Botulinum Toxin Type A for the Treatment of Limb Myokymia: Experiences of Three Children

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Abstract

Myokymia is a rare neuromuscular disorder and limb involvement is not common in this disease. To the best of our knowledge, isolated peroneus longus muscle myokymia was not reported before in the literature; and for that reason treatment protocols were not established. Botulinum toxin type A (BoNT-A), which is used in the treatment of a variety of neurologic disorders, was also defined as a treatment option in myokymia. Herein, we will report three cases of peroneus longus muscle myokymia in children in the absence of any other neurological findings, and the successful results of treatment with local BoNT-A injections. BoNT-A is a safe and effective treatment in myokymia when administered by an experienced clinician and should always be considered when the disorder is persistent and affecting the life of the patient.

Keywords: Botulinum toxin type A, child, limb myokymia

INTRODUCTION

Myokymia is defined as involuntary, continuous, and fine contractions of muscle fibers rhythmically. In general, it takes place in a regional or generalized pattern and it can keep on during sleep. Myokymia may develop due to radiotherapy, Guillain–Barré syndrome (GBS), multiple sclerosis, pontine tumors, hypocalcemia, and rattlesnake venom poisoning. However, myokymia can also be idiopathic. Limb myokymia is quite uncommon. Herein, we will report three pediatric cases with persistent myokymia localized to the peroneus longus muscle in the lower extremity, which is a rare condition. We will also present our experience in the successful treatment of myokymia with botulinum toxin type A (BoNT-A) in a short time.

Case 1

A 7-year-old girl presented with complaints of involuntary contractions on the right side of her right leg and concomitant retractions on her foot for about 2 months. These complaints were fluctuating during the day and improved throughout sleeping. Her medical and family history was unremarkable. There were visibly ongoing contractions in the right peroneal muscle and tendon [Video 1a and 1b]. Other findings of her physical and neurological examinations were normal. Routine laboratory tests, calcium and magnesium levels, and thyroid function tests were within normal limits. Contactin-associated protein-like 2 antibodies (CASPR2-Ab) and leucine-rich glioma inactivated protein 1 antibodies (LGI1-Ab) were negative. Her brain and spinal cord magnetic resonance imaging (MRI) and the nerve conduction studies were normal. Needle electromyography (EMG) performed in peroneus longus muscles revealed spontaneous, repetitive, irregular, grouped discharges of motor units suggestive of myokymia [Video 1c]. Carbamazepine treatment (200 mg/day) was started for the patient. However, there was no significant improvement in the follow-up after 2 weeks. Then 30 units of BoNT-A were applied to this location. In the follow-up, the patient’s involuntary movements decreased within 7 days but complete remission could not be established after 4 weeks, and 50 more units of BoNT-A were administered again. Her complaints were completely resolved 6 weeks later [Video 1d]. The complaints did not recur during the 1-year follow-up. The patient’s consent was obtained for videos.

Case 2

A 9-year-old girl presented with complaints of involuntary contractions in the foot tendon on the right side of her leg for about 3 months. It was stated that these complaints were fluctuating. Physical examination revealed continuous myokymic contractions in the right peroneal muscle and tendon [Video 2]. All other findings of the physical examination were normal. Her medical and family history was unremarkable. Routine laboratory tests and thyroid function tests were within normal limits. Contactin-associated protein-like 2 antibodies (CASPR2-Ab) and leucine-rich glioma inactivated protein 1 antibodies (LGI1-Ab) were negative. Her brain and spinal cord magnetic resonance imaging (MRI) and the nerve conduction studies were normal. Needle electromyography (EMG) performed in peroneus longus muscles revealed spontaneous, repetitive, irregular, grouped discharges of motor units suggestive of myokymia [Video 1c].
normal limits. CASPR2-Ab and LGI1-Ab were negative. Brain and all spinal MRI findings were also normal. Nerve conduction studies were normal. The needle EMG revealed the presence of myokymia [Figure 1]. Carbamazepine treatment was started (400 mg/kg/day in two doses). However, 3 weeks later, there was still no significant improvement in her complaints. Therefore, 50 units of BoNT-A were administered to the patient. During the follow-up, it was observed that the patient’s involuntary movements completely resolved within a week. Carbamazepine treatment was discontinued within 1 month by tapering. The complaints did not recur during the 1-year follow-up. The patient’s consent was obtained for videos.

Case 3
A 14-year-old girl presented with complaints of involuntary contractions in the foot tendon on the right side of her leg for about 1.5 months. Her complaints were fluctuating during the day and greatly decreased when she slept. Myokymic contractions were observed in the right peroneus longus muscle location [Video 3a]. Other physical examination findings of the patient were normal. Routine laboratory tests and thyroid function tests were within normal limits. CASPR2-Ab and LGI1-Ab were negative. Brain and spinal MRI were also normal. Nerve conduction studies were unremarkable. The needle EMG showed myokymia [Video 3b]. Carbamazepine treatment was started on the patient (400 mg/day). However, 3 weeks later, there was still no significant improvement in her complaints. Therefore, 50 units of BoNT-A were applied to this location. In the follow-up, the patient’s involuntary movements improved within 3 weeks [Video 3c]. Carbamazepine treatment was discontinued within 1 month by tapering. Her complaints did not recur during 1-year follow-up. The patient’s consent was obtained for videos.

Discussion
All three cases were females presenting with isolated peroneus longus muscle myokymia. Any etiological cause was not found in the examinations performed in any of them. Hence, they were considered idiopathic. All three cases were successfully treated with BoNT-A injections without any complications.

Myokymia is a clinical phenomenon due to the spontaneous, regular repetition of action potentials that carry the configuration of motor unit potentials. It presents with the spontaneous, worm-like slow movements of the muscle fiber groups that last for many seconds. Adjacent groups of muscle fibers contract separately and slowly and this continues constantly. In electrical evaluations, myokymic waves are rhythmic, grouped, and spontaneous repetitive discharges of the same motor unit. Typically, the firing frequency within the burst is 5 to 60 Hz. The number of potentials within a burst differs broadly and may vary from burst to burst. The intraburst frequency is typically very slow (< 2 Hz) and it produces a characteristic sound on EMG. Myokymic discharges generally accompany clinical myokymia which is defined as a fine persistent trembling or rippling of muscles. Although focal myokymia is more common, myokymia may also be generalized. Focal myokymias are often seen on the face and especially in the eyes.[5,6] To the best of our knowledge, a case that developed myokymia in the pediatric age group and on peroneus longus muscles has not been reported before in the literature.

Biochemical alterations in the microenvironment of the nerve due to demyelination caused by a toxin, edema, or a decrease in ionized calcium concentrations are the main reason for the development of myokymia. Myokymic discharges arise anywhere in the motor axon. There is hyper-excitability in the axon membrane. Both auto-excitation and changes in the microenvironment of these axons are of great importance in the formation of myokymic discharges.[5,7]

It is reported that myokymia resolves spontaneously over time without treatment. However, the discomfort and pain caused by constant contraction require treatment. Typical treatment of myokymia is by using antiepileptic drugs such as phenytoin and carbamazepine.[2] BoNT-A is widely and successfully used in the treatment of myokymias around the face and eyes, blepharospasm, and hemifacial spasm. BoNT-A is recommended in the treatment of myokymia due to its rapid action and low side effect profile.[8,9] Dave et al.[9] administered 100 units of BoNT-A to a 53-year-old female patient who developed post-amputation residual myokymia in the right tibialis anterior and gastrocnemius muscles and achieved a success rate of 70% in a 1-month follow-up. Since the desired response could not be obtained with carbamazepine treatment in a short time in our cases, BoNT-A was preferred. A full recovery was obtained in all cases in a short time.

In our experience, BoNT-A administration seems to be a good option in the treatment of myokymia because of its rapid effect and low side effect profile.

Author contributions
S.I. was involved in the concept and design of the study. S.I. contributed to patient enrolment and collection of samples.
S.I. performed the assay. The author participated in the interpretation of the data, critical review of the manuscript, and the decision to submit it for publication. S.I. will act as guarantor for the paper.

**Ethical compliance statement**
The study was carried out following the Declaration of Helsinki of the World Medical Association and approved by the Research Ethics Committee of Gaziantep University (Project identification code 2021/373). Informed consent was obtained from each patient or their relatives, after a full explanation of the procedures. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

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