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Persistent Jaw Drop Following Botulinum Injection as the Initial Clinical Manifestation of Spinal and Bulbar Muscular Atrophy

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Dear Editor,

Spinal and bulbar muscular atrophy (SBMA) is a rare, progressive neurodegenerative disorder caused by CAG-repeat expansion in the androgen receptor (*AR*) gene. SBMA is characterized by hand tremor, bulbar weakness, fatigability, and slowly progressive limb weakness.[1] Botulinum toxin (BoNT) is widely administered in various conditions, and it acts by inhibiting acetylcholine release at the neuromuscular junction (NMJ). We report this case to highlight the potential for an exaggerated response to BoNT in SBMA patients, which is possibly due to NMJ dysfunction.

A 47-year-old male with no underlying disease received a 100-unit injection of BoNT into his bilateral masseter and temporalis at a dental clinic for head tremor. One day later he developed jaw drop, which required manual assistance to close his mouth. After 9 months he visited our clinic due to no improvement in his chewing difficulty. A neurological examination showed significant jaw-closing weakness but preserved jaw-opening strength. Additionally, subtle perioral fasciculation, tongue atrophy, dysarthria, and postural hand tremors were observed. Bilateral masseter atrophy was suspected, but limb muscle atrophy was not observed. Also, limb tone, muscle power, sensation, and tendon reflexes were all normal.

Nerve conduction studies revealed low action-potential amplitudes in sensory nerves while motor nerve conduction remained normal. Needle electromyography demonstrated positive sharp waves (2+) in the genioglossus, as well as polyphasic and giant motor-unit action potentials with amplitudes up to 20 mV in the cervical, thoracic, and lumbar segments. Repetitive nerve stimulation (RNS) of right orbicularis oculi, abductor digiti quinti (ADQ), and flexor carpi ulnaris (FCU) at low frequency (5 Hz) induced response decrements of 26.1%, 10.8%, and 13.7%, respectively (Fig. 1A). However, high frequency (30 Hz) RNS of ADQ and FCU induced no incremental responses (Fig. 1B). Antibodies against the acetylcholine receptor (AChR) and muscle-specific kinase were all negative. The creatine kinase level was 85 IU/L (normal range 22−198 IU/L). MRI showed diffusely increased T1-weighted signals in his tongue muscles (Fig. 1C). Genetic testing identified 49 CAG repeats in the *AR* gene, confirming the diagnosis of SBMA. The patient had no family history of SBMA. His score on the SBMA Functional Rating Scale was 51, with deficits only on the bulbar-related subscales. The symptoms did not improve significantly during a 1-year follow-up.

SBMA is caused by the toxic effects of mutant AR protein that lead to the degeneration of anterior horn cells in the spinal cord, motor units, and dorsal root ganglia. Additionally, direct toxic effects on skeletal muscles contribute to the primary myopathic features. Moreover, recent studies have highlighted the involvement of the NMJ in SBMA, such as a lack of AChR colocalization[2] and smaller NMJ.[3] Consistent with these findings, clinical cases have demonstrated decremental responses to RNS[4] and responsiveness to acetylcholinesterase inhibi-

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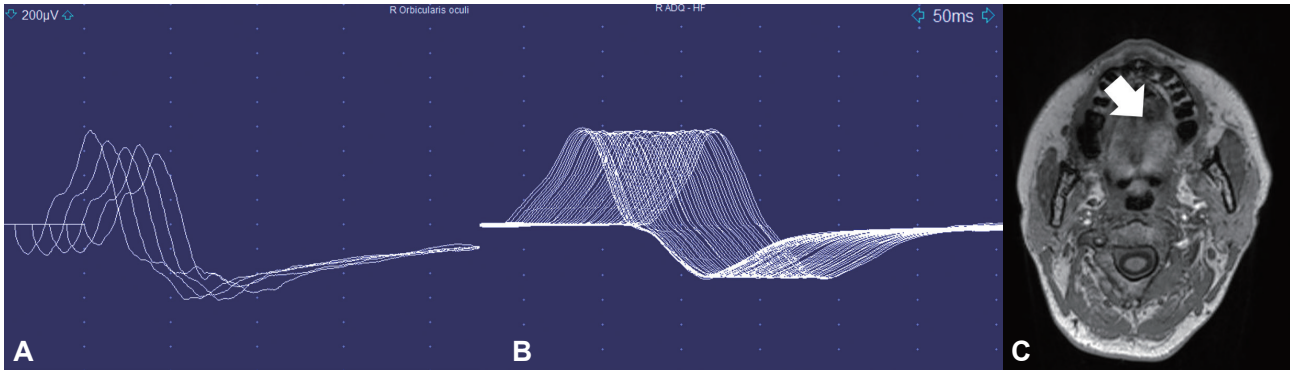

Fig. 1. RNS and brain MRI findings. A: There was a decremental response to low-frequency (5 Hz) RNS of right orbicularis oculi, with a moderate reduction of 26.1% in the amplitude of CMAPs. B: There was no incremental response to high-frequency (30 Hz) RNS of abductor digiti quinti. C: T1-weighted brain MRI revealed a bright tongue sign (white arrow) on the genioglossus muscle. CMAPs, compound motor action potentials; MRI, magnetic resonance imaging; RNS, repetitive nerve stimulation.

tors,[5] further supporting the role of NMJ dysfunction in SBMA.

BoNT acts at the NMJ by cleaving SNARE proteins, which are essential for the release of acetylcholine-containing vesicles from presynaptic neurons, leading to temporary muscle weakness. Its effects typically begin within 1 to 3 days, peak within 10 to 14 days, and gradually wear off over 3 to 6 months.[6] BoNT has been shown to be effective in various neurological disorders, including dystonia, hemifacial spasm, migraine, and amyotrophic lateral sclerosis with sialorrhea. However, in myasthenia gravis, in which NMJ dysfunction is the main pathophysiological mechanism, cautious administration with dose adjustments has been recommended to mitigate potential risks.[7]

The symptoms in our patient appeared on the day after injection, and weakness persisted for over 21 months without improvement. There were decremental responses to RNS in asymptomatic muscles, suggesting subclinical postsynaptic NMJ dysfunction. Since both pre- and postsynaptic structures including the endplate area, AChR compactness, and postsynaptic complexity are affected in SBMA mouse models,[2] BoNT-induced weakness may develop more rapidly and severely. Moreover, SNAP-25 (synaptosomal associated protein-25), a component of the SNARE complex, is expressed not only at the NMJ but also in axonal growth cones,[8] which results in BoNT contributing to NMJ dysfunction as well as axonal growth impairment and denervation. Further research is needed to elucidate the mechanisms underlying the effects of BoNT in SBMA, which could help refine treatment strategies.

While progressive bulbar and limb muscle weakness define SBMA, atypical presentations such as jaw drop[9] and dropped-head syndrome[10] have also been reported. Notably, despite subtle SBMA symptoms, jaw drop accompanied by facial muscle fasciculation and electrophysiological abnormalities—including sensory neuropathy and widespread neurogenic findings—led to an accurate diagnosis in our case. Therefore, maintaining clinical suspicion and conducting a thorough evaluation are important for the early recognition of SBMA.

In conclusion, this case highlights the potential for exaggerated and prolonged effects of BoNT in SBMA, possibly due to NMJ dysfunction. Awareness of this phenomenon is crucial for clinicians administering BoNT in patients with neuromuscular disorders.

Ethics Statement

This case report was approved with a waiver of informed consent by Seoul National University Hospital Institutional Review Board (H-2211-117-1380).

Availability of Data and Material

All data generated or analyzed during the study are included in this published article.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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