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Acute Rheumatic Fever in Adults: A Retrospective Clinical Analysis of 21 patients

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โรคไข้รูมาติกในผู้ใหญ่: การศึกษาย้อนหลังถึงลักษณะทางคลินิกในผู้ป่วย 21 ราย

รัตนวดี ณ นคร

หน่วยโรคภูมิแพ้, อิมมูนโนวิทยาและรูห์มาโตวิทยา, ภาควิชาอายุรศาสตร์, คณะแพทยศาสตร์, มหาวิทยาลัยขอนแก่น

ได้ทำการศึกษาย้อนหลังในผู้ป่วยที่มีอายุมากกว่า 15 ปี ที่ได้รับการวินิจฉัยว่าเป็น acute rheumatic fever และได้รับการรักษาที่ภาควิชาอายุรศาสตร์ โรงพยาบาลศรีนครินทร์ ระหว่างปี พ.ศ.2527-2530. มีผู้ป่วยทั้งหมด 21 ราย อายุเฉลี่ย 22 ปี อัตราส่วนหญิง:ชาย = 1:1.3 ส่วนใหญ่มีประวัติของ acute rheumatic attacks มาก่อน อาการสำคัญที่พบมากเป็นอันดับหนึ่งได้แก่ carditis (80%) อันดับสองได้แก่ arthritis (47%). ผู้ป่วยที่มี carditis ส่วนใหญ่ฟังได้ murmur (82%) โดยเกิดจาก Mitral regurgitation และ Mitral stenosis ในอัตราส่วนที่เท่ากัน. การเกิด carditis นั้นอาจเกิดขึ้นเป็นครั้งแรกหรือเกิดซ้ำในผู้ป่วยที่เป็น rheumatic heart disease มาก่อนก็ได้. การรักษาส่วนใหญ่ได้ผลดี, ไม่มีผู้ป่วยที่เสียชีวิตในระหว่างที่เกิด acute rheumatic attacks. อาการแสดงทางคลินิกอื่น ๆ, ผลการตรวจทางห้องปฏิบัติการ, การป้องกันและการเกิดซ้ำ จะได้กล่าวและวิจารณ์ในรายละเอียดต่อไป

A retrospective clinical analysis of adult acute rheumatic fever was performed in 21 patients who were admitted in Srinagarind Hospital between 1984-1987. The mean age was 22 yr, sex ratio was F:M = 1:1.3 and most of them had previous rheumatic attacks. The most common major criteria was carditis (80%) and the second was arthritis (47%). Most of carditis patients had auscultatory murmurs (82%). Mitral regurgitation and mitral stenosis were equally found. The carditis could occur as the new carditis or on-top preexisting rheumatic heart diseases. All of the patients responded well to therapy and no one died in the acute phase of acute rheumatic attack. Other clinical manifestations, laboratory findings, antibiotic prophylaxis and relapse are discussed in details.

INTRODUCTION

The clinical presentation and natural history of acute rheumatic fever (ARF) and rheumatic heart diseases are not as well known in adults as in children.[1] While juvenile ARF may be overdiagnosed, on the contrary ARF may be underdiagnosed in adults because of lack of awareness of attacks in this age group.[2] Although there have been many well documented reports of ARF in adults,[1,3-14,23-25] however ARF still predominantly affects children and younger adults, but middle-aged patients may also be affected.[25]

The purpose of this clinical analysis is to consider the clinical presentations, diagnostic problems, natural history, therapeutic responsiveness and mortality in acute phase. Data of 21 patients over the age of 15 years with the diagnosis of ARF are presented and compared with other reports.

MATERIALS AND METHODS

The charts of all the patients with the diagnosis of ARF above the age of 15 years, admitted to Srinagarind Hospital, Khon Kaen University, between 1984-1987 were studied. 29 cases were found, the diagnosis cannot be confirmed in 8. The remaining 17 cases fulfilled the revised Jones' criteria of the American Heart Association for the diagnosis of ARF. Another 4 cases possible diagnosis of ARF were given because they were admitted within the first 10 days following the symptoms of previous streptococcal infection but the data of rising ASO titer were not available despite of suggestive clinical criteria.

Chest X-ray, EKG, complete blood counts, urinalysis, ASO titer, ESR and CRP were routinely performed. Renal function, serum albumin and globulin, rheumatoid factors (RF), and echocardiogram were investigated about half of the patients.

RESULTS

Clinical data

The age and sex incidence of the patients are summarized in Table 1. The female: male ratio was 1:1.3. The age range was 15-39 yr. with the mean of 22 yr.

Twelve patients (57%) were farmers, the others were students and government officer respectively.

Seventeen patients (80%) gave the history of the first attack after the age of 15 yr. and 4 patients (19%) did after 30 yr. The times of relapses, demonstrated in Table 2, sixteen patient (76%) had experienced rheumatic attacks range from 2-5 times. Of these, the relapses did occur despite of antibiotic prophylaxis in 6 patients (37%). The numbers of relapses were not different among those who had prophylaxis (average 1.5 occurrences per one patient) and those who did not (1.9 occurrences per one patient).

The interval between the first attack and the relapses ranged from 1 month to 6 years (average 2 years).

Table 1 Age and Sex Incidence of 21 Patients with Acute Rheumatic Fever

	No. of Patients	Per cent
Age (yr)		
15-20	11	52.4
21-25	4	19.0
26-30	2	9.5
31-35	1	4.8
36-40	3	14.3
Sex		
Male	12	57.1
Female	9	42.9

Table 2 Numbers of Relapses and Correlation between Relapses and Antibiotic prophylaxis (N=21)

Number of Relapses	No. of total Patients	No. of Patients with Prophylaxis
0	5	-
1	8	3
2	6	3
3	-	-
4	2	-

Nine patients (42%) had the preexisting symptoms of streptococcal infection such as sorethroat, injected pharynx and tonsils and/or cervical lymphadenopthy.

Diagnostic criteria

The major criteria found in this series were carditis, arthritis, chorea and erythema marginatum. As shown in Table 3, the most common major criteria is carditis (80.9%) and the second most common is arthritis (47.6%).

Table 3 Major criteria at the presentation (N=21)

Major criterias	No. of Patient	Per cent
Carditis only	9	42.8
Arthritis only	2	9.5
Both carditis and arthritis	8	38.1
Chorea	1	4.8
Erythema marginatum	1	4.8
Subcutaneous nodule	0	0

Carditis (Table 4)

Seventeen patients (80%) had carditis, fifteen of these (88%) had previous rheumatic attacks. The diagnosis of carditis was based on combination of cardiac symptoms, increase in cardiac size, EKG and/or echocardiographic findings. CHF is the most common cardiac symptom. Auscultatory cardiac murmurs were found in fifteen cases (88%), the other two who did not have cardiac murmur were diagnosed by other cardiac symptoms and EKG changes (ST-T change and/or prolonged PR). MS and MR murmurs were equally found and combination of murmurs were audible in about half of our patients.

Echocardiography was performed in 9 patients all of them, the valvular lesions were demonstrated. Four patients had pericardial effusion and three of which were asymptomatic.

Table 4 Findings in 17 patients who presented with active carditis.

Finding	No. of Patients	per cent
History of pre-existent rheumatic attacks	15/17	88.2
Preexisting valvular lesions	11/17	64.7
Patients with RHD who developed carditis (compared with total number of patients with RHD)	10/11	90.0
Patient without RHD who developed carditis (compared with total number of patients without RHD)	7/10	70
Cardiac symptoms	14/17	82.3
CHF	13/17	
Chest pain	5/17	
Auscultatory murmurs	14/17	82.35
Single murmur		
MS	2	
MR	3	
AR	3	
Combination of murmurs		
MS MR	3	
MS AR	1	
MS TR	1	
MS MR AR	1	
Auscultatory pericardial rub	1/17	5.8
Echocardiographic performed	9	53
valvular lesions (all had murmurs)	9	
pericardial effusion	4	
Cardiomegaly (CXR)	12/17	70.5
EKG		
Chamber enlargement	14	82.3
PR prolong	5	29.4
arrhythmia (AF)	4	23.5
non specific ST-T change	3	17.6
Treatment		
ASA only	10	58.8
Prednisolone only	1	5.9
ASA and prednisolone	5	29.4
no antiinflammatory drug	1	5.9

Arthritis

About 10 cases (47%) of the patients presented with acute arthritis, mostly occurred together with carditis. Only 3 patients (30%) had classical migratory polyarthritis, another 3 (30%) had additive pattern, only 1 case (10%) had monoarticular arthritis and the rest were not classified in the records.

These series did not include 7 patients (33%) who presented with arthralgia. The sites commonly involved were wrists, knees, ankles and elbows; shoulders and metacarpophalangeal joints (MCP) were occasionally involved, but the interphalangeal joints (IP), hip joints and sternoclavicular joints were infrequently affected. Plantar fasciitis was found in only 1 cases.

Chorea

Only one-15 year-old male patient had the presentation as chorea, a single major criteria. Low grade fever, injected tonsils, elevation of ASO titer and ESR were also detected on physical examination and laboratory investigations.

Erythema marginatum

A female patient of 23 yr had the third rheumatic attack as erythema marginatum. She experienced the first and the second attack at 6 and 1 years previously with carditis and arthritis. She also had fever, murmurs of MR and AR associated with elevation of ASO titer, ESR and serum globulin.

Physical examination

Approximately 80% of the patients had fever more than 38.5 ° c and 2 patients (9.5%) had no fever. Epitaxis was found in 5 patients (23%), none of these had coagulopathy. Signs of streptococcal infections, such as injected tonsils, pharynx and cervical lymphadenopathy, were found in seven cases (33%). There was neither hepatomegaly in the absence of congestive heart failure nor splenomegaly.

Laboratory findings (Table 5)

Throat swab cultures were done in 11 cases, none had positive culture for streptococci. ASO titers were normal in 4 patients (19%) as previously mentioned. ESR was elevated in 19 patients (90%). Average hemoglobin concentration was 11.6g%; 75% of the patients had hemoglobin concentration between 10-12.5g% except in one case with G-6-PD deficiency of whom Hb was 8.6g%. Fourteen patients (67%) had WBC more than 10,000/cumm., five patients had WBC more than 15,000/cumm. (range 7,950-26,000). 70% of the patients had PMN $\geq$ 70% in differential count (average PMN 74%).

Table 5: Laboratory Finding

Laboratory data	no. of positive test per no. of evaluated patients	per cent
- Throat swab cultures positive for streptococcal infection	0/11	0
- High ASO titers	17/21	90.9
- Elevation of ESR	19/21	80.5
- Hemoglobin concentration		
>12.5 g%	4/21	19
10-12 g%	16/21	76.2
<10 g%	1/21	4.8
- Leukocytosis		
WBC >10,000/cumm	14/21	66.6
WBC >15,000/cumm	5/21	23.8
- proteinuria	5/21	23.8
- Azothemia	3/12	25
- Hyperglobulinemia	7/11	63.6
- Hypoalbuminemia	6/11	54.5

Table 6 The Correlation between ASO titers and Serum Globulin

A: ASO titers in 7 patients who had hypergammaglobulinemia

Case no.	1	6	7	9	12	13	14
ASO titers	N	>2500	333	>2500	625	833	1250

B: ASO titers in 4 patients who had normal serum globulin

Case no.	2	3	16	18
ASO titers	N	250	333	N

N =normal

Five patients (24%) had mild proteinuria (not more than 1+), the others had normal urinalysis. BUN, creatinine were performed in 12 patients, three (25%) had mild azotemia and only one had renal insufficiency.

Albumin and globulin were evaluated in 11 cases, seven (63%) had hyperglobulinemia and six (54%) had hypoalbuminemia. Most of the ones who had hyperglobulinemia also had high ASO titers. (Table 6)

Treatment

Twelve (57%) patients were treated with aspirin alone in a dose of 80-100 mg/k/day. Six patients (28%) received aspirin followed by prednisolone (dose 30-60 mg/day), and one received prednisolone alone. Two patients received neithef aspirin nor prednisolone,one of those received major transquilizer for chorea and another improved after conventional treatment of CHF.

Of the seventeen carditis patients (Table2), ten (59%) were treated with aspirin alone, one received prednisolone alone and five (29%) got both. About half of these, fever disappeared within a few days and none had sustained fever beyond the first week. Symptoms and signs of CHF improved in 1-4 days, except one patient, first presented with carditis with MR and AR, had developed intractable CHF even if steroid therapy, and his EKG also showed ST depression in II, III, AVF at the following time. Nine patients (52%) required mainteinance of digitalis, all were indicated by congestive heart failure and half of them had AF.

Two cases who had only acute arthritis responded well to aspirin therapy.

Four in eighteen patients (22%) had aspirin side effects, one had gastric irritation and three had vertigo, the latter tolerated well after lowering the initial doses.

One case of chorea was treated with benzodiazepine and haloperidol, his symptons improved after the first week but were not completely recovered.

Sixteen patients (76%) were admitted, average hospital days was 13.2 days (range 6-39 days), the one whom 39 days admitted was first diagnosed as FUO and was investigated for 30 days prior to the diagnosis of ARF.

None in this series died in the acute phase of ARF.

Discussion

ARF is not infrequently found in adults. It was slight more commonly found in male in our series whereas sex ratio in other series[3,4,7-9,11,15,16] varied from male to female. Most of them (80%) had the first rheumatic attack after the age of 15 yr and 19% after 30 yr. The reasons why does it attack late are unknown, may be associated with differences immunologic response of host due to streptococcal infection or environment factors. It occurs follow asymptomatic streptococcal infection more than fifty per cent, and can relapse even if they have antibiotic prophylaxis, that may be due to irregular treatment which we could not be truely confirmed. The longest interval between first attack and relapse was 6 years which we should consider-: how long the prophylaxis should be continued.

All of the major criteria, except subcutaneous nodule, were found. The most common major criteria in adult was carditis (80%) and the second was arthritis (47%), which contrasts to the previous reports that arthritis was the majority.[3,4,7-9,11,14-16,23] Most of the carditis patients had auscultatory murmurs that were MS, MR, AR, TR, but no AS at all. Patients without preexisting RHD were able to develop carditis nearly as in patient with preexisting RHD. Valvular lesions is the most common cardiac involvement, pericardial involvement was commonly asymptomatic but the percentage cannot put into the conclusion because echocardiography was not performed in all cases.

Migratory polyarthritis, the characteristic of joint involvement in ARF was not commonly found.[24] Large joints, except hip joint, are frequently affected but incidence of small-joint involvement of hands is higher in adults than in children.[8-9] The one with monoarthritis also had carditis, he was diagnosed as FUO and was investigated for more than 1 month before diagnosis of ARF. The natural history of arthritis in ARF in adults is the same as in children-: acute and transitory, without sequelae. Jaccoud-type arthritis was not found in this series and was described in only one patient from all of the series.[12]

Chorea, found only 1 case in this series, is rare in adult ARF. It is more commonly found in female after puberty and associated with carditis more than arthritis; ASO titer and ESR are usually normal because of long latent period.[17] In this case the evidence of streptococcal infection still persisted may be coincident finding rather than the causative evidence.

Erythema marginatum was only found in 1 case as mentioned. In the reference series no report case of chorea, erythema marginatum and subcutaneous nodule was found.

Other clinical manifestaions such as erythema nodosum was not found but epitaxis was found in 23% compared with 4-7% in other series.[4-7]

Anemia has long been recognized in ARF[18] but the mechanism is unclear.[19] Mild to modereate anemia is found in the range of 70-90%[1,17,19] in other series, and 75% in the present series. However it cannot put in the conclusion that anemia in these data was due to ARF alone because many investigations of anemia were not done such as serum iron and hemoglobin typing which are the most common cause of anemia in this North-East part of Thailand.

Despite of occasional reports of acute glomerulonephritis (AGN) in ARF,[1,4,23,27-30] no AGN was found in this series. Only mild proteinuria (urine albumine $< 1+$) was 24% found, so that the combination of ARF and true nephritis is considered most uncommon.

Hyperglobulinemia was 63% found, it might be associated with immunologic response to streprtococcal infection as in table 5.

Most of the patients had a good response to the treatment. About half of the carditis responsed well to aspirin therapy

and also all of arthritis with or without carditis.

None had died in the acute phase of ARF. The mortality rate in ARF which had been reported was 1.2%[3,7,9,12], they had severe RHD, cardiac failure and atrial fibrillation before their fatal attack. Such patients are vulnerable to any intercurrent infection (eg. pneumonia), their death may not have been due to the relapse of ARF per se.

Even if the ones who were given antibiotic prophylaxis had been able to developed recurrent rheumatic attacks, we cannot conclude that the prophylaxis is unnessesary because we have no data about the ones who had prophylaxis without relapses. These failure may be due to irregular self responsive treatment of the patients. The longest interval between the first attack and relapse was 6 years, which we should bring into the consideration about duration of prophylaxis. The decision of duration of antibiotic prophylaxis in ARF also depends on : (1) risk of recurrence; (2) incidence of valvular complications; (3) risk of prolonged antibiotic administration.[20-22] Four groups of adult patients may be considered with respect to prophylaxis: (1) patients with single attacks of ARF without carditis, (2) patient with single attacks of ARF with carditis (3) patient with recurrent attacks of ARF with or without carditis, and (4) patient with RHD. The key issue is the presence or absence of carditis, since this is the most important prognostic factor. Patients in the second and third groups should probably continue prophylaxis which they are at risk environment eg, during child-rearing, or military survice, or throughout their careers in the case of school teachers. Patients in group 4 should continue indefinitely in the hope of minimizing further valvular damage.

The patient must be intelligently instructed concerning the nature of the illness and its natural history in order to ensure good compliance and sensible self-referral for treatment.

Summary

The retrospective clinical analysis of acute rheumatic fever in adults was performed in 21 patients. Male was slightly preponderant and the mean age was 22 yerars. In contrast to other series of clinical analysis, carditis is the most common major criteria (80%) and the second common is arthritis (47%). Chorea and erythema marginatum was found only one each. There was no subcutaneous nodule in this series. Epistaxis was another clinical manifestation of ARF (23%). 88% of the patients had the history of pre-existent rheumatic attack and 64% had preexisting valvular lesions. The majority (82%) of carditis had ausculatory murmurs. MS and MR were equally common ; pericarditis was not uncommon but most of them were asymptomatic. Classical migratory arthritis occurred only in 30%, and commonly involved the large joints. There was no residual deformity among these. Laboratory findings in acute phase were rising ASO titers (85%), elevation of ESR (90%), positive CRP (71%), mild to moderate anemia (75%), mild proteinuria (24%) and hypergammaglobulinemia (63%). The reponse to treatment was good except one patient who developed intractable CHF from the first severely attack of acute carditis. No patient died in the acute phase of AFR. An average hospital days was 13.2 days.

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