Clinical Presentations of Atypical Arthritis in Egyptian Children with Acute Rheumatic Fever

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Abstract: Introduction: The diagnosis of acute rheumatic fever (ARF) remains difficult and complex. This difficulty is mainly attributed to the changing pattern of the disease with a variety of clinical manifestations, which are not included in the latest updated-revised Jones criteria (WHO 2004).Classic acute migratory polyarthritis involving large joints is not always present highlighting the potential diagnostic problems of ARF. **Objective:** The aim of this study was to describe the clinical manifestations of atypical arthritis in children with ARF admitted to Al-Zahraa Hospital, AL-Azhar University, Cairo, Egypt. Also to assess the adequacy of the latest revised WHO Jones criteria (2004) in diagnosis of ARF. **Methods:** We retrospectively studied the records of 201 patients previously diagnosed to have ARF and rheumatic heart disease (RHD) between January 2003 to December 2008.Out of 201 medical records reviewed, 44 cases of acute arthritis and concomitant carditis were selected after exclusion of isolated arthritis, isolated carditis, rheumatic chorea and chronic RHD. **Results:** Atypical arthritis was presented in 86.36 % of ARF patients, while 13.64% presented typical acute migratory polyarthritis of large joints. An atypical pattern of rheumatic arthritis was based on the following criteria: oligoarthritis in 19 patients (43.18%), Monoarthritis in 12 patients 27.27%, polyadditive in 7 patients (15.90%), small joints of the hand in 4 patients (9.09%) and feet in 2 patients (4.54%). Our results revealed association of these atypical arthritis with late or insidious onset carditis in 8 patients (18.18%) and also with silent carditis in 2 patients (4.54%) making the diagnosis more difficult. **Conclusion:** we concluded that atypical arthritis was present in significant proportion of the acute rheumatic fever attacks, making the diagnosis of this intriguing disease even more difficult. The diagnosis of atypical arthritis need more attention, as strict adherence to the revised WHO (2004) Jones criteria would results in under diagnosis of ARF. Our study reinforces the need to interpret the latest modified Jones criteria, possibly incorporating the atypical presentation and to support the view that echocardiographic finding as a major criterion for diagnosis.

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1.Introduction

Acute rheumatic fever (ARF), a disease known over a century (it was first described in 1889)[(1)], still represents one of the most difficult diagnosis in pediatrics.

ARF is a non-suppurative cardiovascular complications of group A beta hemolytic streptococcal (GABHS) pharyngitis. It remains medical and public health problem in both developed and developing countries, even at the beginning of 21th century[(2)].

Till now, there is no specific clinical pathognomonic sign or laboratory test established to confirm its diagnosis. Its diagnosis depends on the fulfillment of Jones criteria established in 1944[(3)].

Dr. Duckett Jones[(3)] clearly defined a set of criteria to establish the diagnosis and limit the over diagnosis of rheumatic fever (RF). These original Jones criteria, as they since became known, were successively modified several times. The latest modification published by the World Health Organization in 2004[(4)], to improve the diagnostic specificity of the updated 1992 Jones criteria, as in daily medical practice the interpretation of some clinical situations of ARF becomes a diagnostic challenge.

In these criteria, arthritis is one of the most frequent major manifestations. The classical description of joint involvement in ARF consists of a clinical status of migratory polyarthritis, which affects especially the large joints and appears around 2 to 3 weeks after oropharyngeal streptococcal infection. The pain, typically intense and disproportional to the signs observed on physical examination and can be quickly reduced with the use of nonsteroidal anti-inflammatories notably salicylate (dramatic response to salicylate). Arthritis characteristically heals without sequelae [(5)].

Several investigators **Sharma *et al.*[(6)], Pereira *et al.*[(7)] and Chen *et al*[(8)].**, reported presence of an atypical clinical presentation of ARF, such as atypical arthritis and silent carditis, leading to remarkable diagnostic problems. Consequently, arthritis especially when it occurs isolated is associated with an increased difficulty of the diagnosis.

Atypical joint involvement in some patients with ARF may be mono or oligo rather than polyarticular, additive and symmetric rather than migratory, involving small joints of the hands and feet, and persisting for weeks if not properly treated[9-11].

The presence of these atypical joint involvement, which do not satisfy the revised WHO Jones criteria (2004) reflecting a remarkable change in the clinical pattern of ARF making its diagnosis more difficult and may lead to misdiagnosis or delayed diagnosis of certain cases especially in those without carditis.

The objective of the present study is to describe the clinical characteristic and the occurrence of atypical rheumatic arthritis in children admitted to Al-Zahraa Hospital, Al Azhar University for Girls, Cairo, Egypt during an acute attack of rheumatic fever. We also assessed the reliability of the revised WHO criteria (2004) in diagnosis of ARF.

2.PATIENTS AND METHODS

We retrospectively analyzed medical record of inpatients who were treated at Al-Zhraa Hospital, Al-Azhar University for Girls, Cairo, Egypt with diagnosis of ARF. Our study was carried out for a period of five years from 2003 to 2008.

Out of 201 medical records reviewed with diagnosis of ARF and chronic heart disease, 44 cases were selected, being retrospectively examined. Before 2004, updated (1992) Jones criteria were applied for the diagnosis of ARF,and after 2004 all the files re-evaluated using revised WHO criteria (2004).

Inclusion criteria were: 1) presence of concomitant rheumatic arthritis and active carditis, 2) diagnosis of active carditis established by fulfilling revised WHO Jones criteria (2004) for the first and recurrent attacks, and also for the late onset carditis, 3) joint involvement classified as an atypical: in presence of polyadditive or oligoadditive (not migratory), presence of monoarthritis, and involvement of small joints of the hands or feet,and 4)-cases incompletely satisfying Jones criteria (silent carditits with atypical arthritis) were included in this study under the fallowing conditions: a)-echocardiographic diagnosis of silent carditis revealed rheumatic valve lesion, b)- patients satisfied two or more minor manifestations, 5)- patients with one year follow up.

Exclusion criteria were: 1) - patients with isolated rheumatic arthritis without evidence of carditis, 2) - patients with arthritis for which an alternative causes were found (rheumatoid arthritis, systemic lupus erythematosus, viral infection, Mediterranean fever…etc 3) - patients were treated as septic arthritis, 4) patients with less than one year follow-up.

The study group was analyzed in two groups depending on the clinical features at admission: 1) patients with initial or first attack of RF (27 cases), 2) patients with recurrence of RF (17 cases).

After case selection, comprehensive revision of the patients' files was done and the following information was recorded: 1) demographic data, 2) clinical features at presentation,3) past history of RF, and 4) presence of RF/RHD in other family member. Laboratory features included: 1) total leucocytic count > 10.000 mm^2 , ESR above 20 mmHg/ first hour and positive C-reactive protein (CRP) were considered abnormal, 2) Antistreptolycin-o titres (ASOT) more than 200 international units was considered to be abnormal and it revealed a recent evidence of streptococcal infection, 3) plain chest radiography for evidence of cardiomegaly and congestive heart failure, 4) ECG for estimation of PR interval, and 5) echocardiograpy /2 DM mode colour was carried out in all patients for establishment of cardiac valvular lesions.

We carried out a descriptive analysis of the demographic, clinical, laboratory variable. All observed at diagnosis and at follow up consultations and adjusted for one year interval.

3.RESULTS

Out of revised 201 files of ARF and chronic RHD disease, 44 cases of acute rheumatic arthritis with concomitant carditis were selected. Age at onset varied from 4 to 15 year in patients with initial attack and from 4 to 12 year in patients with recurrence. Overall gender distribution was 25 (56.81%) females and 19 (43.18%) males, history of recurrent tonsillitis was described in 9 (25%). All patients received regular prophylaxis (Table 1).

Table (1): Characteristics of the study group.

	Initial (first) attack of RF (n=27)	**Recurrence of RF with RHD(n=17)**	**Total (n=44)**
Age :(year) Sex	Range:4-15 Male: 12(44.44%) Female: 15(55.55%)	Range:10-15 Male: 7(41.67%) Female: 10(58.82%)	Range:4-15 Male: 19(43.18 %) Female: 25(56.81%)
Age at onset:(year)	Range: 4-15	Range:4-12	Range:4-15
Positive history of recurrent tonsillitis or sore throat	8 (29.62%)	1 (5.88%)	9 (20.45%)
Positive family history	5 (18.51%)	6(35.29%)	11 (25%)
Regular prophylaxis	27(100%)	17(100%)	44(100%)

Out of 44 cases, 27 (61.36%) had the first episode of ARF, while 17 cases (38.64) had recurrent attacks (Fig. 1).

In relation to the characteristics of joint involvement, an atypical pattern was observed in 38 of 44 (86.36%), while typical migratory polyarthritis was observed in 6 of 44 (13.63%) (Fig. 2).

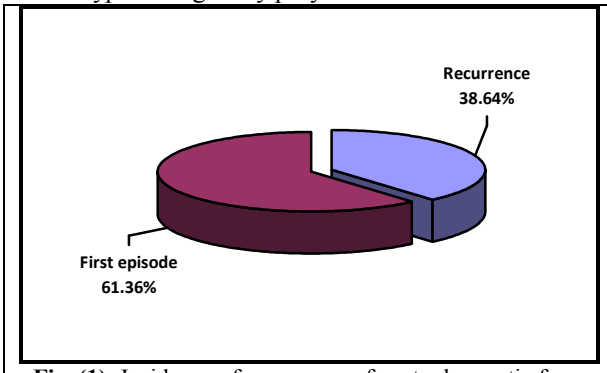

Fig. (1): Incidence of recurrence of acute rheumatic fever.

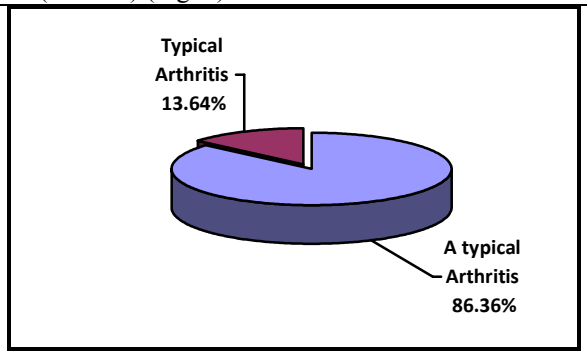

Fig. (2): Incidence of the typical and atypical rheumatic arthritis.

Clinical features of Jones major and minor criteria of ARF at admission to the hospital during the first and recurrent attacks are presented in (Table 2). Rheumatic arthritis associated with classic carditis was observed in 33 patients (75%), of whom, 28(63.63%) had atypical arthritis and 5 patients (11.37%) had typical migratory polyarthritis. While rheumatic arthritis with late onset carditis was observed in 9 patients (20.45%) of whom 8 patients (18.18%) had atypical arthritis and one patient (2.27%) had typical arthritis. Atypical arthritis with silent carditis with was observed in 2 patients (4.54%).

The frequency of clinical Jones minor criteria were: history of fever in 35 patients (79.54%) and arthralgia in one patient (2.27%). The frequency of laboratory minor criteria were: leukocytosis in 19/38 (50%) patients, as the total leukocytic count missed in 6 files. High ESR and positive C-reactive protein were observed in 88.63 % (39 of 44) and 90.90 % (4o of 44) of patients respectively. ESR not elevated in 5 patients had severe carditis with heart failure. Anti-streptolycin O titer (ASOT) higher than 200 IU/ml were found in 79.54% (35 of 44) of patients, it varied from 300 to 1200 IU/ml. No evidence of previous streptococcal infection (ASOT <200 IU/ml) was observed in 9 patients (20.45%) with late onset carditis.

Table (2): Frequency of major and minor Jones criteria among the study group.

	Initial(first) attack of RF(n=27)	**Recurrent attack of RF(n=17)**	**Total (n=44)**
Major manifestations:			
Arthritis with classic carditis	22	11	33(75%)
-Atypical			
-Typical	19	9	28(63.63%)
	3	2	5(11.37%)
Arthritis with late onset carditis	3	6	9(20.45%)
- Atypical			
-Typical	3	5	8(18.18%)
	-	1	1(2.27 %)
Arthritis with silent carditis			
Atypical	2	-	2(4.54%)
-Typical			
Minor manifestations:	2	-	2(4.54%)
Fever	-	-	
Arthralgia			
Leukocytosis	19	16	35(79.54%)
High ESR	1	-	1(2.27%)
Positive CRP	10/22	9/16	19/38(50%)*
High ASOT	27(100%)	12(70.58%)	39(88.63%)
	26(96.29%)	14(82.35%)	40(90.90%)
	24(88.88%)	11(64.70%)	35(79.54%)

*: TLC was recorded in 38 cases

Table (3) describes the distribution of an atypical arthritis pattern according to the criteria used to consider them atypical: oligoadditive in 19(34.18%), monoarthritis in 12 (27.27%) and Polyadditive arthritis was observed in 7 (15.15%). It also describes the distribution of atypical arthritis pattern in relation to carditis. Oligoarthritis with classic carditis was found in 15 (34.09%) patients and with late onset carditis in 4(9.09%) patients, while monoarthritis was found with classic carditis in 8(18.18%) patients, late onset carditis in 3 (6.81%) patients, and silent carditis in one patient (2.27%). Polyadditive arthritis with classic carditis was found in 5 (11.36%) patients, late onset carditis in one patient (2.27%), and silent carditis in one patient (2.27%).

Table (3): Distribution of atypical rheumatic arthritis pattern in relation to rheumatic carditis.

Rheumatic carditis	Rheumatic arthritis			
	Typical 6 (13.63%)	Atypical 38(86.36%)		
		Oligoarthritis	Monoartharitis	Poyadditive
Classic carditis	5 (11.36%)	15 (34.09%)	8(18.18%)	5(11.36%)
Late onset carditis	1 (2.27%)	4 (9.09%)	3 (6.81%)	1 (2.27%)
Silent carditis	-		1 (2.27%)	1 (2.27%)
Total	6 (13.63%)	19(43.18%)	12(27.27%)	7(15.90%)

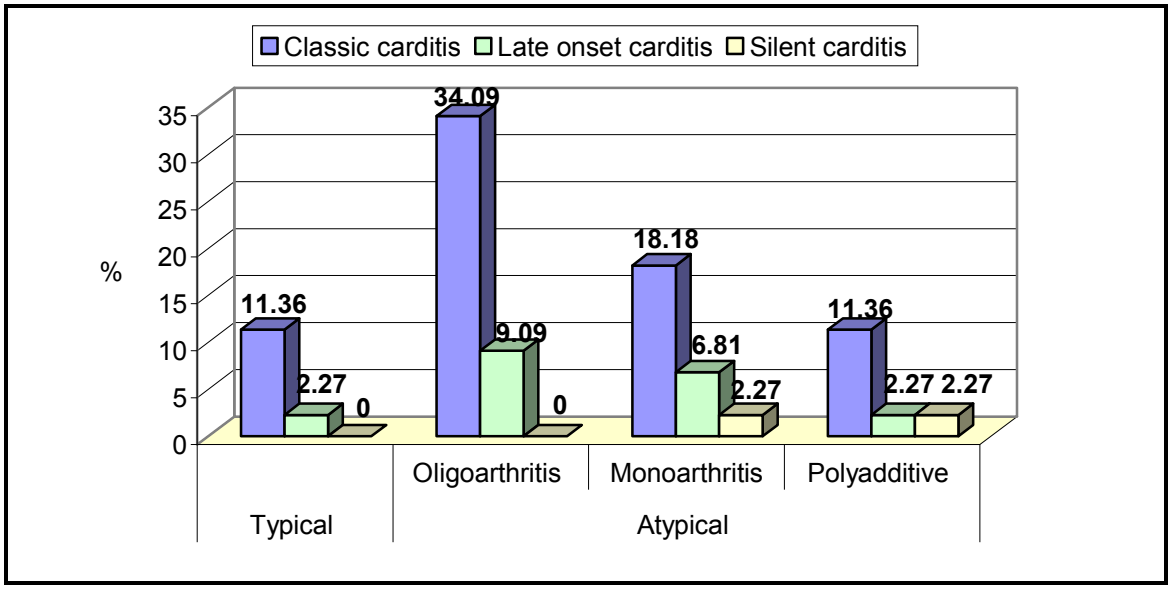

Fig. (3): Distribution of atypical rheumatic arthritis pattern in relation to rheumatic carditis.

Table (4) describes the distribution of the rheumatic arthritis according to involved joints, small joints of the hands were observed in 4(9.09 %) patients and small joints of the feet in 2(4.54 %) patients. While arthritis of the ankle joint was observed in 37(84.09 %) patients, knee joint in 27(61.36%) patients, wrist joint in 6 (13.63%) patients, elbow joint in 2(4.54%) patients and shoulder joint in 2(4.54 %) patients.

Table (4): Distribution of the attacks of rheumatic arthritis according to the involved joints.

Joints	**Initial (first) attack of RF (n=27)**	**Recurrent attack of RF (n=17)**	**Total (n=44)**
Ankle	24 (88.88%)	13 (76.47%)	37 (84.09%)
Knee	14 (51.85%)	13 (76.47%)	27 (61.36%)
Wrist	5 (18.51%)	1 (5.88%)	6 (13.63%)
Elbow	2 (7.40%)	0 0.00	2 (4.54%)
Shoulder	1 (3.70%)	1 (5.88%)	2 (4.54%)
Small joints of the hand	2 (7.40%)	2 (11.76%)	4 (9.09%)
Small joints of the feet	2 (7.40%)	0 0.00	2 (4.54%)

Echo diagnosis of cardiac lesions observed were mitral regurge (14 cases), mitral regurge and aortic regurge (25 cases) and mitral regurge, mitral stenosis and aortic regurge in (2 cases). Echodiagnosis of pericardial effusion was observed in 4 cases.

4.Discussion

Rheumatic fever continuous to be a major health problem in developing as well as developed countries requiring physicians to remain vigilant and to consider ARF in any child with acute arthritis.

The manifestations of ARF according to the Jones criteria were divided into major and minor categories. There are five major criteria such as polyarthritis or carditis and four minor criteria including clinical and laboratory features. The presence of two major or one major and two minor manifestations provide reasonable evidence of rheumatic activity if supported by evidence of preceding group A streptococcal infection[12].

These original Jones criteria, proposed since 1944 have been modified several times, the latest modifications was 2002-2003 WHO criteria, published in 2004[4].

Revised WHO Jones criteria (2004)[4] added some points for the diagnosis of late onset carditis, chorea and recurrent RF and still described articular manifestation typically present as migratory polyarthritis, most often in the large joints. Therefore, strict application of revised WHO (2004) Jones criteria in the diagnosis of rheumatic arthritis with atypical presentations would results in under diagnosis or misdiagnosis of RF[8,13].

In the present study, we describe the clinical characteristics and the occurrence of atypical arthritis in (38) patients with acute rheumatic fever admitted to our pediatric department at Al-Zhraa university hospital, Al-Azhar University for Girls Cairo, Egypt, between Jan. (2003) – December (2008).

Our data do not, however, represent the actual situation of acute rheumatic fever in Cairo, because most of our described cases came from other cities and also, many other cases of ARF may attended other hospitals or private clinic in Cairo.

Forty four (44) patients of acute rheumatic arthritis with concomitant carditis were selected after exclusion of isolated arthritis, rheumatic chorea and chronic rheumatic heart disease. Age at onset ranged from 4 to 15 years. **Sharma *et al.*[6]** reported that the maximum number of cases had ARF was in age group of 5-15 years. They noted that one case was admitted with age less than 5 years.

Female sex predominance (56.8%) was observed as compared to male (43.1%). **Sherma *et al.*** [6] reported male sex predominance, while **Stolerman**[14] reported equal incidence of RF in both .

A history of recurrent tonsillitis or sore throat was evident in 20.45 % (9/ 44) of our patients. **Khrriesat and Najada**[15], reported that a history of sore throat may not be evident especially in young children as they are poor in localising sites of infection.

A positive family history for rheumatic fever was found in 25 %(11/44) of our patients. The data in Egypt reported by **Kotbby *et al.***[16] showed that it was 3.9%, while other authors, (**Eissa *et al.*** [17] **and Kassem *et al.*** [18]) reported it 9%. This familial predisposition to rheumatic fever suggests a genetic susceptibility.

Several studies have reported that genetic susceptibility to rheumatic heart disease is linked to HLA class II alleles [19, 20].

Specific human leukocytic antigen (HLA) class II haplotype conferred strong protection from RF, where others increased the risk of rheumatic disease in Egyptian children [19, 21].

Studies have identified a B cell alloantigen D8/17), present in a high percentage of B cell from patients with ARF and their family members[11, 22, 23].

The classical migratory polyarthritis of ARF described originally in updated Jones criteria (1992) and revised WHO (2004) criteria are not always present.

Several investigators **Pileggi and Ferriani**[5], **Chen *et al.*** [8] **Khriestal and Najada**[15] **and Carapetis *et al.*** [24] reported cases with atypical features of arthritis that are not included in the revised WHO Jones criteria (2004).

An atypical pattern of Joint involvement was observed in 86.36 % of our studied cases, while 13.64 % presented with typical migratory polyarthritis, thus contributing to increase difficulties of the initial diagnosis of ARF. The presence of carditis or cardic sequelae in all our studied patients suggesting a diagnosis of RF, however the diagnosis will be more difficult if carditis was silent.

In 1975, **Stollerman**[25] observed that 32% of the children with ARF in his study population did not present by the classical pattern of joint involvement considering increased duration of the attack, clinical status of monoarticlar arthritis and/or unsatisfactory response to salicylate as atypical articular pattern. Other description of atypical articular status of RF have been reported in the study carried out by **Pileggi and Ferriani**[5], they classified joint involvement as atypical if at least one of the following characteristic had to be present: 1) Duration longer than 3 weeks, 2) Involvement of small joints and/or cervical spine

and/or hip joints, 3) Presence of monoarthritis and 4) Unsatisfactory response to salicylates.

In the present study the most frequent atypical criterion found was related to the area and pattern. The presence of monoarthritis (27.27%), involvement of small joints of the hands (9.09%), and the feet (4.54%) were considered atypical presentation. These findings were in concordance with **Pileggi and Ferriani**[5] and **Sharma *et al.*** [6].

Atypical pattern with symmetric additive polyarthritis (15.90%) and additive oligoarthritis (43.18%) were reported in our cases. **Da. Saliva and Pereira**[9] reported that joint involvement in some patients with ARF may be additive and symmetric rather than migratory. Also may be monoarthritis(23%) or oligo (35%) rather than polyarticular.

The areas of joint involvement in order of frequency were ankle (84.09%), knee (61.36%), elbow (4.54%) and wrist (13.63%). Our findings were in agreement of **Pileggi and Ferriani**[5]. Atypical articular monoarthrites was observed by **Khriesats and Najade** [15] and **Carapetis and Currie**[26].

The incidence of monoarticular arthritis in our study was (34.21%). Monoarticular arthritis as a possible major criterion for the diagnosis of rheumatic fever was extensively discussed by the **workshop participants of AHA**[27]. However, they acknowledged that this finding must be interpreted within the clinical and epidemiological setting of RF prevalence in various populations.

The latest, **revised WHO criteria**[4] notified that, patients with monoarthritis with several (3 or more) other minor manifestations together with evidence of recent GABHS considered as cases of probable rheumatic fever once other diagnosis are excluded. On the other hand **the National Heart Foundation of Australia (NHFA)** have agreed a new criteria and guidelines for the diagnosis of acute rheumatic fever in high and low risk population in Australia[28]. **The Australian guidelines (2005)**[28] and the **updated Australian guidelines (2012)**[29] considered aseptic monoarticular arthritis as major manifestation in high risk population and as minor manifestation in lower risk group.

Our results supporting the view that articular monoarthitis could be included as a major criterion for diagnosis of ARF.

Atypical arthritis with small joints involvement and additive pattern may need differential diagnosis with post streptococcal reactive arthritis[30]. The greatest confusion in the differential diagnosis of ARF follows the description of post streptococcal reactive arthritis (PSReA). PSReA has been considered to be a separate entity of arthritis, but others still believe that it is part of spectrum of RF[31]. We do not consider the atypical arthritis in our series a part of PSReA, because none of our patients fulfilled the proposed clinical criteria suggested by **Ayoub and Ahmed**[32]. In addition to this our patients showed excellent response to salicylate. This response was considered as the most important differential criterion between PSReA and RF[4].

Insidious or late onset carditis is a rheumatic carditis of insidious onset and slow progression. Revised WHO criteria[4] considered the insidious onset rheumatic carditis as one of the main diagnostic categories of RF and facilitate its diagnosis in the absence of other major manifestation or supporting evidence of GABHS infection.

Surprisingly in the present study 18.18 % (8/44) of our patients had insidious or late onset carditis with concomitant atypical acute arthritis. This unusual and unexpected presentation may lead to misdiagnosis or delayed diagnosis of such cases. Insidious or late onset carditis presented in patients who came to medical attention months after the onset of RF, and may have insufficient supporting evidence of a recent GABHS to fulfill the Jones criteria. Insidious onset carditis and rheumatic chorea presented the relatively late phase of the disease with delayed manifestations of RF, when antistreptococcal antibody titre suggestive of preceding streptococcal infection had already normalized. **Pileggi and Ferriani**[5] reported presence of atypical arthritis concomitant with carditis and chorea in 7% of their series. Also **Carvalho *et al.*** [33] reported presence of rheumatic chorea with acute arthritis in 4.5% of their studied series. While no available data, to our knowledge, about the concomitant occurrence of atypical acute arthritis with insidious or late onset carditis.

With suboptimal auscultation skills, an echo Doppler investigation will quickly confirm the presence or absence of valvular involvement when a clinically detectable murmur is present[34]. Two (5.26%) of our patients with atypical arthritis had silent carditis and the diagnosis was established only after echocardiography (echocarditis). **Khriesal and Najada**[15] reported presence of atypical arthritis concomitant with silent cardities in 2 of their 4 studied cases.

Several studies, **Figuerr *et al.*** [34], **Saxena**[35], **Hilario and Terreri**[36], and **Chebab**[37] confirmed that the yield of carditis with valvular regurgitation will be increased with the used of echocardiography in patients with isolated rheumatic arthritis or rheumatic chorea. These findings highlight the importance of repeating echocardiography over the next 3-4 weeks, as valvular involvement which was absent initially, may appear later supporting the view that echocardiographic findings should be considered as a major criterion of the diagnosis of ARF. However, the role of

echocardiography has not been defined in the last revised WHO Jones criteria (2004). **Revised WHO Jones criteria**[4] stated that Doppler echocardiographic finding alone should not be classified as either major or minor criteria at this time. On the other hand an **Australian guideline (2005)**[28], **and updated Australian guidelines (2012)**[29] for the diagnosis of ARF included echocardioagraphic evidence of subclinical valuvular disease as major manifestations in high risk groups for ARF.

Leucocytosis, an acute phase reactant was available in 19/38 of our cases. The count of more than 10.000/cubic mm was taken as significant[6]. **Sharma *et al.*** [6] reported 32% in their series. It is important to remember that the leukocytosis count will remain elevated if the patient is being treated with steroids. Under these circumstances it therefore loses its value as an index of activity**.**

There is no laboratory marker for ARF and its diagnosis is based on a different combination of clinical and laboratory evidence of previous streptococcal infection. However **Khrriesat and Najada**[15] reported that the conjunction of increase ASOT, high ESR and a positive C-reactive protein level should alert the clinician that ARF is likely when articular symptoms are observed, even in the absence of clinical carditis and before the echocardiogric findings.

ESR was found to be raised in 88.63% of cases in the present study, an incidence similar to that of **Sharma *et al.***[6]**,** and **Saxena**[33]**.** In our study patients presented by severe carditis with heart failure had decreased ESR.

C-reactive protein, another acute phase reactant was positive in 90.90% of our patients CRP is neither specific nor does it indicate accurately the degree of severity. It is a sensitive indicator of inflammation. Absence of CRP is strongly against the diagnosis of acute rheumatic fever[38]**.** Presence of CRP however is not diagnostic since it becomes positive in many respiratory infections.

The tests of acute phase response, ESR and C-Reactiv protein showed a wide variation in published series in different countries [5,33,39]**, Carvalho *et al.*** [33] attributed this to the different laboratory techniques that might have influenced these results in the same way for antistreptolysin O.

An important clue for diagnosis ascertainment is high or rising ASOT[33]**, it is** raised in 79.54% patients in our study group. ASOT titers of more than 200 I.U were taken as significant. Wide variations are observed in several published series in different countries. **Sharma *et al.***[6] in their Indian series found significant rising ASO titers in (96%), **Carvalho *et al.*** [33] reported it to be 58.2% in Brazilian Series. Moreover, systematic review recently published by **Costa *et al.*** [39] comparing all Brazilian series published since 1980's, indicated a wide variation in ASOT from 48.7% to 84.5% in different studies.

In the present study, 9 patients (20.46%) had insignificant ASO titers of less than 200 IU. Such cases usually presented in the relatively late phase of the disease (late carditis) or with delayed manifestations of RF when ASOT suggestive of preceding streptococcal infection had already normalized. Therefore, late onset carditis of RF was subsequently excluded from the requirement of elevated ASOT[4]**. Sharma *et al.***[6] in their series found insignificant ASOT (<200 IU) in 4% of patients had rheumatic chorea.

ASO titers while of considerable value for diagnosis show no clear relationship to inflammatory activity of the disease. It is very important to have serial estimation of ASO titers, rising titers are of more significance for recent evidence[6]**.** Also, **Carvalho *et al.***[33] stressing the importance of serial determination over the first two months.

Chen *et al.*[8] reported that the diagnosis of RF remains difficult and complex with tendency for atypical features, therefore it is essential to develop new pathogenic diagnostic techniques. They suggested that lymphocyte procoagulant activity (PCA) and antibody to streptococcal polysaccharide (ASP), not only are the evidence of prior streptococcal group A infection, but also reflect immune state.

Echocardiography is useful in evaluating patients suspected of having rheumatic valve disease[40]**.** In the present study, echocardiogram of patients revealed that 100 % of our patients had valvulitis of whome 2 patients (4.54%) had silent valvulitis with no clinical asscultatory findings. Also echocardiography helps the diagnosis of pericardial effusion in 4 patients (9.09%).

In conclusion, our study shows that atypical articular manifestations of ARF, which do not fulfill the last revised Jones criteria, were present in a high percentage of cases. This may represent an additional difficulty for establishing the diagnosis.

This study warns that ignoring atypical cases with lacking ineffective secondary prophylaxis regimen would result in a cardiac sequelae with possible increase incidence of RHD.

Egyptian physicians must remind that ARF remains an important part of our clinical vocabulary in Egypt. However, till now any clear cut guidelines for Egyptian patients' scenario are not existent.

References

1- Holmer C and Shulman ST (1991) Clinical aspects of acute rheumatic fever. J Rheumatol 18:2-13.
2- Pastore S, De Cunto A,Benettoni A *et al.* (2010) The resurgence of rheumatic fever in a developed country area: the role of echocardiography. Rheumatology 50(2):396-400
3- Jones TD (1944) Diagnosis of rheumatic fever JAMA 126:481-484
4- WHO Expert Consultation on Rheumatic Fever and Rheumatic Heart Disease. Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consultation, Geneva, 29 Oct-1 Nov 2001. Geneva: WHO, 2004.(WHO Technical Report Series No 923.).
5- Pileggi GCS, and Ferriani VPL (2000) Atypical arthritis in children with rheumatic fever. J Pediatr (Rio) 76(1):49-54.
6- Sharma SD, Gupta RK, Gupta R *et al.* (2007): Clinical Laboratory and Echocardiographic Profile of Rheumatic Fever in Children 9(1) :1-4.
7- Pereira BA, da Silva NA, Andrade LE *et al.* (2007) Jones criteria and under diagnosis of rheumatic fever. Indian J Pediatr 74 :117-121.
8- Chen L, Xie X, Gu J *et al.* (2009) Changes of manifestations of 122 patients with rheumatic fever in South China during last decade. Rheumatol Int 30:239-243.
9- Da-Salvia and Da- Pereira BA (1997) Acute Rheumatic fever Still a challenge.Pediatric Rheumatology 23(34):545-568.
10- Williamson L, Bowness P, Mowat A, and Smith I (2000) Lesson of the week Difficulties in diagnosing acute rheumatic fever-arthritis short lived and carditis silent. BMJ.320:362-365.
11- Stollarman GH (2001) Rheumatic fever in the 21st Century. Clinical Infection Disease 33:806-814.
12- Dajani AS (1992) Guidelines for the diagnosis of rheumatic fever (Jones criteria 1992 update) JAMA.268:2069-2073.
13- Bakiler AR and Arun- Ozer E (2008) An unusual case of acute rheumatic fever presenting with unilateral pulmonary edema. The Turkish Journal of Pediatrics 50 :589-591.
14- Stolerman GH (1997) Rheumatic fever .Lancent 349: 935-942.
15- Khriesat I and Najada AH (2003) Acute rheumatic fever without early carditis: an atypical presentation. Eur J Pediatr 162:868-871.
16- Kotby AA, Abd EL-Monim MT (1996) Assesment of rheumatic fever and rheumatic heart disease in the children's hospital ,Ain Shams University (1981-1995). The Egyptian Journal of Pediatrics 13(3-4):183-205.
17- Eissa AM , Kafay A, Hussein S, Saad MA, Maged M and EL-Sisy N (1988) Ten years follow up study on rheumatic children in EL-Hussein University Hospital. Gaz Egypt Paed Ass.36(3-4) :183-188.
18- Kassem AS, Zyan R, and Zaher SR (1995) Rheumatic fever and rheumatic heart disease in Alexandria, Egypt: present status .EHJ. Feb 129-136.
19- Guedes Y, Kotby A, EL-Demellawy M *et al.* (1999) HLA Class II Association with Rheumatic Heart Disease Are More Evident and Consistent Among Clinically Homogeneous Patients.Circulation 99(21): 2784-2790.
20- Stanevicha V, Eglite J, Sochneves A *et al.* (2003) HLA Class II Association with Rheumatic Heart Disease Are More Evident and Consistent Among Clinically Homogeneous Patients in Children in Latvia. Arthritis Research and Therapy 5(6) :340-346.
21- El Banna H, Zaki ME, Ismil SK, Mamzy E and Ibrahim S (2007) Molicular and immunological studies in children with rheumatic fever. Sc J Az Med Fac.(girl) 28: 1593-1603.
22- Hollander E, Del Giudize-Asch G, Simon L (1999) B-lymphocyte antigen D8/17 and repetitive behaviors in artism . Am J Psychiatry 156(2) : 317-320.
23- Chanderashekhar and Narula (2007) Rheumatic fever in Willerson JT, Wellens HJJ, Cohn JN, and Holwer DR (eds): Cardiovascular medicine, third edition, section III. Springer London, 431-439.
24- Carapetis JR, Steer AC, Mulholland E K, *et al.* (2005) The global burden of group A streptococcal diseases. Lancet infect Dis 5:685-694.
25- Stolerman GH (1975) Rheumatic fever and streptococcal infection . New York, Grune and Stratton.
26- Carapetis JR and Currie BJ (2001) Rheumatic fever in a high incidence population the importance of monoarthritis and low grade fever. Arch Dis Child 85:223-227.
27- Firrieri P (2002) Preceedings of the Jones criteria Workshop for the Jones criteria working group. Circulation.106:2521-2523.
28- Carapetis JR, Brown A, Wilson N J *et al.* (2007) An Austeralian guidline for rheumatic fever and rheumatic heart disease: an abridged outline. MJA 186(11): 581-586.
29- RHD Australia (ARF/RHD writing group), National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Australian guideline for prevention, diagnosis

and management of acute rheumatic fever and rheumatic heart disease (2nd edition). 2012

30- van der Helm-van Mil AH (2010) Acute rheumatic fever and post-streptococcal reactive arthritis reconsidered. Curr Opin Rheumatol 22(4): 437-442.

31- Ayoub and Majeed (2000) Post-streptococcal reactive arthritis. . Curr Opin Rheumatol 12:306-310.

32- Ayoub EM and Ahmed S (1997) Update on complications of group A streptococcal infections. Curr Prob Pediaer 27:90-101

33- De Cavalho SM, Dalben I, Corrente J E *et al.* (2012) Rheumtic Fever Presentation and outcome: a case- series report.Rev Bras Reumatol 52(2):236-246.,

34- Figueroa FE, Fernandez MS, Valdes P, Welson C, Lamas F,Carrion F, Berrios X and Valdes F (2001) Prospective comparison of clinical and echocardiographic diagnosis of rheumatic carditis : long term follow up of patients with subclinical disease .Heart 85(4): 407-410.

35- Saxena A (2000) Diagnosis of acute rheumatic fever: current status of Jones Criteria and role of echocardiography .Indian J Pediatr 67:283-286.

36- Hilario MO and Terreri MT (2002) rheumatic fever and post-streptococcal arthritis.Best Pract Res Clin Rheumatol 16(3):481-494.

37- Chebab G (2001) Subclinical carditis during an initial attack of acute rheumatic fever, contribution of colored Doppler echocardiography and therapeutic advantages. Med Liban.49(6):311-315.

38- Tandon R (2001) Acute Rheumatic Fever.In: Ghai OP(ed) Ghai Essential Pediatrics 5th edn New Delhi, Interprint 274-258.

39- Costa LP, Domiciano DS and Pereira RMR (2009) Caracteristicas demograficas. Clinicas, laboratories e radiologicas da febre reumatica: revisao sistematica. Rev Bras Reumatol 49(5):606-616.

40- Kumar P and Clark M (2005) Echocardiography. In Kumar and Clark clinical medicine, 6th edition, El Sevier Saunders.

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