Hereditary Geniospasm: Two Cases of Hereditary Geniospasm One Treated with Btx TypeA

Herediter Geniospazm: Biri Botulinum Toksini ile Tedavi Edilen Herediter Geniospazmlı 2 Olgu

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ABSTRACT Hereditary geniospasm (HG) is an autosomal dominantly inherited disease characterized by involuntary spasm localized to the chin. Some researchers proposed that it is a kind of essential myoclonus. Attacks generally begin in early childhood but sometimes just after birth. This disease is rare and only a few cases treated by botulinum toxin (BT) injection were reported. Electromyography (EMG) records of mental muscles of a father and his daughter and their clinical findings were discussed with the literature. The younger one was successfully treated by BT injection. Interestingly situs inversus totalis was determined in a case.

Key Words: Electromyography, botulinum toxins

ÖZET Herediter geniospazm (HG), otozomal dominant geçişli, çenede lokalize istemsiz kasılmalarla karakterize bir hastalıktır. Bazı araştırmacılar esansiyel miyoklonusun bir varyantı olduğunu öne sürmüştür. Ataklar erken çocukluk döneminde, bazen doğumdan hemen sonra başlar. Bu hastalık nadir görülür ve botilinum toksini (BT) ile tedavi edilebildiğine dair az sayıda bildiri vardır. Bu makalede, baba-kız herediter geniospam olarak değerlendirilen iki olgunun mental kastaki elektromiyografi (EMG) aktivitesi ve klinik bulguları literatür eşliğinde tartışıldı. Genç olgu BT enjeksiyonları ile başarılı bir biçimde tedavi edildi. Olgulardan birinde ilginç olarak situs inversus totalis saptandı.

Anahtar Kelimeler: Elektromiyografi, botulinum toksin

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Hereditary geniospasm (HG), also known as hereditary chin trembling/ tremor, is a rare autosomal, dominantly inherited disease with involuntary spasms localized to the chin. Researchers have also proposed that it is a kind of essential myoclonus. Attacks generally begin in early childhood and sometimes just after birth. Stress, concentration, and emotional situations can aggravate the symptoms.[1,2] In a study, the responsible gene locus were demonstrated on the long arm of chromosome 9q13-q21.[3] The gender ratio was reported as 1.3/1 (male/female).[2]

In this paper, two cases of HG as a father and his daughter with clinical findings and electromyographic features were presented. Botulinum toxin (BOTOX®, Allergan Pharmaceuticals, Ireland) was injected to the mentalis muscle of the daughter and she was treated successfully.

CASE REPORTS

CASE 1

A 26-year-old woman with continuous, involuntary movement in the chin was referred to the outpatient clinic of the neurology department. It was declared that her symptoms were observed just after the birth without intermittence and aggravated in crowded places, with stress, and have never ceased during sleep. In the neurological examination, continuous involuntary spasm prominent on the left side of chin was observed. No other pathological findings were found during the examination. Interestingly situs inversus totalis was detected by the physical examination which was also known by the patient.

CASE 2

The father, aged 56 had the same complaint of continuous, involuntary movement in the chin since his childhood. He could not know about the precise beginning time of these movements. He did not complain about his movement and did not accept BT injection. He declared that his symptoms gradually decreased by age. In his neurological examination, the spasm was barely visible.

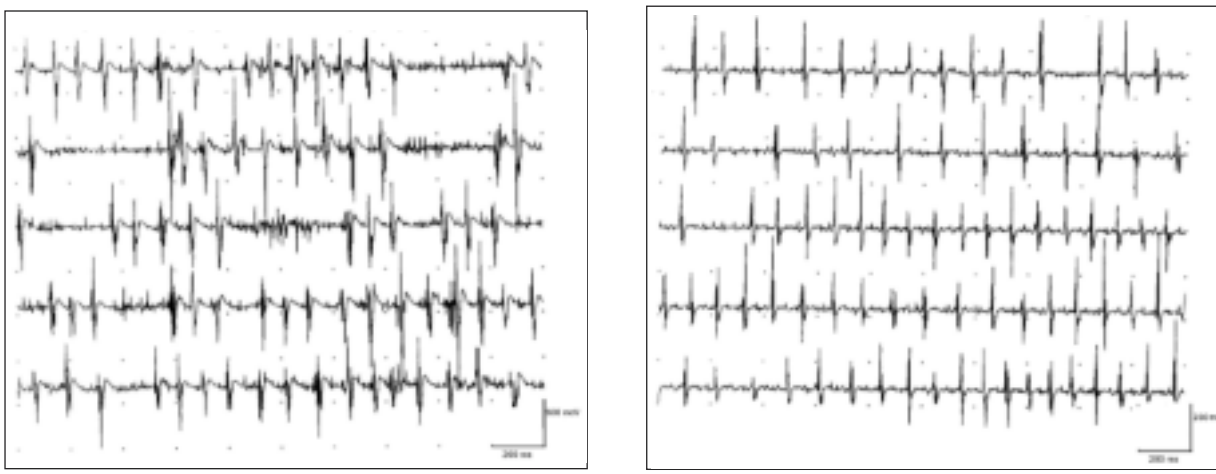
As we could not identify any other patient with similar symptoms in the questionnaire of his relatives, we can not propose an inheritance pattern.

Video recording of both patients were done for the documentation of the continuous, involuntary spasm of the chin.[4] In the routine laboratory results of the daughter no positive finding was revealed.

Seven and half, and 2.5 units of BT was injected into each left and right mentalis muscles of the daughter. More than 90% improvement was observed one month after the injection. Initially in the clinical examination very fine and intermittent involuntary spasm was barely observed. In order to obtain a complete suppression of movements a total of 20 units (left 15 units, right 5 units) BT was applied four and half months 4.5 months after the first injection. However, no additional improvement was observed.

Electrophysiological Investigation

Nerve conduction studies were normal. Needle EMG recordings of the patients were showed in Figure 1 a, b. While the subjects were awake, muscle action potentials (MUAP) were recorded simultaneously from both left and right mentalis muscles using concentric needle electrodes and conventional EMG system. The recordings of both patients showed continuous muscle fiber activity. We measured 50 interpotential intervals and peak



A B

FIGURE 1: (A) Potentials obtained with a needle electrode from the left mentalis muscle in the proband. **(B)** Potentials obtained with a needle electrode from the left mentalis muscle in the proband's father. Pay attention to sensitivity scales which are different.
We received illuminated approval from patients.

TABLE 1: Potentials values obtained from both cases.

	Mean interpotential interval (±SD) (range)	Mean amplitude (±SD) (range)	Mean frequency
Proband	145.85(±119.68)* μs (56-528)¥	792.78(±213.93)** μV (388-1555) ¥¥	6.85/s
Father	129.43(±40.79)*μs (84-264)¥	282.22(±72.46)** μV (133-444) ¥¥	7.72/s

Unpaired t test, *:T=0.918 p: 0.36 **: T=15.98 p=0.000, (95% CI*:-19.35-52.18 **:446.66-574.45)
Comparison of variances (Levene's test), ¥:F= 14.50 p= 0.000 ; ¥¥:F= 22.80 p= 0.000
SD: Standard deviation, μs: microsecond, μV: microvolt .

to peak amplitude of potentials on both offline traces. While the means of interpotential intervals were not different, the mean amplitude of potentials in the daughter was higher than her father's.

Both variances of interpotential intervals and amplitude were different (Table 1). EMG was not applied concurrently; BT injections were not performed under EMG guidance. Video displays of the patient were recorded before and after the BT application.

DISCUSSION

Since HG was first defined in 1894, more than 350 cases in 27 families have been reported in Europe and America.[1] It is a paroxysmal movement disorder of the mentalis muscle with onset in infancy.[5] Neither the genetic basis of the peculiar movement disorder nor its pathophysiology has yet been fully elucidated.[1,6]

It should be differentiated from myokimia, which is a palatal tremor and an essential tremor in which facial muscles are affected.[3] Involuntary movement episodes in HG typically begin during early childhood.[2] Essential tremor rarely begins in infancy and childhood.[7] While the symptom of the daughter was observed after the birth the beginning of the father's symptoms was not precisely defined. Symptoms are more prominent in adulthood, but frequency of the attack and intensity tend to decrease with advancing age.[2] Essential tremor can also be seen in chin as an atypical variant, but patients often have severe symptoms.[8]

Facial myokymia is in fact very different from what was found in our patients. It is unilateral, rhythmic, regular and localized but includes several muscles and is not affected by stress or emotional changes.[2] They are more rapid and neurophysiologic aspects are different: Myokymic discharges are not observed in electromyography.[5,9,10] Also, myorhythmia can be excluded because it is slower and usually involves the face, eyes, and limbs.[11]

Finally because of these five factors as mentioned below we thought hereditary geniospasm as the diagnosis:

1) The abnormal involuntary movement is related to quick jerks of the mentalis muscle.

2) Involuntary muscle activity at the chin was provoked or aggravated by emotional or physical stress and was observed during sleep.[2]

3) The peak frequency of the involuntary movements with HG varies between 5.7- 10.3 Hz as in our patients.[2]

4) Involuntary movement episodes in HG typically begin during early childhood.[7]

As in one of our patients.

5) Geniospasm is transmitted as autosomal – dominant trait that has a high penetrance.[12] We examined a 56 -year-old man and one of his daughter (26 year) to prove that geniospasm has an autosomal – dominant pattern of inheritance.

Both of the patients experienced continuous symptoms, not paroxysmal. When the two patients were compared each other on the basis of needle EMG recordings it was observed that the daughter exhibited MUAP's higher frequency and amplitude. The amplitude and interpotential intervals of MUAP's of the daughter were in wider range. We proposed that HG amplitude and interpotential intervals will be stabilized with age and decided to follow up the daughter by the needle EMG with certain intervals for many years to confirm this observation. The peak frequency of the involuntary movements in HG was reported to be 5.7- 10.3 Hz as we report for our patients (Tablo 1).

Regular injection of BT in mentalis muscle was reported to be effective for the treatment of HG in some of the studies.[4] A subject with sporadic HG without family history was treated with 25 units of BT A and achieved %95 improvement.[13] Jankovic et al, describe a 74-year-old man with familial, childhood-onset chin tremor, and a 3-year history of progressive hand tremor, gait difficulty, and other parkinsonian features.[14] Since chin tremor often occurs in Parkinson's disease (PD), a coexistent HG may not be recognized unless past and family history of tremor is carefully explored.[14] Another subject with PD was also reported, but BT was not administered in that case.[14]

Channelopathies are a recently delineated, emerging group of neurological disorders united by genetically determined defects in ion-channel function.[15] These disorders are characterized by a prominent genetic and phenotypic heterogeneity that can make them challenging and bewildering to understand.[16]

To categorize these disorders according to their predominant clinical manifestations (i.e., myotonia, weakness, migraine, ataxia, epilepsy, and movement disorders) molecular basis of recognized clinical syndromes should be known.[15]

Ion channels are large transmembrane proteins which are essential for the normal function of all eukaryotic cells.[12] Ion channel dysfunction is often susceptible to external factors such as stress and changes in pH, ion concentration, and temperature, and many respond to acetazolamide. Strong CNS candidate diseases including paroxysmal movement disorders such as paroxysmal dystonic choreoathetosis and familial geniospasm.[1,6] If HG is a neurological channelopathy, BT injection will be a more proper treatment.[17]

Situs Inversus (SI) (also called situs tranversus) is a congenital condition in which the major visceral organs are reversed or mirrored from their normal positions.[18] The normal arrengement is known as situs solitus. SI is generally an autosomal recessive genetic condition although it can be X linked or found in identical mirror twins.[18] SI totalis occurs at an incidence of 1 in 10000-50000 live births.[19] About %25 of individuals with SI have an underlying condition known as primary ciliary dyskinesia (Kartagener Syndrome).[20] SI totalis was determined in only one of our patient. As far as we known coexistence of HG and SI totalis has not been documented yet. There may be a genetic link between these two conditions (HG and SI) but coexistence may be completely fortuitous.

In conclusion, amplitude and interpotential intervals may show a more stabilized tendency with the advanced age in HG. Regular injection of BT in the mentalis muscle is an effective way in the treatment of HG.

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