Sydenham's Chorea with a Pediatric Neurologist's Point of View

Çocuk Nörolojisi Bakışı ile Syndenham Koresi

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ABSTRACT

Objective: Sydenham's chorea, which is an autoimmune and hyperkinetic movement disorder seen following pharyngitis caused by group A streptococci, is the neurological manifestation of acute rheumatoid fever. This study aims to present the demographical and clinical features in addition to patient management and outcomes in patients diagnosed with Sydenham's chorea.

Material and Methods: Thirty-three children and adolescents who were admitted to the Ankara Education and Research Hospital pediatric neurology clinic between September 2016 and September 2019 and were diagnosed with Sydenham's chorea were included in the study. Demographic, clinical and laboratory data, treatments and responses to treatments along with outcomes were evaluated in a retrospective and cross sectional manner.

Results: The average age of the patients was 119.6±29.2 months and 24.2% were male. In 30 (90.9%) of the patients, carditis as reported by echocardiography accompanied Sydenham's chorea. Hemichorea was present in 11 (30%) patients while chorea was more prominent in the extremities in 12 patients, in the trunk in 8 patients and in the face in 1 patient. Antistreptolysin-O titers were elevated in 28 (84%) patients. Twenty-eight (84.8%) patients were given haloperidol, 3 (9%) patients were given carbamazepine and 2 (%6) patients were given sodium valproate for an average of 6.8±1.1 months. Clinical remission was achieved in 6.9±1.2 months. The only adverse effect observed was parkinsonism caused by haloperidol prescribed for acute symptomatic treatment. The patients were followed up for 9.6±4.2 months after the symptoms had subsided and no recurrence was observed.

Conclusion: Sydenham's chorea is one of the major criteria for acute rheumatoid fever which classically limits itself but may cause loss of function and adversely affect the quality of life. Here, we aimed to show the clinicians clinical practice and results of management of Syndenham chorea in a wide range of pediatric patients.

Key Words: Chorea, Movement disorder, Sydenham's chorea

ÖZ

Amaç: A grubu beta hemolitik streptokokkal farenjit sonrası gelişen otoimmun, hiperkinetik bir hareket bozukluğu olan Syndenham koresi, akut romatizmal ateşin nörolojik klinik bulgusudur. Bu çalışmada Syndenham koresi tanısı alan hastaların demografik ve klinik özellikleri yanısıra hasta yönetimi ve sonuçlarının literatüre sunulması amaçlanmıştır.

Gereç ve Yöntemler: Ankara Eğitim ve Araştırma Hastanesi, Çocuk Nörolojisi Polikliniğinde Eylül 2016-Eylül 2019 tarihleri arasında başvuran Syndenham koresi tanısı alarak izlenen 33 çocuk ve adolesan hasta çalışmaya alınmıştır. Hastaların demografik, klinik ve laboratuvar özelliklerine ait bilgiler, verilen tedaviler ve tedavi yanıtları ile hastaların prognozları retrospektif ve kesitsel olarak değerlendirilmiştir.

Bulgular: Yaş ortalaması 119.6 ± 29.2 ay olan %24.2'si erkek cinsiyetteki 33 hastanın 30'unda (%90.9) ekokardiyografik kardit syndenham koresine eşlik ediyordu. Hemikore 11 hastada (%30) izlenirken, 12 hastada ekstremitelerde, 8 hastada

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gövdede, 1 hastada yüzde belirgin kore izlendi. Anti-streptolizin-O yüksekliği 28 hastada (%84) saptandı. Ortalama 6.8±1.1 ay süre ile Yirmi sekiz hastaya (%84.8) haloperidol, 3 hastaya karbamazepin (%9), 2 hastaya sodyum valproat (%6) tedavisi verildi. Klinik remisyon ortalama 6.9 ±1.2 ayda sağlandı. Haloperidol kullanımına bağlı parkinsonizm, akut semptomatik tedavi için haloperidol verilen bir hastada tek yan etki olarak kaydedildi. Semptomlar gerileyip tedavi sonlandırıldıktan sonra ortalama 9.6±4.2 ay izlenen hastalarda rekürrens görülmedi.

Sonuç: Klasik olarak kendi kendini sınırladığı bilinen ancak işlevselliği bozan, hayat kalitesini negatif yönde etkileyen Syndenham koresi, akut romatizmal ateşin majör kriterlerinden birisidir. Burada, Syndenham koresi yönetiminde klinik pratikteki uygulamalar ve sonuçları geniş bir pediatrik hasta popülasyonunda tartışılarak klinisyenlere ışık tutulması amaçlanmıştır.

Anahtar Sözcükler: Kore, Haraket bozukluğu, Syndenham koresi

INTRODUCTION

Sydenham's chorea is the sole neurologic manifestation of acute rheumatoid fever (ARA) in addition to being one of the major diagnostic criteria (1,2). Sydenham's chorea is present in approximately 25% of patients diagnosed with ARA (2). It is an autoimmune inflammatory disease where the immunologic response to group A beta hemolytic streptococci (GABHS) causes an autoimmune damage to basal ganglia (1). Chorea is the main finding in Sydenham's chorea which is the most common acquired and acute onset movement disorder in the pediatric age group (1,2). However, behavioral problems and cognitive symptoms often accompany chorea (3).

Findings of carditis have been reported in 70% of the patients in this self-limiting and usually monophasic disease (4). Although Sydenham's chorea is generally accepted as benign, it may seldom be refractory or recur (1,2). There is no internationally accepted consensus on the definitive and symptomatic treatment for chorea, antibiotics directed at active GABHS infection and preventing reinfection are the most common steps taken in clinical practice. In addition to these modalities, immunomodulatory treatment for the control of symptoms and prevention of persistence or recurrence of neurologic and psychiatric symptoms has been reported in the literature (5).

The aim of this study is to present the demographic and clinical features, treatments, and responses to these treatments in a large pediatric population diagnosed with Sydenham's chorea in a retrospective manner.

MATERIAL and METHODS

Thirty-three children and adolescents who were admitted to the Ankara Education and Research Hospital with a diagnosis of Sydenham's chorea between September 2016 and September 2019 were included in the study. Demographic, clinical and laboratory data of the patients were obtained from patient files in a retrospective manner.

Ethics committee approval for the study was obtained from the local ethics committee of the Ankara Education and Research hospital (180/2019) The study was conducted in accordance with the Helsinki criteria.

In addition to the demographic data of the patients included in the study, clinical features during admission, laboratory findings, clinical and laboratory features during follow up, treatment and outcomes were also evaluated. Demographic variables such as date of birth, age, gender, the age on admission and the last follow up in addition to neurological examination findings, treatment and response, duration of follow up and time to cure were recorded. Autoimmune marker levels, antistreptolysin-O titers (ASO), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, echocardiography, electroencephalography and cranial magnetic resonance imaging results were also evaluated.

Statistical analysis

The IBM SPSS (Statistical Package for the Social Sciences) version 21 was used for statistical analyses. Results of descriptive analyses have been reported as minimum, maximum and average ± standard deviation (X±SD) for numerical variables while non-numerical values have been reported as number (n) and percentage (%).

RESULT

A total of 33 children adolescents of which 8 (24.2%) were boys were included in the study. The youngest patient on admission was 68 months old while the oldest was 180 months old and the average was 119.6±29.3 months. The shortest follow up duration was 4 months while the longest was 24 months and the average was 9.7±4.9 months. Twenty-five (75.8%) of the patients were born via spontaneous vaginal delivery while only two (6%) of these patients had a history of preterm delivery. A total of 6 (18.1%) patients, including two patients with a history of preterm delivery, were born via Cesarean section. None of the patients had a positive family history of Sydenham's chorea or movement disorders.

All patients were given antibiotics to treat or prevent the recurrence of acute pharyngitis. Intramuscular benzathine penicillin G 1.2 million units was prescribed which was to be repeated every 3-4 weeks. Haloperidol (Nörodol®, drops) 0.25-15 mg/kg/day, carbamazepine 5-10 mg/kg/day and sodium valproate 10-40 mg/kg/day is recommended to control choreiform and psychiatric symptoms. Twenty-eight (84.8%) patients were given haloperidol, 3 (9%) patients were given

Table I: Neurological examination findings of the patients diagnosed with Sydenham's chorea.

Neurological examination findings	n=33 (100%)
Chorea	33 (100 %)
Unilateral (hemichorea)	11 (33.3 %)
Right extremity	9 (81.8 %)
Upper and lower extremities	12 (36.4 %)
Face and extremities	1 (3.0 %)
Trunk > extremities	8 (24.2 %)
Milking phenomenon	27 (81.8 %)
Hypotonia	4 (12.1 %)
Dysarthria	3 (9.0 %)
Failed ocular fixation test	3 (9.0 %)
Psychiatric symptoms	2 (6.0 5)

carbamazepine and 2 (6 %) patients were give sodium valproate. All patients had movement disorders, i.e. chorea as the chief complaint on admission. Choreiform movements were more prominent on the extremities for 12 (36.4%) patients and on the whole body for 8 (24.2%) patients while 11 (33.3%) patients had one sided chorea, who were diagnosed with hemichorea. Of the hemichorea patients, 5 (15.1%) had facial involvement. Choreiform movements were very prominent on the head and neck for one (3%) patient. No patients had additional movement disorders. Two (6%) patients had emotional instability and anxiety in addition to chorea.

Neurological examination findings of the patients have been summarized in Table I.

High ASO titers were detected in 28 (84.8%) of the patients and 16 (48.5%) had high ESR while 18 (48.5%) patients had elevated CRP levels. Twelve of these patients had all three parameters elevated while three patients had normal ASO titers and elevated ESR and CRP levels. All patients were negative for antinuclear antibody (ANA), anti-dsDNA, anticardiolipin and antiphospholipid immunoglobulin M and G which were routinely measured.

Cardiac auscultation revealed 32 patients with I-III/VI apical systolic murmur while 30 (93.8%) had echocardiographic findings of carditis and these patients were taken into follow up for subclinical carditis by pediatric cardiology.

All patients underwent cranial MRI on admission. The MRIs were performed within average 8.7±0.8 days after the onset of symptoms and all were reported as normal.

All patients were given antibiotics in order to treat or prevent the recurrence of acute pharyngitis. Intramuscular benzathine penicillin G 1.2 million units was prescribed which was to be repeated every 3-4 weeks. Haloperidol (Nörodol®, drops) 0.25-15 mg/kg/day, carbamazepine 5-10 mg/kg/day and sodium valproate 10-40 mg/kg/day is recommended in order to control choreiform and psychiatric symptoms. Twenty-eight (84.8 %) patients were given haloperidol, 3 (9%) patients were given carbamazepine and 2 (6%) patients were give sodium valproate.

During the follow up, one patient had to be changed to carbamazepine from haloperidol (8 mg/kg/day divided into three doses) due to parkinsonism and 3 (9%) patients required the addition of carbamazepine due to chorea resistant to haloperidol. There were no adverse effects attributable to carbamazepine or valproic acid. Acute symptomatic treatments were tapered off when the symptoms disappeared and these treatments lasted for 3 months 10 days minimum, 10 months 2 days maximum, with an average of 6.8±1.1 months. Average remission period for all patients was 6.9±1.2 weeks, 6.7±0.8 weeks for 24 (72.7%) patients who used only haloperidol, 8.8 ±0.4 weeks for 3 (9%) patients who used only carbamazepine and 6.5±1.8 weeks for 2 (6%) patients who used only sodium valproate. None of the patients were given immunomodulatory treatment. The patients were followed up for 4 months at minimum and for 24 months maximum (average of 9.6±4.2 months) and there was no recurrence.

DISCUSSION

Sydenham's chorea has been investigated widely in the literature owing to its status as the major criterion for ARA, the sole neurologic criterion, and the most frequent cause of acquired movement disorders of the childhood. It is more frequent in girls who are 8-9 years old (1,2). Similarly, there was a predominance of females in our study and the average age of onset was 9 old.

Although Sydenham's chorea is usually considered self-limiting, lack of proper antibiotic prophylaxis (6). There was no recurrence during the 10 months follow up period following the remission of symptoms in 33 children who were diagnosed with Sydenham's chorea in the pediatric neurology clinic of our hospital. This is an exceptionally low incidence considering the 20-46% recurrence incidence reported in studies investigating pediatric and adult patients (7-8).

This difference can be explained by the fact that the follow up period was shorter and antibiotic prophylaxis was more meticulously controlled in our study. Cases of chorea which last for 2 years have been reported and existence of active carditis and female gender have been listed as risk factors for persistence (9). Another study has reported the duration of chorea as 4,8 weeks with prednisolone treatment and 11.7 weeks without prednisolone treatment (7). In our study, average remission duration regardless of treatment was 6.9±1.2 weeks while it was 6.7±0.8 weeks for patients (72.7%) who were given haloperidol only. Average remission period for the few patients who were given carbamazepine and valproic acid were consistent with the literature (10-13).

Neuroleptics control the chorea by inhibiting the dopaminergic activity in the basal ganglia. Pimozide and haloperidol are the most prescribed neuroleptics for this purpose and haloperidol is reported be more reliable and faster in controlling the movement disorders. However, adverse effects have been reported more frequently for haloperidol (14). Parkinsonism, dystonia, sedation and cognitive disorders are the most common side effects of haloperidol (15). Only one patient in our study had parkinsonism as a side effect of haloperidol, which disappeared following the discontinuation of the drug.

Valproic acid and carbamazepine are the most frequently prescribed antiepileptic drugs for the symptomatic treatment of the chorea (11-13). These drugs can be chosen in case of adverse effects of neuroleptics or refractoriness and various authors have stated that less negative effect on cognitive performance, lower level of sedation and decreased risk of causing additional movement disorders such as parkinsonism or dystonia can be the reason of choice for acute symptomatic treatment (10-15). In our study, carbamazepine was added to haloperidol for the treatment of refractory chorea in 3 (9%) patients, carbamazepine for 3 (9%) and sodium valproate for 2 (6%) patients was chosen as the first line of treatment due to concerns about patient and parent cooperation.

Chorea is defined as arrhythmic, rapid, involuntary, jerky, or fluid movements with low amplitude which is often observed in the distal extremities. Chorea is the main clinical finding of Sydenham's chorea (2,4) and it frequently effects the face, trunk, and extremities. Hemichorea is present in 20% of all cases (16). We aimed to classify anatomical regions based on the dominance of chorea and observed that chorea was more prominent in extremities in 36.4 %, in the whole body in 24.2% and in the form of hemichorea in 33.3% of the patients.

Emotional instability and anxiety were present in 6 % of the patients as psychiatric symptoms accompanying chorea. On the other hand, hyperactivity disorder, obsessive compulsive disorder, or depression, which are reported to more frequent in the literature, were not present (17-19). This can be explained by the fact that psychiatric symptoms are not deemed as important as the etiology and treatment of chorea and it shows that patients with Sydenham's chorea must be evaluated for neuropsychiatric involvement. Similarly, the incidence of migraine is reported to be higher in patients with Sydenham's chorea however, we did not question our patients concerning migraine in the follow up (20).

Existence of ARA diagnostic criteria in addition to elucidation of other causes of chorea are the most important parts of the diagnostic algorithm for Sydenham's chorea. Our patients were evaluated for infectious, vascular, and autoimmune causes. Carditis is reported to be present in 70% of the patients with Sydenham's chorea thus, electrocardiography and echocardiography was applied to all patients (4). The incidence of clinical and subclinical carditis accompanying Sydenham's chorea in our study was 90.9%. Neuroimaging techniques are advised in cases with atypical presentations. Cranial MRI was performed for all patients in our study despite the extra cost and the need for sedation in the pediatric patient population to detect different etiologies (vascular or infectious) and all were reported as normal.

CONCLUSION

Sydenham's chorea is a benign phenomenon which classically limits itself and a diagnosis of acute rheumatoid fever can be made by its existence alone. Antibiotic treatment/prophylaxis for the treatment and prevention of the active infection along with acute symptomatic treatment are mandatory for pediatric patients presenting with Sydenham's chorea and diagnosed with acute rheumatoid fever. Diagnosis of ARA and ruling out other reasons of chorea are the mainstay of the diagnostic algorithm. The lack of an international consensus for diagnosis and treatment makes different management algorithms in different centers relevant. Our study has some limitations such as its retrospective and cross-sectional nature in addition to some points mentioned in the discussion. Prospective multidisciplinary clinical studies which evaluate diagnosis, treatment and accompanying systemic findings are necessary.

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