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Sydenham's Chorea: A Clinical Follow-Up of 65 Patients

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Sydenham's chorea, the neurological manifestation of rheumatic fever, is the most common acquired chorea of childhood. In this retrospective study, the authors aim to present the clinical and laboratory findings of 65 Sydenham's chorea patients, followed up in a clinic over less than 7 years. The mean age at the onset of the symptoms was 11.7 ± 2.6 years (range, 6-17 years). Of the patients, 63% were female and 37% were male (male/female: 1.7/1). Chorea was generalized in 78.5% of the patients, right hemichorea in 12.3%, and left hemichorea 9.2%. There was a history of rheumatic fever in 30.8% of the patients. Echocardiographic study showed cardiac valve involvement in 70.5% of 61 patients. Brain magnetic resonance imaging, which was performed on only 18 patients, was evaluated as normal in all. Electroencephalography was also performed on only 18 patients and showed abnormal waves in 50% of them. Pimozide was mostly the first choice of drug therapy. Nevertheless, drug therapy was not needed in 18.5% of the patients. The recovery period of the first attack of the chorea was 1 to 6 months in 51.7% of the patients. The recurrence rate was 37.9%. In conclusion, Sydenham's chorea is still an important health problem in Turkey with respect to its morbidity.

Keywords: rheumatic fever; Sydenham's chorea

Chorea is characterized by rapid, involuntary, irregular, jerky movements of the limbs, face, and trunk. Sydenham's chorea, the most common acquired chorea of childhood, is the neurological manifestation of rheumatic fever in which antistreptococcal antibodies are believed to cross-react with neuronal tissue, particularly in the basal ganglia.[1-6]

In the developing world, a decline in the incidence of rheumatic fever and associated Sydenham's chorea was observed along with the improved socioeconomic conditions and extended use of antibiotics against group A beta-hemolytic streptococci. But since the 1980s, the incidence has increased, and it has been again a major health concern in developing countries.[7,8] Rheumatic fever and Sydenham's chorea are still an important problem in Turkey with respect to its considerable morbidity and mortality.[9,10]

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In this study, we aim to present clinical and laboratory features and outcome of 65 patients with Sydenham's chorea, followed up in our clinic over less than 7 years.

Patients and Methods

We reviewed the medical records of 65 inpatients and outpatients diagnosed with Sydenham's chorea, followed up between December 1995 and September 2002, in the Department of Pediatrics, Selçuk University, Meram Medical Faculty, Konya, Turkey.

Sydenham's chorea was diagnosed by clinical observation of chorea and the absence of any other underlying cause.[2] Total physical examination and a standard clinical examination for chorea, including localization of the chorea, darting tongue, milkmaid grip,[4] and laboratory tests including antistreptolysin O, C-reactive protein, erythrocyte sedimentation rate, thyroid, liver and kidney functions, rheumatoid factor, antinuclear antibody, anti-DNA, serum copper and ceruloplasmin levels, chest x-ray, electrocardiography, echocardiography, electroencephalography, and brain magnetic resonance imaging, were performed.

A Hewlett-Packard Sonos 1000 system ultrasonic imager was used for echocardiographic assessments. Appropriate transducers of 2.5, 3.5, and 5 MHz were used to define the cardiac structures. The echocardiographies were obtained in the standard precordial positions,

following the recommendations of the American Society of Echocardiography.[11]

With magnetic resonance imaging (PICKER, 1.5 T, Picker Internationals, Highlands Heights, Ohio), transaxial and coronal sections of brain were obtained at the acute phase of the chorea.

Scalp electroencephalography was recorded by using electroencephalographic equipment, an 8-channel and a 16-channel system with the electrodes arranged according to the 10-20 system in Sydenham's chorea patients at the acute and the recovery phase (6 months to 1 year later).

The effectiveness of the drugs, used in the treatment of the chorea, was compared by Student's *t* test. A *P* value of <.05 was considered statistically significant.

Results

The mean age at the onset of the symptoms was 11.7 ± 2.6 years (range, 6-17 years). Of 65 patients, 63% were female and 37% male (1.7:1). Of 65 patients, 55.4% were evaluated first in our clinic, but 44.6% were referred from other clinics. The onset of the symptoms of 33.8% patients was in winter, 26.2% was in spring, 30.8% was in autumn, and 9.2% was in summer. Consanguinity was present in 15.4% of the patients. An upper respiratory tract infection was experienced in 23.1% of the patients several weeks prior.

The presenting complaints of the patients are seen in Table 1, the physical examination findings are presented in Table 2, and some clinical features are featured in Table 3. A history of rheumatic fever was present in 30.8% of the patients. The interval between rheumatic fever findings and the onset of the chorea was from 1 to 96 months. Echocardiography could have been performed in 61 patients, and valve involvement was detected in 70.5% of the patients. The histories and the findings of arthritis and carditis are seen in Table 4.

Laboratory studies were as follows: antistreptolysin O 610.8 ± 383.9 Todd unit (range, 106-1688 Todd unit), erythrocyte sedimentation rate 21.2 ± 20.6 mm/h (range, 4-90 mm/h), and leukocytes 7816 ± 2460 × 10^9/L (range, 3600 ± 12 000 × 10^9/L). Tests of rheumatoid factor, antinuclear antibody, anti-DNA, thyroid function, serum copper, and ceruloplasmin levels were negative or in the normal range.

Brain magnetic resonance imaging was performed on 18 patients and evaluated as normal in all.

Electroencephalography was performed on only 18 patients and showed abnormal findings in 50% of them at the acute phase. These findings were continuous and irregular slow activity in 88.9% of the patients, paroxysmal bursts in 55.6%, sharp waves in 33.3%, and alpha asymmetry in 11.1%. The localizations of these waves were in the parietooccipital area in 88.9% of the patients. The abnormal waves were lateralized in 55.6% of the patients. Hyperventilation and photic stimulation did not influence the records. The control electroencephalographic study was performed in the recovery phase (6 months to 1 year later) on the patients having electroencephalographic abnormalities, except for 1 patient. The electroencephalographic records in the recovery phase (n = 8) indicated that the abnormal findings improved in 62.5% and persisted in 37.5% of the patients.

Pimozide was the first choice in 26 patients, haloperidol in 23, phenobarbital in 2, carbamazepine in 1, and haloperidol together with pimozide in 1. No drug therapy

Table 1. Presenting Complaints of Sydenham's Chorea Patients (n = 65)

Complaints	%
Involuntary movements	100
Speech disorder	36.9
Impairment in handworks	21.5
Unbalanced walking	20
Writing disorder	16.9
Anxiety, sleepiness, exhaustion	7.7
Impairment in school success	6.2
Character changes	4.6
Quick tempered	1.5

Table 2. Physical Examination Findings of Sydenham's Chorea Patients (n = 65)

Features	%
Generalized chorea	78.5
Right hemichorea	12.3
Left hemichorea	9.2
Chorea in face	6.2
Chorea in head-neck	6.2
Milkmaid grip	26.2
Darting tongue	18.5
Decreased tendon reflexes	10.8
Increased tendon reflexes	1.5
Decreased muscle tonus	3.1
Decreased muscle power	9.2

Table 3. Clinical Features of Sydenham's Chorea Patients

Features	
Age, y, mean ± SD	11.7 ± 2.6
Duration of chorea until admission, days, mean ± SD	162 ± 557 (range, 2-4000)
Duration of improvement of the first attack of the chorea (n = 29), %	
0-1 month	13.8
1-6 months	51.7
6-12 months	3.4
12-24 months	20.7
Over 24 months	10.3
Number of recurrences (n = 29), %	37.9
Time to recurrence, days, mean ± SD	366 ± 294 (range, 60-860)

Table 4. Arthritis and Carditis Features of Sydenham's Chorea Patients

Arthritis and Carditis Features	%
Histories (n = 65)	
Arthritis	18.5
Carditis	4.6
Arthritis and carditis	7.7
Acute arthritis (n = 65)	1.5
Echocardiography findings (n = 61)	
Valve involvements	70.5
Mitral	95.3
Aort	23.3
Tricuspid	7
Pulmonary	2.3
Normal	29.5
Artralgia (n = 65)	13.8

Table 5. Treatment With Haloperidol and Pimozide of Sydenham's Chorea Patients

	Pimozide	Haloperidol	*P*
Time to onset of the clinical recovery, days, mean ± SD	29.5 ± 42.9	14.5 ± 10.7	<.05
Time to complete remission, days, mean ± SD	109.5 ± 115.5	42.7 ± 29.9	<.05
Total duration of the drug use, days, mean ± SD	84.3 ± 102.6	51 ± 22.5	<.05

was needed in 18.5% of the patients. Thirty-six patients did not come to follow-up regularly. For the rest of the patients (n = 29), haloperidol did not become useful in 3 patients, pimozide in 5, and haloperidol together with pimozide in 1. Because of the adverse effects of the drugs (haloperidol in 3 patients, pimozide in 1 patient), treatment was ended in 4 patients. Observed adverse effects of haloperidol were dystonia, Parkinsonism, sleepiness, absentmindedness, and forgetfulness. Those of pimozide were sweating, sleepiness, headache, dry mouth, and numbness. Pimozide was used as a second-choice drug in 7 patients, haloperidol in 6, carbamazepine in 4, and valproic acid in 1. Because most of the patients did not come to follow-up regularly after the onset of the treatment, we could not have collected the outcome as properly as we had wished. However, we compared the time to onset of the clinical recovery, complete remission, and total duration of haloperidol and pimozide use by using the data that we could obtain (see Table 5).

Discussion

In 1686, Thomas Sydenham accurately described Sydenham's chorea, differentiating it from the other movement disorders. Three centuries later, Taranta and Stollerman established a causal relationship between streptococcal infection and Sydenham's chorea, and now Sydenham's chorea has been accepted as a major manifestation of rheumatic fever.[2,5]

Although the pathophysiology of Sydenham's chorea is still unclear, the cross-reactivity of a streptococcal antibody with basal ganglia and the brain cross-reactive epitopes of streptococcal M proteins are indicated in patients with Sydenham's chorea.[12,13] The main symptoms of Sydenham's chorea, including abnormal movements and hypotonia, are believed to result from an imbalance among the dopaminergic system, the intrastriatal cholinergic system, and the inhibitory gamma-aminobutyric acid system.[14] In addition, imaging studies performed by positron emission tomography and single-photon emission-computed tomography show hypermetabolism in the basal ganglia.[15-18]

Sydenham's chorea occurs in 10% to 20% of the patients with rheumatic fever, predominantly at 5 to 15 years old, with a peak incidence at 8 to 9 years and a female predominance of 2:1.[1,3-6] In our series, the mean age of the onset of the chorea was 11.7 years, and the ratio of female to male was 1.7:1.

Sydenham's chorea usually shows remission after a mean period of 6 to 9 months, although in some patients, it lasts 2 years, and in rare subjects, it remains as a lifelong condition. Although 51.7% of our patients showed remission in a period of 1 to 6 months, chorea remained more than 1 year in 10.3% of the patients. It is reported that 20% to 35% of the cases relapse usually in the first few years.[5] In our series, 37.9% of the patients had relapsed in a mean time of approximately 1 year.

As Sydenham's chorea lacks a specific biologic marker, its diagnosis relies on the recognition of acute chorea clinically and the absence of an underlying cause. Although other manifestations of rheumatic fever strongly support the diagnosis of Sydenham's chorea, their presence is not mandatory, according to the modified Jones criteria.[2,5] It remains unclear why not all subjects with rheumatic fever develop Sydenham's chorea, and conversely, it is also unclear why not more than the 20% of Sydenham's chorea patients show any other clinical manifestation of rheumatic fever.[5] Cardiac involvement in Sydenham's chorea has been reported in 23% to 84% of patients with rheumatic fever, whereas the association with arthritis does not exceed 30%.[5] In our series, a history of rheumatic fever had been taken from 30.8% of the patients. Cardiac valve involvement was detected in 70.5% of the patients, and arthritis was experienced in 27.7% of them. Hemichorea was observed in 21.5% of the patients. In the literature, hemichorea is encountered in up to 20% of the patients.[5,6]

Tests of acute phase reactions are usually normal in Sydenham's chorea. Increased antistreptolysin O titers exist in two thirds of the cases. These tests are much less helpful in Sydenham's chorea than in other forms of rheumatic fever because of the long latency between the infection and the onset of the chorea.[1,3-6]

Brain magnetic resonance imaging, performed in 18 patients, did not indicate any pathologic finding in the basal ganglia and thalami. In some studies, although magnetic resonance imaging has revealed signal changes and swelling in the basal ganglia,[15,19-22] in most cases, pathology has not been observed.[5] Giedd et al[21] reported that a signal change was demonstrated in 2 of 24 patients with Sydenham's chorea.

Electroencephalographic abnormalities in Sydenham's chorea are nonspecific and seen in 29% to 85% of the patients.[23,24] In the present study, abnormal electroencephalographic records were detected in 50% of 18 patients. Electroencephalographic records, reported in Sydenham's chorea, are mostly paroxysmal and slow wave in the parietooccipital area.[23,25-27] In our study, parietooccipital localization was found in 8 patients, slowing was seen in 8, and paroxysmal activity was seen in 5. Of these cases, 3 patients showed no improvement in electroencephalographic records despite the clinical recovery. Although electroencephalographic abnormalities in Sydenham's chorea are expected to improve, it is not necessary to show parallelism with clinical recovery.[26,27] Nevertheless, persistent electroencephalographic abnormalities in Sydenham's chorea are also reported.[25] In our series, there was no relationship between the lateralized waves in 5 patients and the localization of the chorea. Although it is reported in Sydenham's chorea,[25] we did not observe spikes in electroencephalographic records or any epileptic attack.

Because the disease is usually self-limited, bed rest and stress avoidance may suffice for the treatment. If the choreic movements are prolonged or severe or associated with psychological dysfunction, drug treatment becomes necessary.[1,3-5] Sedatives such as phenobarbital or diazepam,[5,6] dopaminergic receptor antagonists such as haloperidol and pimozide,[1,3,5,28-30] reserpine,[31] tetrabenazine,[32] corticosteroids,[33] phenothiazines,[5] valproic acid,[34,35] and carbamazepine[36,37] have been used with varying degrees of success.

Successful control of the choreic symptoms by using dopaminergic blockers (haloperidol, pimozide) has provided evidence that increased dopaminergic activity is, at least in part, responsible for the involuntary movements.[28-30] Shannon and Fenichel[30] suggest that pimozide, a dopaminergic blocker, may have fewer side effects than haloperidol. They suggest that it has virtually no effect on norepinephrine receptors, and so low doses (2 mg, twice a day) and short-term treatment have a lower risk for the appearance of tardive dyskinesia while improving Sydenham's chorea symptoms. Haloperidol is frequently associated with side effects such as parkinsonism and dystonia.[38] In our series, although haloperidol seemed to be more effective than pimozide, it was the cause of more frequent and serious adverse effects. An appropriate comparison could not have been performed for the other drugs because of insufficiency of the follow-up.

An important point of view in the follow-up of Sydenham's chorea is whether prophylaxis with penicillin or sulfonamides is necessary. Although a few reports mention that prophylactic treatment does not have any effect on recurrences[39] or clinical course,[40] common opinion differs.[1,3-6] The prophylaxis must be continued to the age of 12 years if carditis does not exist.[1,5,6] We inform our patients with cardiac valve involvement about performing lifelong prophylaxis.

In conclusion, Sydenham's chorea is still an important health problem despite being known for centuries. Sydenham's chorea needs more effective medical effort because of its long duration, recurrences, impairment of school success, accompanying heart disease, and requirement of prophylaxis for years.

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References

1. Gilroy J. *Basic Neurology*. 3rd ed. New York: McGraw Hill; 2000.
2. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council on Cardiovascular Diseases in the Young of the American Heart Association. Guidelines for the diagnosis of rheumatic fever: Jones criteria, 1992 update. *JAMA*. 1992;268:2069-2073.
3. Carter S. Sydenham chorea. In: Powland LP, ed. *Merritt's Textbook of Neurology*. 8th ed. Philadelphia: Lea & Febiger; 1989:645-647.
4. Haslam RHA. Chorea. In: Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson Textbook of Pediatrics*. 16th ed. Philadelphia: W. B. Saunders; 2000:1840-1841.
5. Cardoso F. Infectious and transmissible movement disorders. In Jankovic J, Tolosa E, eds. *Parkinson's Disease and Movement Disorders*. 3rd ed. Baltimore: Williams & Wilkins; 1998:945-965.
6. Paulson GW, Reidre CR. Movement disorder in childhood. In Watts RL, Koller WC, eds. *Movement Disorders: Neurologic Principles and Practice*. New York: McGraw-Hill; 1997:661-672.
7. Cardoso F, Eduardo C, Silva AP, Mota CC. Chorea in 50 consecutive patients with rheumatic fever. *Mov Disord*. 1997;12:701–703.
8. Bitar FF, Hayek P, Obeid M, et al. Rheumatic fever in children: a 15-year experience in a developing country. *Pediatr Cardiol*. 2000;21:119–122.
9. Karademir S, Demirceken F, Atalay S, et al. Acute rheumatic fever in children in Ankara area in 1990–1992 and comparison with a previous study in 1980–1989. *Acta Paediatr*. 1994;83:862.
10. Karaaslan S, Oran B, Reisli I, Erkul I. Acute rheumatic fever in Konya, Turkey. *Pediatr Int*. 2000;42:71–75.
11. Feigenbaum H. *Echocardiography*. Philadelphia: Lea & Febiger; 1994.
12. Bronze MS, Dale JB. Epitopes of streptococcal M proteins that evoke antibodies that cross-react with human brain. *J Immunol*. 1993;151:2820-2828.
13. Kiessling LS, Marcotte AC, Culpepper L. Antineuronal antibodies in movement disorders. *Pediatrics*. 1993;92:39-43.

14. Marques-Dias MJ, Mercadante MT, Tucker D, Lombroso P. Neuropsychiatry of the basal ganglia. *Psych Clin North Am*. 1997;20:809-820.
15. Goldman S, Amrom D, Szliwowski HB, et al. Reversible striatal hypermetabolism in a case of Sydenham's chorea. *Mov Disord*. 1993;8:355-358.
16. Weindl A, Kuwert T, Leenders KL, et al. Increased striatal glucose consumption in Sydenham's chorea. *Mov Disord*. 1993;8:437-444.
17. Dilenge ME, Shevell MI, Dinh L. Restricted unilateral Sydenham's chorea: reversible contralateral striatal hypermetabolism demonstrated on single photon emission computed tomographic scanning. *J Child Neurol*. 1999;14:509-513.
18. Lee PH, Nam HS, Lee KY, et al. Serial brain SPECT images in a case of Sydenham chorea. *Arch Neurol*. 1999;56:237-240.
19. Castillo M, Kwock L, Arbelaez A. Sydenham's chorea: MRI and proton spectroscopy. *Neuroradiology*. 1999;41:943-945.
20. Ikuta N, Hirata M, Sasabe F, et al. High-signal basal ganglia on T1-weighted images in a patient with Sydenham's chorea. *Neuroradiology*. 1998;40:659-661.
21. Giedd JN, Rapoport JL, Kruesi MJ, et al. Sydenham's chorea: magnetic resonance imaging of the basal ganglia. *Neurology*. 1995;45:2199-2202.
22. Emery ES, Vieco PT. Sydenham's chorea: magnetic resonance imaging reveals permanent basal ganglia injury. *Neurology*. 1997;48:531-533.
23. Heye N, Jergas M, Hotzinger H, et al. Sydenham chorea: clinical, EEG, MRI and SPECT findings in the early stage of the disease. *J Neurol*. 1993;240:121-123.
24. Ganji S, Duncan MC, Frazier E. Sydenham's chorea: Clinical, EEG, CT scan, and evoked potential studies. *Clin Electroencephalogr*. 1988;19:114-122.
25. Ch'ien LT, Economides AN, Lemmi H. Sydenham's chorea and seizures: clinical and electroencephalographic studies. *Arch Neurol*. 1978;35:382-385.
26. Aminoff MS. *Electrodiagnosis in Clinical Neurology*. 3rd ed. New York: Churchill Livingstone; 1992.
27. Westmoreland BF. Sydenham's chorea. In: Niedermeyer E, Lopes da Silva FH, eds. *Electroencephalography*. Baltimore: Urban-Schwarzenberg; 1982:228.
28. Miyakawa M, Ohkubo O, Fuchigami T, et al. Effectiveness of haloperidol in the treatment of chorea minor. *No To Hattatsu*. 1995;27:191-196.
29. Harries-Jones R, Gibson JG. Successful treatment of refractory Sydenham's chorea with pimozide. *J Neurol Neurosurg Psychiatry*. 1985;48:390.
30. Shannon KM, Fenichel GM. Pimozide treatment of Sydenham's chorea. *Neurology*. 1990;40:186.
31. Naidu S, Narasimhachari N. Sydenham's chorea: a possible presynaptic dopaminergic dysfunction initially. *Ann Neurol*. 1980;8:445-447.
32. Hawkes CH, Nourse CH. Tetrabenazine in Sydenham's chorea. *Br Med J*. 1977;1:1391-1392.
33. Green LN. Corticosteroids in the treatment of Sydenham's chorea. *Arch Neurol*. 1978;35:53-54.
34. Daoud AS, Zaki M, Shakir R, al-Saleh Q. Effectiveness of sodium valproate in the treatment of Sydenham's chorea. *Neurology*. 1990;40:1140-1141.
35. Alvarez LA, Novak G. Valproic acid in the treatment of Sydenham chorea. *Pediatr Neurol*. 1985;1:317-319.
36. Artigas Pallares J, Lorente Hurtado I. Carbamazepine in paroxysmal choreoathetosis in Sydenham's chorea. *An Esp Pediatr*. 1989;30:41-44.
37. Roig M, Montserrat L, Gallart A. Carbamazepine: an alternative drug for the treatment of nonhereditary chorea. *Pediatrics*. 1988;82:492.
38. Shields WD, Bray PF. A danger of haloperidol therapy in children. *J Pediatr*. 1976;88:301-303.
39. Gebremariam A. Sydenham's chorea: risk factors and the role of prophylactic benzathine penicillin G in preventing recurrence. *Ann Trop Paediatr*. 1999;19:161-165.
40. Ghram N, Allani C, Oudali B, et al. Sydenham's chorea in children. *Arch Pediatr*. 1999;6:1048-1052.