arthritis was noted more in boys than in girls but the difference was not statistically significant. We had a few cases of Sydenham chorea, which occurred more in girls than in boys. The observation of female majority among patients with chorea is in agreement with the general opinion.

The clinical signs of ARF are the same throughout the world, with arthritis^{3,19} and carditis^{9,18} remaining the most commonly reported major manifestations. In this study, the dominant feature was carditis, which was found either alone or in combination with other manifestations in as many as 65%. In another study from the same region (Ankara), the frequency of carditis was found to be increased in 1990-1992 in comparison with 1985-1989¹⁶. Similarly, in the pediatric Greek population, carditis was found in 70% of patients with ARF from 1980-1997²⁰. The dominant feature was detected as carditis in the intermountain area outbreak in 1985-1992⁹. In fact, the distribution of the major criteria in these studies and ours is slightly different from that described in the literature¹. We believe that these results are partly explained by the recent use of more frequent echocardiographic examinations for the evaluation of patients with ARF. In our study, 19 (14%) patients with isolated arthritis and

pure chorea had silent carditis demonstrated by echocardiographic investigation but without any significant murmur.

The mitral valve was the most commonly affected valve (97%), followed by the aortic valve (35.2%). These findings are in line with the observations of others^{3,17-18}. Mild to moderate carditis was present in 68 patients (80%); severe carditis was diagnosed in 16 (19%). In our study, carditis was a dominant presenting manifestation, but appeared to be mild or moderate, and this observation is parallel to other studies^{9,17}. We know that more than 50% of the episodes of ARF include carditis, which often progresses gradually to chronic rheumatic heart disease¹². Our results indicate that carditis continues to be a dominant feature of the disease, and echocardiography may become a valuable tool in the diagnosis and follow-up of carditis.

In most Western series, the mortality rate during the acute stage is less than 1%¹⁹, while it is higher in some developing countries¹⁸. In our series, there was no mortality in ARF in the acute period.

An important feature of the persistence of ARF in our community has been the lack of clinical symptoms of a preceding streptococcal infection sufficiently severe to precipitate medical attention. ARF can be prevented if streptococcal infection is treated within nine years²¹, but there was no history of preceding pharyngitis in 41% of the patients in our series. Different results have been reported in the literature (28%, 50%, 55%, 73%)^{10,17,18,20}. In another recent series from the same region, a history of a preceding respiratory illness was obtained much more frequently than in our series (81%)¹⁶. Even with a higher incidence of a history of respiratory infection, medical attention has not always been sought. These are the most significant limiting factors in primary prevention of ARF. In the present study, nine patients with positive throat culture with group A streptococcus had received inadequate antibiotic treatment.

A recurrence rate of 8.5% in our series is parallel with other studies^{9,19}. Recurrences of ARF are more likely in children and less likely after puberty. We had three patients aged over 15 years. Carditis more commonly recurs in patients with a history of carditis, thus prophylaxis should be continued for a longer

period in such patients²². Carditis was detected in 65% of patients in our study with a first episode of ARF and in 90.9% of patients with recurrences. Similarly, Karaaslan et al.³ reported carditis in 91% of patients with recurrences. In another study from New York, 9 of 10 patients who had recurrent rheumatic fever had developed carditis in the period from 1969 to 1988¹⁹. Carditis was found significantly less frequent (61.4%) in first episodes compared to those having recurrent episodes (96.2%) in a recent study²³. It is important that, in this study, penicillin prophylaxis had been discontinued in 10 of 11 patients with recurrences. These findings also point out the importance of secondary prophylaxis, because we know that recurrences of rheumatic fever cause further damage to the heart valves.

Several studies have suggested that genetic susceptibility to rheumatic fever (RF) may be linked to HLA Class II alleles. Hallioglu et al.²⁴ suggested that the HLA DQA1*03 allele may be a protecting factor in Turkish children with RF. Their results also suggest that the combination of the DRB1*04 and DQA1*03 alleles may be a stronger protective factor than the DQA1*03 allele alone.

Rheumatic fever and rheumatic heart disease have a considerable adverse economic impact in developing countries. Most of the patients need hospital admission repeatedly. Primary and secondary penicillin prophylaxis has become of medical practice in developed countries and is believed to be the cause of a dramatic decline in the incidence of rheumatic fever in these countries.

In conclusion, ARF exists in the pediatric Turkish population. Carditis is a dominant presenting manifestation. Streptococcal infection is still a significant health care problem. Our study reaffirms the need for effective preventive programs for these infections.

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