Sydenham's Chorea in Jerusalem: Still Present

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Abstract

Background: In developed countries the incidence of Sydenham's chorea, a major sign of rheumatic fever, has declined, but outbreaks are still encountered worldwide.

Objectives: To report the characteristics of a cohort of SC patients in the Jerusalem area.

Methods: We conducted a prospective assessment of rheumatic fever and SC between 1985 and 2002. The diagnosis of rheumatic fever was based on the revised Jones criteria. Other etiologies of chorea were excluded. Recurrence was defined as the development of new signs lasting more than 24 hours and separated by a minimum of 2 months from the previous episode. Patients were followed for 1 to 14 years following the initial SC episode, and at least one year after recurrence.

Results: Among 180 children with rheumatic fever, 24 had SC. Most of them came from large families of Ashkenazi origin. In 19 patients (79%) the chorea was associated with other rheumatic fever signs, while 5 had pure chorea. Due to the systematic use of two-dimensional color Doppler echocardiography, cardiac involvement was detected in 75% of the patients. Ten patients (42%, 7 females) developed 11 recurrent episodes of chorea 3 months to 10 years after the initial episode. At recurrence, chorea was the sole rheumatic sign in all nine patients who recurred once. None of the patients had persistent chorea.

Conclusions: SC is still prevalent in the pediatric population of Jerusalem, and may recur years later. Recognition of the disease and adequate treatment is necessary.

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Sydenham's chorea is the central nervous system manifestation and one of the major criteria of rheumatic fever [1]. The prevailing hypothesis is that the chorea in rheumatic fever is mediated by group A Streptococcus infections triggering an autoimmune response directed at the basal ganglia [2,3]. However, with no definite laboratory confirmation, the diagnosis of SC is based on the clinical context and requires exclusion of other conditions [2,4,5]. It is recommended that patients with SC be treated with penicillin prophylaxis to prevent recurrent attacks, even if they do not appear to have rheumatic heart disease [4].

SC is usually a monophasic event. Recurrences are observed in 20% of the patients, usually within several months of the initial episode, and are considered rheumatic fever relapse [6].

SC = Sydenham's chorea

Although the decline in rheumatic fever incidence in developed countries has been associated with a decrease of SC [7], there are still outbreaks of both rheumatic fever and SC worldwide [2,4,8–10]. In June 2000 Habib and colleagues [11] reported 44 patients with acute rheumatic fever identified over a decade in two hospitals of the Nazareth area. Surprisingly, none of them had chorea.

Over a period of 17 years, 24 children from the Jerusalem region were diagnosed at Bikur Cholim Hospital as having SC. We summarize our clinical experience with these patients.

Patients and Methods

All patients diagnosed with rheumatic fever between 1985 and 2002 at the Bikur Cholim Hospital, Jerusalem, were screened for SC. Diagnosis of rheumatic fever was based on the revised Jones criteria [1]. Cardiac involvement was assessed clinically and by echocardiography in all patients [12–15]. The diagnosis of SC was made after exclusion of other etiologies [2,5,16]. All patients underwent routine blood tests, throat culture, C-reactive protein, erythrocyte sedimentation rate, thyroid function tests, rheumatoid factor, antinuclear antibodies, anticardiolipin antibodies, anti-streptolysin O titers, serum ceruloplasmin, electrocardiogram, two-dimensional echo-Doppler cardiography, electroencephalogram and brain computed tomography [5,16]. Patients were considered to have pure chorea if there was no evidence of other signs of rheumatic fever. Chorea severity was graded as minimal, moderate, or severe [17]. At the time of diagnosis all SC patients received prophylaxis with 250 mg of oral penicillin twice daily until the age of 18 years.

Recurrence was defined as the development of new signs lasting more than 24 hours and separated by a minimum of 2 months from the previous episode. At the time of recurrence patients were assessed for rheumatic fever activity. Workup consisted of clinical examination, echo-Doppler cardiography, ECG, ESR, CRP, ASLO, ANA, ACL, and throat culture. Patients were followed for 1–14 years after the initial SC episode and at least one year after the recurrence.

For statistical analysis categorical variables were compared by the Fisher exact test, and continuous variables were compared by Student's *t*-test.

ESR = erythrocyte sedimentation rate
CRP = C-reactive protein
ASLO = antistreptolysin O titers
ANA = antinuclear antibodies
ACL = anticardiolipin antibodies

Results

Patients

Of 180 patients with rheumatic fever, 24 had SC. Their clinical characteristics are shown in Table 1. The female/male ratio was 2:1. Age at onset ranged from 4 to 13 years. Most patients (18/24) came from large families of 4 or more siblings. Sixteen patients had at least one parent of Ashkenazi origin (East European). Familial chorea/rheumatic fever was present in only two cases. Chorea severity was minimal in 8 patients, moderate in 12 and severe in 4. Chorea was mostly bilateral at presentation (19/24); hemichorea was detected in 5 patients. Aside from the chorea, the neurologic examination was normal in 12 patients, hypotonia was found in 10, and unilateral weakness ipsilateral to the hemichorea in 2. Four cases with very mild chorea resolved without treatment. Moderate chorea resolved with valproic acid alone (14 patients). Haloperidol or thioproperazine had to be added in three patients with moderate chorea resistant to valproic acid, and was the initial treatment in three patients with severe chorea. The duration of chorea was several weeks in most patients, but lasted for 1.5 years in one child. There were no cases of persistent chorea.

In all patients, laboratory workup for other etiologies aside from rheumatic fever was negative, and brain CT was normal. Electroencephalogram was unremarkable in all but two patients who had abnormal tracings with intermittent slow wave activity.

SC diagnosis was easily established in 19 patients (79%), based on the clinical setting and the presence of other major rheumatic fever signs, which coincided with the appearance of chorea in 11 patients, preceded the chorea for 6–12 months in 6 patients and appeared 3 months to 1 year after the chorea in 2 patients. Major signs included cardiac valvular pathology in 18 patients and arthritis in one. In five patients with pure chorea there were no other major rheumatic fever signs or any laboratory evidence for an acute rheumatic fever attack, except for increased ASLO titer in one patient. In these patients, diagnosis was based on exclusion of other etiologies.

Cardiac pathology

The results of the cardiac evaluation are detailed in Table 2. They were detected clinically in eight patients only. In 55% of the heart-involved patients positive echocardiographic findings were found in spite of negative auscultation. Mitral regurgitation was the typical finding in all patients with cardiac involvement: isolated in 16, or associated with mitral stenosis or tricuspid insufficiency (1 patient each).

Recurrences

Eleven recurrences were recorded in 10 (7 females) of the 24 patients with SC [Tables 1 and 3]. The time interval between the initial episode and the recurrence ranged from 3 months to 10 years. Eight recurrences occurred within the first 18 months after the primary episode. One patient had a second relapse 2.5 years

Table 1. Clinical characteristics of all patients with SC

	n=24	%
Age at onset (range)	4–13 yrs	
Females	16	66
Large families (>4 children)	18	75
Ashkenazi origin	16	66
Familial chorea/rheumatic fever	2	8
Chorea severity		
Mild-minimal	8	33
Moderate	12	50
Severe	4	16
Chorea characteristics		
Bilateral symmetric	13	54
Bilateral asymmetric	6	25
Hemichorea	5	21
Neurologic findings		
None	12	50
Hypotonia	10	42
Ipsilateral weakness	2	8
Treatment		
None	4	16
Valproic acid	14	58
Neuroleptic agents	6	25
Presence of other rheumatic fever major signs	19	79
Pure chorea	5	21
Persistent chorea	0	0
Recurrences	11 (10 patients)	42
Follow-up	1–14 yrs	

Table 2. Cardiac pathology at first attack

Total no. of patients	24	%
Positive clinical auscultation	8	33
Positive echocardiographic findings	18	75
Positive echocardiographic findings with negative auscultation	10	42
Mitral regurgitation alone	16	66
Mitral regurgitation with mitral stenosis	1	
Mitral regurgitation with tricuspid insufficiency	1	

Table 3. Clinical characteristics of patients with recurrence

Gender	Age at 1st chorea episode	Other rheumatic fever signs around 1st attack	Time elapsed between 1st and recurrent chorea	Rheumatic fever activity during recurrence
F	12 yrs	No	6 mos	No
F	13 yrs	Yes	16 mos	High ASLO
F	9 yrs	Yes	15 mos	No
F	9 yrs	Yes	10 yrs	ASLO borderline
F	8 yrs	Yes	3 mos	No
M	10 yrs	Yes	6 mos	No
F	12 yrs	Yes	5 mos	No
M	7 yrs	Yes	12 mos	No
M	9 yrs	Yes	5 yrs	No
F	10 yrs	Yes	6 mos	No
			2.5 yrs	High ASLO, cardiac changes

later, and in two others it appeared 5 and 10 years after the initial event. ASLO titer at recurrence was elevated only in two patients and borderline in one. In the nine patients with only one recurrence, chorea was not associated with any clinical evidence for active rheumatic fever. In the patient with two recurrent episodes, mitral regurgitation developed into mitral stenosis discovered at the second episode.

Discussion

The age and sex distribution and the clinical profile of our SC patients are similar to those reported in other series [3–5,16]. However, there were notable differences from the report of Habib et al. [11]: none of the Nazareth patients had chorea, and a high prevalence of rheumatic fever was observed in our institution. This might be partly explained by the different genetic background, since 66% of our patients were of Ashkenazi origin and members of large families. These findings could be comparable with a report describing acute rheumatic fever among adult Hassidic Jews in the United States, which might suggest a possible genetic predisposition [18].

In most of our patients the presence of other rheumatic fever signs established the rheumatic origin of the chorea and indicated antibiotic prophylactic therapy. The use of two-dimensional color Doppler echocardiography in our patients raised the sensitivity of detecting cardiac involvement from 33% (clinical diagnosis) to 75% [Table 2]. The rate of carditis, documented by Habib's team and based on clinical findings alone, was 34% [11]. This highlights the current debate regarding the use of echocardiography as the sole criterion of rheumatic carditis without accompanying auscultatory findings [9].

In the present study a relatively high rate of recurrence was observed (42% in our patients) as compared to previous reports: 25% in Australia [19], and 20% in Brazil [16], Israel [10] and the USA [20]. This could be attributed, in part, to the long follow-up period (the recurrence of chorea in three patients occurred more than 2, and up to 10 years, following the initial episode). Thus, SC recurrences might be underestimated. However, in contrast to a recent publication [16], none of our patients had persistent chorea, nor did any develop PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection) after the choreic episode [21].

Surprisingly, rheumatic fever recurrence was clinically restricted to CNS involvement in nearly all cases (10/11), and only one patient had a change in cardiac involvement during recurrence. Moreover, at the time of SC recurrence and up to one year of follow-up, none of the nine other patients showed other major rheumatic fever signs. In the majority of the recurrence episodes no clinical or laboratory evidence could support linking the relapse of the chorea with rheumatic fever activity, suggesting that recurrent chorea in patients with a history of previous SC is not always due to rheumatic fever activity [22,23].

In conclusion, SC is still manifest in the pediatric population of Jerusalem, and represents a treatable movement disorder. Recognition of the disease and antibiotic prophylactic long-term treatment is necessary.

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