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Original article

Articular manifestations in patients with atypical rheumatic fever

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ABSTRACT

Objectives: To describe the clinical characteristics and the occurrence of atypical arthritis in children diagnosed with rheumatic fever (RF) and followed in tertiary care clinics in Salvador, Bahia, Brazil.

Methodology: A descriptive study of a case series, of the initial clinical presentation, and of recurrence in 41 children diagnosed with RF.

Results: Of the patients studied (n=41), 61% were male, mean age of 9.2 years, and mean age at diagnosis between 5 and 16 years. Arthritis was present in 75.6% of patients; carditis in 75.6%; chorea in 31.7%; erythema marginatum in 14.6%; and subcutaneous nodules in 4.9%. An atypical pattern was observed in 22 of 31 cases of arthritis (70.9%): involvement of small joints and/or axial skeleton in 12 cases (38.7%); >3 weeks of duration in 9 (29%); inadequate response to NSAIDs in 2 (6.5%); oligoarthritis (≤ 4 joints) in 22/31 (71%), with monoarthritis in 6/31 (1 in the foot, 1 in the ankle, and 4 in the knee). Fever was present in 78% of the cases, and 82.9% of patients were regularly on secondary prophylaxis.

Conclusion: Atypical arthritis was present in most patients presenting with joint involvement, being a confounding factor against a proper diagnosis and of therapeutic delay.

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Manifestações articulares atípicas em pacientes com febre reumática

RESUMO

Objetivos: Descrever as características clínicas e a ocorrência de artrite atípica em crianças com diagnóstico de febre reumática (FR) acompanhadas em ambulatórios terciários em Salvador, Bahia.

Metodologia: Estudo descritivo, de uma série de casos, do quadro clínico inicial ou recorrência de 41 crianças com diagnóstico de FR.

Resultados: Dos pacientes estudados (n=41), 61% eram do sexo masculino; com média de idade de 9,2 anos e idade no momento do diagnóstico entre 5 e 16 anos. Artrite esteve

Palavras-chave:

Febre reumática

Crítérios de Jones

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presente em 75,6% dos pacientes; cardite em 75,6%; coreia em 31,7%; eritema marginado em 14,6% e nódulos subcutâneos em 4,9%. Um padrão atípico foi observado em 22 dos 31 casos com artrite (70,9%): envolvimento de pequenas articulações e/ou esqueleto axial em 12 casos (38,7%); duração maior que três semanas em nove (29%); resposta inadequada ao AINH em dois (6,5%), oligoartrite (\leq quatro articulações) em 22/31 (71%), sendo monoartrite em 06/31 (uma em pés, uma em tornozelo e quatro em joelho). A febre esteve presente em 78% dos casos e 82,9% dos pacientes utilizavam a profilaxia secundária de forma regular. **Conclusão:** Artrite atípica esteve presente na maioria dos pacientes que cursaram com acometimento articular, constituindo um fator de confundimento diagnóstico e atraso terapêutico adequado.

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Introduction

Rheumatic fever (RF) is a late, inflammatory, non-suppurative complication of the infection of the upper airways by the group A beta-hemolytic streptococci.¹⁻⁴ It can affect different tissues, including the heart, the joints and the central nervous system,⁴ and occurs mainly among genetically predisposed children and adolescents between the ages of 5 and 15.⁴⁻⁶

The diagnosis of RF remains one of the most difficult problems in the paediatric area, thanks to the polymorphism of its clinical presentation and to the lack of specific or pathogenomic laboratory tests for the disease.⁷⁻¹⁰

The Jones criteria were established in 1944, with the goal of reducing the occurrence of diagnostic errors and delays.¹¹ Despite its usefulness in clinical practice, these criteria do not include the difficulties in establishing the diagnosis of RF, especially in the presence of atypical articular manifestations, which may lead to errors or to delays in diagnosis.⁷ This diagnostic difficulty is accentuated in patients who present with arthritis as the only clinical manifestation of the disease.^{4,12,13}

The classic description of arthritis of RF consists of a picture of migratory polyarthritis, mainly of large joints of the lower limb, and with its onset around 2-3 weeks after a streptococcal infection of the oropharynx. The typically intense pain responds well to the use of non-steroidal anti-inflammatory drugs (NSAIDs), and usually has no more than 3 weeks in duration.^{2,8} The most commonly affected joints are knees and ankles.

Atypical joint manifestations have been increasingly described in the literature, being characterized by a monoarticular picture lasting longer than six weeks, poor response to salicylates, and an additive arthritis, as well as an unusual involvement of joints such as hips, cervical spine, and small joints.^{1,7,9} This possible pattern of joint involvement in RF was first mentioned in 1975 by Stollerman, when this author noted that 32% of children with rheumatic fever did not show the classical pattern of joint involvement.¹⁴

Terreri et al. rated the articular pattern in 93 patients with RF. The arthritis was additive in 27% of cases; small joints, such as the metacarpophalangeal and proximal and distal interphalangeal joints, were affected with a frequency of 2%-8%; arthritis with more than six weeks duration was observed in 10%; no response to acetylsalicylic acid occurred in 15% of the cases, and monoarthritis was found in 6% of patients.⁷

These atypical manifestations further hamper the diagnosis of RF, especially if the doctor is not aware of the possibility of this kind of event.

The present study was conducted aiming to evaluate the characteristics of joint involvement and the occurrence of atypical arthritis in children during the initial outbreak and in recurrence of RF.

Patients, materials and methods

Forty-one medical records of 41 children and adolescents diagnosed with RF and treated at the Paediatric Rheumatology Service, Hospital Professor Edgard Santos, Universidade Federal da Bahia, and at the Paediatric Cardiology Service, Hospital Ana Nery, both in the city of Salvador, Bahia, were retrospectively analyzed. The study covered a period of three years, from March 2009 to December 2012. The inclusion criteria were: diagnosis of RF based on modified Jones criteria (1992) and patients aged up to 21 years-old. The variables used in the study were: gender; age; presence and characteristics of major and minor Jones criteria; characteristics of articular involvement; information on the evidence of prior infection by streptococcus (ASLO), and laboratory tests. To take into consideration the presence of an atypical pattern for the joint involvement, at least one of the following features was needed: more than three weeks in duration; involvement of small joints and/or cervical spine and/or hip joint; monoarthritis; and poor response to salicylates.

Data processing and analysis were performed with the help of the Statistical Package for Social Sciences (SPSS®) program, version 12.0, with descriptive data analysis. The mean age of patients and the absolute and relative frequencies of the following variables were analyzed: gender; major and minor Jones criteria; number of joints involved; atypical articular manifestations; description of each atypical feature, and regularity of secondary prophylaxis.

The project was approved by the ethics committee, HUPES (071/2009, Resolution CNS 196/96).

Results

The medical records of 41 children (25 males and 16 females; ratio 1,6:1,0) were reviewed. The patients' age at diagnosis ranged from 5 to 16 years, with a mean of 9.2 years.

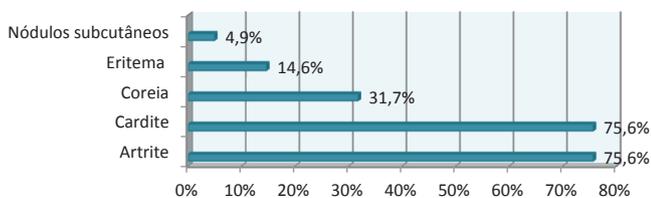


Figure 1 – Frequency of the biggest signs of Jones diagnostic criteria in 41 patients with rheumatic fever diagnosis

The frequency of Jones major signs was: 31 patients with arthritis; 31 with carditis; 13 with chorea; two with subcutaneous nodules; six with erythema marginatum (Fig. 1). Arthritis was isolated in six of 31 cases presenting with this symptom (19.4%).

As to the characteristics of joint involvement, the atypical pattern was observed in a considerable number of cases with arthritis: 22/31 (70.9%). Involvement of small joints and/or axial skeleton occurred in 12 (38.7%); a period greater than three weeks in nine (29%); inadequate response to NSAIDs in two (6.5%), oligoarthritis (≤ 4 joints) in 22/31 (71%), with monoarthritis in 06/31 (foot, 1; ankle, 1; and knee, 4) (Fig. 2). The presence of polyarthritis (≥ 5 joints) occurred in 9/31 patients (29%).

Among these 22 unusual cases, isolated arthritis was found in six patients (19.4%); arthritis associated with carditis was found in 12 cases (57.1%); arthritis associated with carditis and chorea in four cases (19%); arthritis, carditis, erythema marginatum and subcutaneous nodules in one case (4.8%); and arthritis, carditis, chorea and erythema marginatum in one case (4.8%).

Fever was present in 78% of cases, and 82.9% of patients were regularly on secondary prophylaxis.

Discussion

In 1982, Goldsmith and Long highlighted the presence of a clinical picture of arthritis with unusual characteristics (symmetric, longer duration, short latency period after streptococcal infection, and poor response to salicylates),¹⁵ and suggested an immune response change to some kind of antigenic modification of Group A-beta-haemolytic streptococcus.

Since then, many authors are referring to clinical pictures of arthritis after infection with Group A-beta-haemolytic streptococcus with the characteristics above mentioned, not usual to the pattern described by Jones criteria.

The studies in the literature on this form of presentation of arthritis after streptococcal infection are relatively scarce

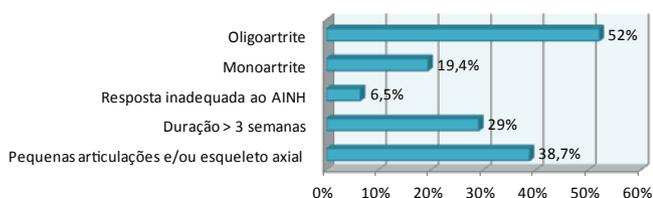


Figure 2 – Percentage of atypical articular manifestations in 41 patients with rheumatic fever diagnosis

and heterogeneous, being often based on reports or series of cases, which limit the clear knowledge of the causation of this form of presentation.

Given the conflicting literature, we proposed, out of curiosity, to map the profile of patients diagnosed with RF at our service, with greater emphasis on the pattern of presentation of articular involvement.

In the present study, patients' age at diagnosis ranged from 5 to 16 years, with a mean age of 9.2 years, a finding similar to results previously described in other regions in Brazil.^{1,9} According to literature, the incidence of RF is higher between 5-15 years, both for the first outbreak and for relapses.¹⁶ Therefore, there were no variations in age of onset for RF with atypical joint pattern.

Among the patients in this study, 61% were male (ratio, 1,6:1). This finding contradicts the results of most authors, which show a higher prevalence of RF in females (55% to 60.5%).^{1,2,17}

As for Jones major criteria, there was no predominance of arthritis over carditis, as in most studies in the literature, with similar prevalences for both clinical manifestations (75.6%). This can be explained by the inclusion of patients from a center of reference in paediatric cardiology (Fig. 1).

The prevalence of arthritis varies in the literature, but our results were similar to the studies of Motta and Meira and of Ferreri et al.,^{1,18} which found arthritis in 71.4% and 70, 5% of their patients, respectively.

In the present study, 51.6% of our patients had involvement of more than one, and up to five joints; 19.4% in just one joint; and 29% in more than five joints. This result revealed a high prevalence of oligoarticular presentation in patients with RF in our community, and these presentations undoubtedly generate diagnostic difficulties and therapeutic delays.

Table 1 illustrates the frequency of monoarthritis in RF in different studies, drawing attention to this possibility in the clinical comparison of RF, in contrast to what was set by Jones criteria.^{12,19-22} An example in clinical practice is the suspicion of septic arthritis in cases of monoarthritis accompanied by fever, causing loss of time with diagnostic procedures and with invasive and unnecessary therapeutic interventions. Mataika et al. described three cases of monoarthritis initially treated as septic arthritis, with subsequent diagnosis of RF in the presence of a developing endocarditis.²³

Among the more involved joints in patients with single joint involvement, the knee joints have prevailed, followed by axial skeleton and ankle joints. Harlan et al.²¹ evaluated 92 patients with RP, and three of these had monoarthritis

Table 1 – Percentage of monoarthritis in rheumatic fever according to different authors

Study	Percentage of monoarthritis
Khriesat I, 2003 ¹²	32%
Carapetis, 2001 ¹⁹	17%
Ralph A, 2006 ²⁰	5.5%
Harlan GA, 2006 ²¹	3.3%
Olgunturk, 2006 ²²	16%
Present study	19.4%

(hips in one patient, knees in two), similarly to Pileggi et al.,⁹ who also found three cases of monoarthritis, two in the knee and one in the hip joint. In our study, single joint involvement occurred in the following joints: knee (4/6), foot (1/6), and ankle (1/6).

Some manifestations described are the involvement of small joints (such as metacarpophalangeal and metatarsophalangeal joints), and of the axial skeleton (spine and sacroiliac and hip joints),^{9,10} and this may cause diagnostic difficulties with juvenile idiopathic arthritis and the juvenile spondyloarthritides (Table 2). The involvement of small joints was present in 18% of cases analyzed by Lin Chen et al.²⁴ In 38.7% of our patients, the involvement of small joints occurred mainly in feet and hands and, in lesser extent, in axial skeleton joints.

In some patients diagnosed with RF, a favourable clinical response after appropriate use of NSAIDs does not occur. This implies a long-term use of these drugs, due to the presence of an arthritis of prolonged evolution. In the present study, despite the early use of this medication in the first days after the diagnosis of arthritis, 4.9% of patients were poorly responsive to NSAIDs. In the study of Ferriani et al.,² this poor response occurred in 19.56% of patients.

The presence of arthritis as the only clinical manifestation is still considered as an unusual clinical manifestation that complicates and delays the final diagnosis of RF; this occurred in 19.4% of patients (6/31). Harlan et al.²¹ demonstrated that the time for diagnosis of RF was superior to 4 weeks in 59% of patients with atypical arthritis, as compared to 35% in other patients.²¹

Another aspect that complicates the diagnosis of RF is the laboratory diagnosis. In addition to being non-specific, laboratory abnormalities may not be present in a significant percentage of patients due to various factors: the period of collection, a previous administration of antibiotics, and accessibility to these tests in a timely manner, among others. Looking specifically at patients presenting with atypical manifestations, evidence of inflammatory activity was positive in only 56%, and ASLO was present in 44% of patients.

Thus, the results reveal a considerable percentage of patients with atypical articular manifestations, corroborating observations made for some time by other authors (Fig. 3), and again calling attention to the need to keep in mind this possibility of articular presentation in patients with RF.

Table 2 – Joints affected in patients with rheumatic fever according to different authors

Joints	Pileggi (2000) ⁹ %	Hilário (1995) ¹⁰ %	Present study %
Knee	75	76	74.2
Ankle	79	62	61.3
Elbow	19	29	29
Wrist	25	28	32.3
Small joints (feet and/or hands)	32/26	13/15	22.6
Shoulder	19	12	12.2
Cervical spine	26	15	9.7
Lumbar spine	4	07	6.5

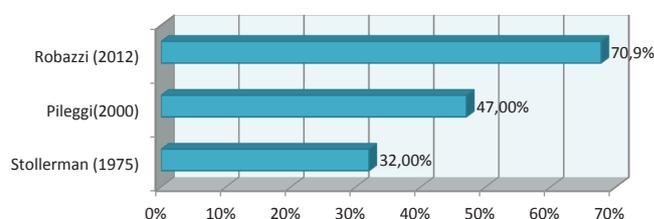


Figure 3 – Comparison of percentage of atypical manifestations among various authors

Conclusion

From the results of this study, we may stress the importance of the recognition, by rheumatologists, paediatricians and even internists, of atypical articular presentations in the clinical picture of RF, thus avoiding unnecessary diagnostic delays and, consequently, therapeutic delays, with risk of irreversible cardiac sequelae.

This diagnostic suspicion should be addressed in the case of a patient with evidence of infection with Group A-beta-haemolytic streptococcus; who do not fulfil modified Jones criteria for the diagnosis of RF; and who develop a clinical picture of acute outcome, oligo or single joint, symmetrical or asymmetrical, usually non-migratory arthritis that may affect any joint and with a poor response to acetylsalicylic acid.

Conflicts of interest

The authors declare no conflicts of interest.

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