

## **SYDENHAM'S CHOREA – CLINICAL AND EVOLUTIVE CHARACTERISTICS**

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### **ORIGINAL ARTICLE**

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## **ABSTRACT**

**CONTEXT:** During the last 12 years we have observed an increase in the frequency of Sydenham's chorea (SC) in our country. We observed that some of our patients presented recurrence of chorea despite regular treatment with penicillin benzathine.

**OBJECTIVE:** The aim of our study was to evaluate clinical and evolutive characteristics of SC in a group of patients followed in our Pediatric Rheumatology Unit.

**TYPE OF STUDY:** Retrospective study.

**SETTING:** Section of Pediatric Rheumatology – Discipline of Allergy, Clinical Immunology and Rheumatology – Dept. of Pediatrics – UNIFESP – EPM.

**PARTICIPANTS:** Two hundred and ninety patients with rheumatic fever (RF) followed between 1986 and 1999.

**METHODS:** We reviewed the charts of 290 patients with rheumatic fever (RF) followed between 1986 and 1999. All patients were diagnosed according to revised Jones criteria (1992). We included 86 patients that presented SC as one of the major criteria (one or more attacks) and evaluated their clinical and evolutive characteristics as well the treatment.

**RESULTS:** Fifty five patients were girls and 31 were boys. The mean age at onset was 9.7 y and mean follow-up period was 3.6 y. The 86 SC patients presented 110 attacks of chorea. We observed isolated chorea in 35% of the patients, and 25 (29%) presented one or more recurrences. We included only 17 of the 25 patients with 22 recurrences and 14 attacks of chorea for further analysis, because it was not possible to detect precisely the interval between attacks in the other patients. The approximated interval between the attacks ranged from 4 to 96 months. In 71% of the patients there was no failure in the secondary prophylaxis with penicillin benzathine, which was performed every 3 weeks.

**CONCLUSION:** Despite the regular use of secondary penicillin benzathine prophylaxis, children with RF have a high risk of SC recurrence.

**KEY-WORDS:** Rheumatic fever. Sydenham's chorea. Recurrences. Prophylaxis.

## **INTRODUCTION**

Sydenham's chorea is an enigmatic manifestation of rheumatic fever. Although SC is rare in developed countries, we have observed an increase in its frequency in our country during the last few years.<sup>1</sup>

It may appear as an isolated manifestation of rheumatic fever or precede or accompany an acute attack associated with other criteria of the disease.<sup>2,3,4,5</sup>

The relationship between Sydenham's chorea and rheumatic fever has been the subject of considerable controversy and some aspects continue to be intriguing. Since chorea is generally a late manifestation, it is unusual to find clinical or even immunological (laboratory) evidence of a streptococcal infection and the erythrocyte sedimentation rate (ESR) is usually normal.<sup>6</sup>

In 1985, Berrios and col.<sup>7</sup> described that 32% of their Sydenham's chorea patients suffered a recurrence despite the penicillin prophylaxis and this raised doubts not only about the relationship with the streptococci but also, in some cases, with rheumatic fever itself. We also observed that some of our patients presented recurrence of chorea despite regular treatment with penicillin benzathine. Our aim was to study the clinical and evolutive characteristics of Sydenham's chorea patients and the frequency of the recurrences as well its relationship with regular prophylaxis.

## **PATIENTS AND METHODS**

A retrospective evaluation of the charts of 290 rheumatic fever patients diagnosed according to the revised Jones criteria (1992)<sup>8</sup> was carried out between 1986 and 1999. Patients diagnosed before 1992 were reevaluated to assure if they fulfilled the 1992 Jones criteria.

Children less than 16 years of age, with well-established chorea and a follow-up period equal to or greater than one year were included in the study. Patients with a family history of chorea, or positive antinuclear antibody, were excluded.

The epidemiological data, the clinical characteristics of the attacks (initial and recurrent) and the compliance with secondary prophylaxis (every 21 days) were analysed. We defined recurrence when the patient presented manifestations of chorea after a minimum period of 4 months without symptoms and medication.

The antistreptolysin O (ASO) titer was measured in the majority of patients and considered altered when there was an increase of two or more titer steps in relation to the previous titer (15 days interval) or when one titer was equal to or greater than 800 IU/ ml (in cases with only one measurement).

## **RESULTS**

Of the 290 patients with rheumatic fever, 86 (29.6%) had chorea during the first attack of the disease. There was a total of 100 chorea episodes, including recurrences. Fifty five patients with Sydenham's chorea were female (ratio 1.7:1) and 44 non-caucasian. The mean age at onset of symptoms was 9.7 years old and mean follow-up period was 3.6 years (Table 1).

Sydenham's chorea occurred isolated in 30 (35%) patients and associated with other symptoms in 56 (65%) patients during the first episode of rheumatic fever. In the latter we observed chorea (co) and carditis (ca) in 38 patients, chorea, carditis and arthritis (ar) in 14 and chorea and arthritis in 4 patients. Of the 86 patients who presented chorea at the first attack, 25 (29%) had 32 recurrences, of which 24 were with chorea. This recurrences began after a minimum of 4 months without symptoms and without specific chorea treatment. In 8 patients (10 episodes), it was not possible

to detect precisely the interval between attacks and for this reason, these were not included in the study. We therefore included only 17 of the 25 patients with 22 recurrences and 14 attacks of chorea for further analysis. Within this group, 10 patients were female and 9 were caucasian. The mean age at onset was 9.8 years old and the mean follow-up period 4.8 years (Table 1). The manifestations of the recurrent attacks are described in table 2. Of the 30 patients who presented with isolated chorea at the first attack, 8 (26.6%) had a disease recurrence: 6 with chorea (5 isolated and 1 associated); 1 with carditis and 1 with carditis and arthritis. Of the 56 patients who presented with chorea associated to another major disease manifestation during the first attack, 9 (16%) had recurrences. The intervals between the attacks of chorea can also be found in table 2.

According to the information from the patient or parent 61 (71%) children had no failure in the secondary prophylaxis while 25 (29%) were not compliant.

Of the 17 patients who presented recurrences, 9 (53%) showed good compliance.

ASO was measured in 8/14 patients with disease recurrence and was found normal in all of them.

## **DISCUSSION**

Rheumatic fever is still a prevalent disease in our country and an important cause of morbidity due to chronic cardiopathy.<sup>9</sup>

Sydenham's chorea was described by Thomas Sydenham in 1686 and it has been associated with RF since 1956<sup>10</sup>. It is a major manifestation of RF and, according to the last modification of the Jones criteria in 1992, a sufficient criteria even by itself for the diagnosis of the disease<sup>8</sup>. The incidence of Sydenham's chorea

has been increasing in our country over the last years, as recently published<sup>1</sup>. In a study undertaken in 7 centers of the State of São Paulo (Brazil) with 786 patients, chorea was present in 38 % of Rheumatic fever patients (299 patients).<sup>11</sup>

In our study Sydenham's chorea occurred in 30% of our 290 patients (86 patients), which is similar to the frequency found by Cardoso et al<sup>12</sup>, but higher than the frequency reported in the majority of the studies<sup>8,13</sup>. Interestingly of the 86 patients who presented with chorea at the first attack, approximately 60% had associated carditis. However we did not observe a predominance of isolated chorea, as described in the literature<sup>14</sup>. We speculate that this fact may be related to the referring practice of our patients, where some of them, especially those with isolated chorea, are followed by other specialists. Additional studies are necessary to confirm if this fact may also be related to specific characteristics of our patient population or even to the streptococcal strains involved.

Nevertheless, of the 22 recurrences, only 3 (13.6%) presented isolated or associated carditis, so we did not detect a higher probability of recurrences with cardiac involvement in patients who presented chorea at the first attack, as described in the literature<sup>15</sup>. Cardoso et al suggested that carditis could be related to longer duration of Sydenham's chorea<sup>16</sup>.

Overall 17 children (19.7%) presented with recurrences; of these, 9 used regular prophylaxis and 8 were non-compliant. Since we were unable to determine serum levels of penicillin in these patients, compliance was assessed according to the information of patients and parents.

In 14/22 recurrences chorea was present, either isolated or associated to another manifestation. We did observe a predominance of chorea (63%) in the recurrences, which proves the tendency of chorea to mimic its first attack.<sup>17</sup>

Since we were *intrigued* by the high frequency of recurrences in patients with chorea on regular prophylaxis, we would like to emphasize a few issues:

1. We believe that the recurrences, including those in patients with a short interval (4 months) between the attacks, are not a continuation of the same attack, since those children remained asymptomatic and did not receive any treatment for their chorea during this period. It is important to mention that there is no reference in the literature regarding the minimum time required between two attacks;
2. There is a possibility that a chorea attack may be induced by other non-streptococcal stimuli, apart from those already known (birth-control pills and pregnancy), which could explain the recurrences in patients receiving regular prophylaxis;
3. Efficacy of the antibiotics used in secondary prophylaxis may be limited due to uncertain quality of some products;
4. Other non-rheumatic causes of chorea, such as viral infections, tumors of the central nervous system, degenerative processes, among others<sup>18,19,20,21</sup>, have to be considered specially in those patients who present with recurrent isolated chorea on adequate prophylaxis .

The lack of clinical and laboratory evidence of a prior streptococcal infection and the lack of elevation of acute phase proteins in the great majority of Sydenham's chorea patients lead us to believe that pure chorea is a "special" manifestation of rheumatic fever or that, in some cases, it may be related to another diagnosis. In some individuals the recurrence of rheumatic fever is caused by light or transient streptococcal infections which may remain undetected by culture or immunological

tests.<sup>7</sup> In this study we did not observe a significant increase in ASO titers in any patient.

Kulkarni et al described a 21% relapse rate in cases of Sydenham's chorea, however, data about the clinical characteristics of the patients or their prophylaxis compliance are lacking.<sup>14</sup>

In the opinion of Berrios et al., some of these chorea episodes do not represent distinct attacks but exacerbations in patients who have chronic and persistent choreiform activity, characterizing the natural course of the disease.<sup>7</sup> We believe however, that after a minimum period of 4 months without clinical manifestations *or specific treatment*, the recurrence of choreiform movements rather represent a clinical relapse than ongoing disease.

## CONCLUSION

Despite the regular use of secondary penicillin benzathine prophylaxis, children with rheumatic fever have a high risk of Sydenham's chorea recurrence.

Since the relationship of chorea and its recurrences with other clinical manifestations of rheumatic fever are poorly understood, rigorous prophylaxis with penicillin and periodic follow-up are necessary.

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## RESUMO

**CONTEXTO:** Nós observamos um aumento na frequência de coréia de Sydenham no nosso meio durante os últimos 12 anos. Foi verificado que alguns pacientes apresentaram recorrência da coréia apesar da profilaxia regular com penicilina benzatina.

**OBJETIVO:** O nosso objetivo foi avaliar as características clínicas e evolutivas da coréia de Sydenham em um grupo de pacientes acompanhados no nosso ambulatório de Reumatologia Pediátrica.

**TIPO DE ESTUDO:** Estudo retrospectivo.

**LOCAL:** Setor de Reumatologia Pediátrica, Disciplina de Alergia, Imunologia clínica e Reumatologia, Departamento de Pediatria, Universidade Federal de São Paulo/Escola Paulista de Medicina.

**PARTICIPANTES:** 290 pacientes com febre reumática seguidos no período de 1986 e 1999.

**MÉTODOS:** Nós revisamos os prontuários de 290 pacientes com febre reumática seguidos no período de 1986 a 1999. Todos os pacientes tiveram o diagnóstico de febre reumática de acordo com os critérios de Jones revisados (1992). Foram incluídos 86 pacientes que apresentaram coréia de Sydenham como manifestação maior (um ou mais surtos) e avaliamos suas características clínicas e evolutivas bem como tratamento.

**RESULTADOS:** 55 pacientes eram do sexo feminino e 31 do masculino. A idade média de início da doença foi 9,7 anos e o tempo médio de evolução 3,6 anos. Os 86 pacientes com coréia de Sydenham apresentaram 110 surtos de coréia. Nós observamos coréia isolada em 35% dos pacientes e 25 (29%) apresentaram uma ou mais recorrências. Foram incluídos para o estudo apenas 17 de 25 pacientes com 22 recorrências e 14 surtos de coréia, pois não foi possível detectar o intervalo entre os surtos nos outros pacientes. O intervalo entre os surtos variou de quatro a 96 meses. Em 71% dos pacientes não ocorreu falha na profilaxia secundária com penicilina, que foi realizada a cada três semanas.

**CONCLUSÃO:** Apesar do uso regular de profilaxia com penicilina benzatina, as crianças com FR têm um maior risco de recorrência de coréia de Sydenham.

**PALAVRAS-CHAVE:** Febre reumática. Coréia de Sydenham. Recorrência. Profilaxia.

**Table 1. Patients with Sydenham's chorea in the first attack and recurrences, according the gender, race, age at onset and follow-up period.**

Chorea	N	Gender (F:M)	Race (C:NC)	Age at onset - years (mean)	Follow-up period – years (mean)
First attack	86	55:31 1.7:1	42:44	9.7	3.6
Recurrence	17	10:7 1.4:1	9:8	9.8	4.8

F: Female  
M: Male

C: Caucasian  
NC: Non-caucasian.

**Table 2. Age and clinical characteristics of Rheumatic Fever patients with Sydenham's chorea at the first attack and presented recurrences (n = 17)**

Patient	Gender	1 <sup>st</sup> attack		1 <sup>st</sup> recurrence		2 <sup>nd</sup> recurrence		3 <sup>rd</sup> recurrence	
		Age (years)	Jones Major Criteria	Age (years)	Jones Major Criteria	Age (years)	Jones Major Criteria	Age (years)	Jones Major Criteria
1	Fem.	12	co	13	co+ar	14.5	Ar		
2	Male	4	co	4.7	co				
3	Fem.	12.6	co	13	co				
4	Fem.	11.9	co	12.3	co	12.6	Co		
5	Fem.	6.9	co	7.2	co				
6	Fem.	11.1	co	13.2	ca				
7	Fem.	8.2	co	10.1	co				
8	Male	11.7	co	14.1	ca+ar				
9	Male	12.7	co+ca	13.1	co				
10	Male	11	co+ca+ar	15	co+ar				
11	Male	9.2	co+ar	9.9	ca+ar				
12	Male	9.3	co+ca+ar	10.8	ar				
13	Fem.	10.8	co+ca+ar	11.2	co	12.2	Co		
14	Fem.	10.1	co+ar	10.6	ar	13	Ar	14.3	co+ar
15	Fem.	9.4	co+ca	13	ar				
16	Fem.	7.6	co+ca+ar	15.6	co				
17	Male	9	co+ca	14.5	co+ar				

Fem.- female

co- chorea

ca- carditis

ar- arthritis.