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Two Cases of Hemifacial Spasm Completely Recovered after Repeated BTX-A Treatment

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Abstract

Hemifacial Spasm (HSF) refers to the intermittently involuntary clonic twitch or painless rigidity of one or two sides of facial muscles. Patients with hemifacial spasm generally have a decline in quality of life, accompanied by anxiety, depression and other emotional problems, which further aggravate hemifacial spasm symptoms. BTX-A injection is the first choice for treatment of HFS, which can not only relief the symptoms of HFS but also improve the mood problems. There have been no reported cases of HFS cured by drugs or BTX-A. Here we reported two HFS patients recovered after multiple BTX-A treatments without recurrence for 3-8 years, which might provide a clue for further exploration of the pathogenesis of HFS.

Keywords: Hemifacial spasm • BTX-A • Curing • Pathogenesis • Emotion

Introduction

Hemifacial spasm is a kind of peripheral nerve diseases, which is characterized by unilateral or bilateral, involuntary contraction of the muscles innervated by the facial nerve and aggravated by tension, fatigue, and autonomous movements. It was first reported by Edouard Brissaud, a French neuropsychiatries in 1893, who also suggested several possible etiologies for the involuntary movements of his patient, including the possibility of arterial malformations compressing the origin of the facial nerve [1]. Though Neurovascular Compression (NVC) in the exit region of facial nerve root (root exit zoon, REZ) is considered as the main cause of this disease, the exact causes of the disease have still remained unknown until now. In the United States, the average annual incidence and prevalence rates of HFS are 0.74 per 100,000 males, 0.81 per 100,000 females, 7.4 per 100,000 males, and 14.5 per 100,000 females, respectively [2].

The ratio of male to female is 1.0:1.8, and the mean age at onset is (46.6 ± 11.5) years [3]. HFS is a chronic disorder, with rare spontaneous recovery. A natural history study of 104 patients with HSF showed that 11 (10.6%) were aggravated, 40 (38.5%) were stationary for 6-42 years (mean 13 years), 10(9.6%) improved partially for 7-18 years (mean 11 years) and 43 (41.3%) were in remission for between 2 months and 23 years (mean 6.4 years) after onset and required no further treatment for 5 months to 13 years (mean 5.7 years) [4]. Micro vascular decompression and intramuscular injections with BTX-A type A (BTX-A) are the main recommended therapies [5]. BTX-A injection is the first choice, which has also been shown to have a positive influence on mood and affection [6]. The BTX-A treatment had an overall success rate of 88% in relieving spasms. The mean duration of response was about 20 weeks. There have rarely been reported cases of completely recovered after repeated BTX-A treatment. Here we reported two cases, one of which has been spasm-free for 3 years after multiple Botox injections and the other has been for 8 years.

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Case Report

We reported two cases completely recovering from injections of BTX-A.

Case 1

An 88-year-old male has developed right blepharospasm with no obvious cause since 1996, which gradually progressed to the right side of his face. He complained that the spasms were intensified by stress and anxiety, and the symptoms disappeared during sleep. Cranial MRI showed no obvious abnormality. He was treated with BTX-A since 1998. Symptom remission lasted for six months, and BTX-A treatment was given twice a year. The patient had no history of hypertension, diabetes, heart disease and other underlying diseases. Moreover, the patient acknowledged mild anxiety and depression since 1998, the main symptoms of which were low mood, difficulties in falling asleep, light sleep, decreased working motive. Long-term oral administration of mirtazapine 7.5 mg QN, clonazepam 2 mg QN, and estazolam 2 mg QN improved his mood and sleep. The patient received his last BTX-A injection 3 years ago and had no recurrence of hemifacial spasm since then, and his cranial MRI showed encephalatrophy at that time. Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale showed 0 and 0 on April 16, 2021 (Video 1).

Case 2

A 78-year-old male has presented with right hemifacial spasm 23 years

Video 1. Disappearance of hemifacial spasm in patient 1 on April 16, 2021.

ago without obvious cause. He had received acupuncture treatment without effect. He had no anxiety and depression as assessed. From 1998 to 2013, he received BTX-A injections twice a year, with six months of relief each time. He had hypertension for 40 years and diabetes for 7 years. In 2009, he suffered a cerebral infarction with weakness in his left limb as a sequel. Since 2009, he has been hospitalized several times for cerebral infarction. In 2013, he was found to have multiple intracranial aneurysms. In the same year, his hemifacial spasm alleviated, and there has been no recurrence of hemifacial spasm during follow-up until now (Video 2). There was no history of facial pain or weakness, facial or head trauma, prior exposure to neuroleptics, or other movement disorders for both patients. According to the condition, they received injections into orbicularis oculi muscle and face at about 15 points, and the injection volume at each point was 0.1 ml, containing 2.5-5U of BTX-A (freeze-dried crystalline type A botulinum toxin produced by Lanzhou Institute of Biological Products, China), a total of 50U each time (Figure 1).

Discussion

There have rarely been cured cases of HFS by drugs or BTX-A. In these two cases, the symptoms of HFS disappeared after repeated injection of BTX-A, and the hemifacial spasm did not recur during several years of follow-up, which was considered to be cured. For the pathogenesis of HFS has not been clear, the mechanisms are worth exploring. As for the aggravation and alleviation factors of hemifacial spasm, different investigations currently drew inconsistent conclusions. Stress, tension, fatigue and facial autonomous activities aggravated the spasm, while relaxation and drinking alleviated it. Patient 1 had significant emotional problems prior to the BTX injection. He told us that when he was young, he would have unilateral facial involuntary twitching before exams, which relieved spontaneously and was closely related to anxiety and nervousness. Psychogenic Facial Spasms (PFS) are often classified as psychogenic dystonia, but they may be difficult to differentiate from HFS when occurring alone or presenting unilaterally. There are overlapping clinical features between organic and psychogenic facial spasms [7]. As this case is retrospective, the classification of the patient's facial spasms is hard to be stated. However, from the following aspects, it tended to be psychogenic.

Video 2. Disappearance of hemifacial spasm in patient 2 on July 16, 2021.

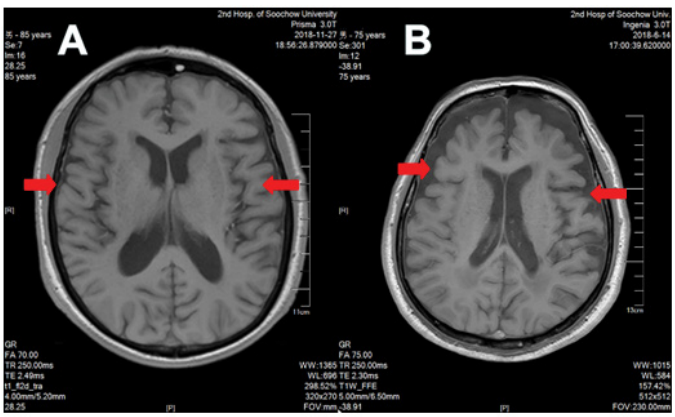

Figure 1. A. Cranial MRI of Patient 1 showed that multiple intracerebral infarction with the formation of partial softening lesions and senile brain atrophy; B. Cranial MRI of Patient 2 showed that multiple intracerebral infarction with the formation of partial softening foci, changes in deep cerebral white matter ischemia foci, and brain atrophy.

1. No facial spasms during sleep. In a previous study, up to 80% of organic HFS patients had reported persistence of facial movements during sleep [8].
2. No worsening of spasms during voluntary facial muscle movements.
3. Brain MRI/MRA did not reveal any vascular abnormalities or occupying lesions. Neurovascular anatomic abnormalities or dolichoectatic vessels have typically been demonstrated in patients with HFS.
4. The patient has a clear history of anxiety and depression, with relevant drugs for a long time. Degree of facial spasms was closely related to emotion.

As is known, tension and anxiety aggravate hemifacial spasm, while the inconvenience of life caused by the disease itself further aggravates emotional problems, which is a vicious circle. Chengyun Wang et al. reported that patients with HFS are often accompanied by somatization, interpersonal sensitivity, depression, anxiety, and phobia, which could also be improved by BTX-A injection [9]. Weijia Chen et al. proved it from the mechanism that peripheral unilateral injection of BTX-A could inhibit anxiety-like behaviors [10]. Therefore, it is reasonable to speculate that BTX-A treatment of hemifacial spasm can improve the negative emotion which aggravates the symptoms of spasm, and turn the vicious circle into a virtuous one, making HFS healed, especially for the patients with psychogenic facial spasms. High quality of life promotes good mental shape, and good mental shape further improves the quality of life, both of which are conducive to relieving HFS symptoms. In turn, the alleviation of facial spasm symptoms is also conducive to the improvement of both. This may be the reason for the recovery of facial spasm. This mechanism is even more persuasive on PFS. The two patients are both advanced intellectuals with mental work, and the work pressure is self-evident. Both patients are now retired and reduced stress at work and happiness in retirement may also play a role in their recovery.

Although currently researches on the causal relationship between hemifacial spasm and mental factors are few, it's reasonably believed that the occurrence of hemifacial spasm is significantly related to mental factors. Chronic mental stress makes excessive secretion of pressure-boosting hormone, causing elevated blood pressure. Leong Jia-Li et al. performed a meta-analysis on the relationship between hypertension and hemifacial spasm, which highlights a positive correlation between hypertension and HFS. The results of the meta-analysis showed that there is indeed a higher prevalence of hypertension among HFS patients as compared to non-HFS controls, which might partially explain the correlation between hemifacial spasm and mental factors [11]. The detailed mechanism between hypertension and HFS should be further evaluation in future studies.

The pathogenesis of hemifacial spasm has not yet been concluded, and there are mainly two hypotheses:

1. Peripheral theory postulates a "pseudo synaptic" short circuit transmission between the damaged facial nerve fibers at the neurovascular compression site. Demyelination of nerve fibers due to compression of blood vessels is the source of spastic abnormal discharges [12].
2. Central theory holds that spasm is caused by overexcitation at the level of the facial nucleus and that abnormal discharge originates from the level of the facial nucleus. The root cause of ectopic discharge is the functional recombination and structural change of some form of facial nerve nucleus [13].

Both patients recovered at an advanced age, and cranial MRI scans revealed encephalatrophy. Consequently, from the perspective of the peripheral theory, we speculate that encephalatrophy enlarges the space around the facial nerve and reduces the compression of the nerve. From the perspective of the central theory, it is reasonable to suspect that encephalatrophy reduces the stimulation of the cortical brainstem bundles to the facial nerve nucleus,

which improves the abnormal discharge caused by over-excitation of the facial nerve nucleus. In short, we reasonably suspect that encephalatrophy in elderly patients plays an important role in the disappearance of spasm. It should be noted that the pathogenesis of the disease is varied in each individual clinically, and further studies are needed for the exploration of the mechanisms on recovering of hemifacial spasm.

Botulinum toxin A is an effective, safe, long-term treatment for patients with hemifacial spasm [14]. The onset effect of BTX-A usually occurs several days after injections with 3-4months duration of clinical improvement thereafter. A small proportion of patients who fail to demonstrate an improvement following BTX-A starting at the onset of treatment are known as 'primary non-responders', while others who show decreased response after repetitive treatments are known as 'secondary non responders'. A possible reason for the latter group's non-response may be partially due to production of circulating antibodies directed against BTX-A along the treatment [15,16]. We retrospectively investigated these two patients who had undergone treatment for ≥ 15 years, and they received injections twice a year with a remission period of 3-6 months after each injection. There was a statistically significant increase in the amount of BTX injected from the first to the last injection. Hsiung et al. showed maintenance of sustained benefit (defined as a continued benefit of 50% or more from baseline) with repeated application, but the benefit in the second and fifth years of observation was respectively 96% and 88% [17]. However, Barbosa ER et al. reported that the difference in the rate of improvement reported by each patient after the initial and the last injection was marginally significant. Compared to a single injection, whether the recovery of hemifacial spasm is related to long-term injection of BTX-A, suggests that a larger study is needed to confirm our hypothesis.

Studies have shown that there are more females than males in patients with hemifacial spasm, and the gender distribution difference may be related to the effect of hormones on neural signals and plasticity. Epidemiological and clinical data suggest that sex hormones influence dystonia, and the mechanism is that estrogen may regulate the dopaminergic system in the substantia nigra striatum, thereby aggravating involuntary motor function. In this case, the two cured patients are both male, which further indicates that the hemifacial spasm symptoms of male may be easier to get better than that of female [18].

Conclusion

We report two patients with hemifacial spasm who did not relapse after repeated BTX-A treatment for more than 3 years of follow-up. It is reasonable to speculate that BTX-A treatment of hemifacial spasm can improve the negative emotion, and turn a vicious circle into a virtuous one, which makes HFS heal. Additionally, we present the hypothesis that the occurrence of hemifacial spasm may have a significant relationship with mental factors, for which anxious and impatient people are easier to have hemifacial spasm. Besides, encephala trophy may play an important role in relief of facial spasms. Absolutely, we need to further observe the prognosis of older patients with hemifacial spasm to explore the inner pathogenesis. Last but not the least; men may be easier to recover from HFS than female.

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