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Does childhood chorea mean sydenham chorea everytime?

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Abstract

Aim: We were retrospectively our experience in Sydenham Chorea and reexamined 39 patients with choreiform movement disorder who were admitted to pediatric neurology and cardiology outpatient clinics between 2010 and 2017.

Materials and Methods: We reviewed these case symptoms, diagnosis period, differential diagnosis and shortening the duration of symptoms with chorea treatment.

Results: Two of 39 patients who diagnosed Sydenham Chorea, were finally diagnosed Systemic Lupus Erythematosus. Symptoms duration time is shorter with neurodol or valproaic treatments.

Conclusion: Although Sydenham Chorea's is the most common movement disorders, the practitioners should aware of the differential diagnosis. The relapse of Acute Rheumatic Fever with chorea can be prevented by administering antibiotic prophylaxis.

Introduction

Acute rheumatic fever (ARF), which usually develops 1-6 months after tonsillopharyngitis caused by Group A Beta-Hemolytic Streptococci (GABHS), is an autoimmune and multi-systemic disease leading to different health issues in joints, heart and neurological systems. The incidence of ARF is 19/100000 in children aged 5-15 years, which is 5 to 10 times higher in developing countries. Chorea, which was first identified in 1686 by Sir Thomas Sydenham and historically referred to as St Vitus' dance, is a complication of ARF characterized by involuntary, rapid and aimless movements in the face, trunk and extremities. One-third of patients with ARF have Sydenham' Chorea (SC). Unlike the involvements in other organs, Sydenham's Chorea may develop in months, even years after streptococcal infection [1]. Other major and minor symptoms of ARF do not often accompany with Sydenham's Chorea, and GABHS cannot be detected because of the long latent duration. Sydenham's Chorea is a clinical diagnosis, which has no practical diagnostic test. Chorea is a delayed ARF squeal with a noisy onset characterized by hyperkinetic movement disorder with single or bilateral involvement. The average recovery is 8-15 weeks, while full recovery may take up to 2 years. Rarely, chorea can relapse. Antiepileptic drugs (valproate, carbamazepine), dopamine receptor antagonists (haloperidol) and steroids are used in prolonged cases of this disease, which can recover without treatment [2]. This study retrospectively evaluated the demographic characteristics, clinical results and treatment options of patients diagnosed with SC in pediatric neurology and pediatric cardiology clinics. We want to underline with this paper that the outpatients with choreiform movement disorders who applied, evaluated carefully at diagnosis, treatment and duration time and differential diagnosis. However, Sydenham's Chorea is the most seen choreiform movement disorders in childhood, we want to emphasize screening differential diagnosis such as Systemic Lupus Erythematosus, Wilson Disease, pediatric autoimmune neuropsychiatric disorders associated with streptococc (PANDAS) etc.[3]. The relapse of Acute Rheumatic Fever with chorea can be prevented by administering antibiotic prophylaxis with lifelong.

Material and Methods

In the study, 39 patients with choreiform movement disorder who were admitted to pediatric neurology and cardiology outpatient clinics between 2010 and 2017 were retrospectively examined. Of them, 37 were diagnosed with Sydenham's Chorea and included in the study. Two

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Table 1. Demographic and clinical characteristics of patients

Results	(n,%)
Age 15.8 ± 3.1	
Female / Male	21.16
Symptom onset time	29.1 ± 34.7 (2-150) (days)
Chorea	37 (100%)
Generalized Chorea	26 (70%)
Hemichorea	11 (30%)
Involvement of facial muscles	6 (16%)
Axial involvement	8 (22%)
Dysarthria	9(24%)
Loss of strength	2 (5%)
Affective disorder	3 (8%)

patients who were diagnosed of Systemic Lupus Erythematous (SLE) in the follow-up process were excluded from the study. Then, the patients were evaluated according to the Modified Jones Criteria for the diagnosis of ARF by using clinical and laboratory results (4). Their demographic characteristics, complaints, laboratory results, ECG, echocardiographic (ECHO) examinations, treatment options, and duration of symptoms were evaluated. This article was approved by The Ethics Committee of Inonu University. The approved number is 2018/12-7 at June, 05, 2018.

Statistical method

Data were analyzed using the SPSS 17.0 (SPSS; Chicago, IL, USA) version for Windows, and reported using descriptive statistics including numbers, percentages, mean and standard deviation.

Results

The study sample consisted of a total of 37 patients with Sydenham's Chorea, including 21 females and 16 males. Their mean age was 15.6 years, and the female/male ratio was 1.3 (21/16). They applied to our clinic in an average of 29 days (2-150 days) after the onset of their complaints. Their physical examination revealed that 70% (n=26) had generalized chorea and 30% (n=11) had hemichorea. Other examination results are given in Table 1. The laboratory examinations performed for diagnosis and differential diagnosis revealed that their values of complete blood count, AST, ALT, Ca, T3, T4, TSH, antiM, antiTg, ceruloplasmin, and urinary excretion of ceruloplasmin were within normal limits. However, two of them with positive ANA and dsDNA were followed up and then diagnosed with SLE, and therefore excluded from the study. In addition, 60% of the patients (22/37) had increased ASO (>250IU) and 13% increased sedimentation (>20 cm/1 hour) (Table 2).

Table 2. Laboratory results of patient.

	Mean ± standard deviation	Abnormal results (n,%)
White blood cell (10^3 cell /mm^3)	9.3 ± 3.2	-
Blood platelets (10^3 cell /mm^3)	291 ± 91	-
Sedimentation (cm/1 hour)	11 ± 14	5(13)
ASO (IU)	483±512	22(60)
CRP		2(5)
GABHS growth in throat culture		1 (3)

In terms of other diagnostic criteria for ARF, 81% had carditis, 10% had arthritis (Table 3), 71% had mitral valve insufficiency, and 19% had aortic valve insufficiency. In the follow-up session with control ECOs performed six months later, sequel valve failure was observed in %16 of the patients (Table 3). Moreover, 36 (97%) patients who were followed up due to diagnosis of Sydenham's Chorea received neurodol, valproic acid (VPA) or steroid therapy. One patient refused to take any medication. In details, 33 patients (89%) used neurodol, 14 (38%) VPA and 6 (16%) steroid. Three out (8%) of 20 (54%) patients who received single drug therapy used only VPA, while 17 (45.9%) used only neurodol. No patient received steroid treatment alone. Furthermore, 10 (26%) out of 16 patients who did not have adequate clinical improvement were treated with neurodol and VPA, 5 (13%) with neurodol and steroids, and 1 (3%) with neurodol, VPA and steroid sequentially. Since clinical improvement was observed in the follow-up of three patients whose treatment was started with VPA, they did not receive additional treatment; however, the treatment plans of 16 patients using neurodol were changed. The treatment administered to patients using only the combination of neurodol and VPA continued for 3-6 months. One patient who did not have adequate clinical improvement was respectively administered neurodol, VPA and steroid for 5 months. The mean duration of treatment was 2 months for the patients receiving haloperidol, and 2.7 months for those using VPA. The choreiform disorder lasted 2.9 months (1-8 months) in average. Aspirin was administered to 6 (16%) patients with arthritis and arthralgia, digoxin to 2 (5%) patients with heart failure, and enalapril to 13 (35%) patients (Table 4).

Discussion

Acute rheumatic fever is a delayed inflammatory and multi-systemic disease that occurs two to three weeks after Group A Beta-Hemolytic Streptococcal Pharyngitis, affecting the heart, joints, skin, and central nervous system. The patients complain of having involvements of carditis, arthritis, chorea, subcutaneous nodule and erythema marginatum. Its prevalence is five times higher in developing countries, especially due to the lack of effective antibiotic use, where 15% of schoolchildren aged 5-14 years are estimated to have it. Its incidence is 19/100,000 across the world and 2-4/100,000 in developed countries [5]. Acute rheumatic fever, which manifests as systemic sequel involvement, affects the central nervous system after a latent period of 1-6 months (or years). This involve-

Table 3. Acute Rheumatic Fever diagnostic clinical and laboratory results.

ARA diagnostic results	(n, %)
Carditis	30 (81)
Within normal limits	2 (5)
Trace MVI	15 (41)
1^0 MVI	5 (14)
2^0 MVI	6 (16)
Trace AVI	6 (16)
2^0 AVI	1 (3)
1^0 TVI	1 (3)
1^0 PVI	1 (3)
Arthritis	4 (10)
Erythema marginatum	0
Subcutaneous nodule	0
Arthralgia	4 (10)
Prolonged PR in ECG	6 (16)
Increased sedimentation	5
CRP positivity	2
CRP positive and increased sedimentation	1
Fever	0

Table 4. Treatment options and durations and follow-up results.

Drugs	Number and percentage of patients (%)
Aspirine	6 (16)
Digoxine	2 (5)
Enalapril	13 (35)
Steroid	6 (16)
Neurodol	33 (89)
VPA	14 (38)
VPA+Neurodol	10(26)
Neurodol+steroid	5(13)
Neurodol+VPA+steroid	1(3)
Neurodol use time	2±1.6
(mean ± standard deviation)	(months)
VPA use time	2.7±3.4
(mean ± standard deviation)	(months)
Duration of	2.9±2 (1-8)
post-treatment symptoms	(months)
ARA relapse	2 (%6)
Chorea relapse	4(%12)

ment, known as Sydenham's Chorea, is a less common complication of ARF. The diagnosis of ARF has been included as major and minor criteria in the guidelines since 1944 [4]. Sydenham's Chorea is characterized by an aimless, uncontrolled and irregular movement disorder affecting the body, extremity and face, which gradually increases over time. The initial complaints of patients generally include impaired speech and gait, weakness in hands, impaired handwriting, and incompetence (such as inability to tie shoes or button knobs), frequently accompanied with mood swings. Involuntary movements disappear with sleep but increase with stress [6]. Despite having dramatic symptoms, Sydenham's Chorea is a self-limiting disease [7]. It is often not possible to prove streptococcal infection due to delayed involvement [7]. Sydenham's Chorea is caused by secondary immune reactivity to the brain, particularly the basal ganglia. In particular, the detection of antibodies against neurons in caudate nucleus supports this hypothesis [8]. However, while the amount of GABA and acetylcholine in basal ganglia decreases, dopaminergic activity increases. This also explains the mechanisms of action of haloperidol, VPA and carbamazepine, which are useful in the treatment of Sydenham's Chorea [2]. Pathological changes in Sydenham's Chorea include decreased neurons in cerebral cortex, basal ganglia and thalamus, changes in cytoplasmic and nuclear cells, gliosis, endothelial swelling, perivascular round cell infiltration, and petechial hemorrhages [9]. The initial clinical results of the patients evaluated retrospectively were generalized chorea and dysarthria. Although hemichorea was the first finding, only 30% of the patients included in this study had hemichorea [10]. The presence of late-stage findings, such as generalized chorea, was often associated with delayed application time (29 days in average). The patients were administered haloperidol, VPA and steroid. Their symptoms disappeared after 2 months of the treatment with haloperidol and 2.7 months with VPA. However, 10 patients who did not recover with haloperidol were first treated with VPA. Then, 6 patients who did not recover with VPA were administered steroids. The total duration of treatment of these patients lasted 3-6 months, and they had no symptoms at the end of the treatment. The mean duration of post-treatment symptoms was 2.9 months for all patients. No side effects were detected after the treatment. The duration of the disease normally lasts up to two years in patients receiving no treatment, but similar to those of the patients included in this study, clinical results can improve in a short time with medical treatment, significantly increasing patients' quality of life. Given that Sydenham's Chorea is an immune-mediated disease; corticosteroids, intravenous immunoglobulin, and plasmapheresis have also been shown to be beneficial in selected cases [11]. In this present study, oral prednisolone was administered at a dose of 1mg/kg/day to 6 patients with persistent symptoms for 4 weeks. At the end of four weeks, all symptoms disappeared. All patients were treated with prophylactic penicillin to prevent the relapse of ARF. Not only chorea, but also tics, emotional and behavioral changes, and dystonic disorders can be observed after streptococcal infections. Obsessive-compulsive disorder, anxiety, attention deficit-hyperactivity disorder, behavior and sleep disorders, PANDAS (pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections) are other health conditions identified so far [6]. Differential diagnosis of patients with choreiform movement disorder should be kept in mind at their first admission to clinics [12]. Especially in cases of recurrent chorea, differential diagnosis should be reviewed for diseases with increased frequency in similar age groups including SLE and Neurowilson. Since some clinical findings of SLE occur over time, clinical follow-up of these patients should be performed. Two patients who had relapsed chorea findings previously followed due to Sydenham's Chorea were diagnosed with

SLE, and accordingly their treatments were planned. Although Sydenham's Chorea was common in the patients included in this study, they were treated correctly without delay due to the diagnosis of SLE, which has completely different complications and treatment process. In particular, Wilson's disease is one of the diseases that should be considered in the differential diagnosis of movement disorders due to the high rate of consanguineous marriages in Turkey. There are some limiting issues in our paper. First of all this paper is designed retrospective so that the groups couldn't be homogeneous. We were screening the patients with the key words that arthritis, chorea and carditis according to ICD-10 diagnosis system. We think that we could miss some patients with ARF and chorea coded another diagnosis codes which we didn't research.

Conclusions

Although Sydenham's Chorea is first investigated in children with choreiform movement disorder, the differential diagnosis is especially important for recurrent cases. Quality of life can be increased by shortening the duration of symptoms with chorea treatment. In developing countries like Turkey, the relapse of ARF can be prevented by administering antibiotic prophylaxis lifelong.

Main points

1. We want to underline in this article that childhood chorea does not always mean Sydenham Chorea. We should make differential diagnosis in every single case. Rarely chore reasons have been seen more than we thought as SLE.
2. In the literature, the authors have advised not to treat the chorea but it has been clearly showed that giving the treatment will be fine at life quality.
3. By the way we have shared our clinical experiences and treatments.

Ethics approval

This article was approved by The Ethics Committee of Inonu University. The approved number is 2018/12-7 at June, 05, 2018.

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