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Botulinum Treatment Induced Dropped Head Syndrome in a Patient With Chronic Migraines and Multiple Sclerosis

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Background: Chronic migraine treatment typically is treated medically by use of medications, such as nonsteroidal anti-inflammatory drugs and triptans; however, for a subset of patients, botulinum toxin (or Botox) has effectively been shown to be an alternative medication.

Case Report: Following Botox administration for chronic headaches, our patient developed unforeseen adverse effects and presented with severe neck stiffness, facial droop, and dysphagia, collectively known as dropped head syndrome, prompting them to seek emergency care. In order to counteract botulinum toxicity, we administered neostigmine, but unexpectedly induced cholinergic toxicity, which led to severe secretions and blurry vision. Glycopyrrolate was administered with responsive resolution of symptoms.

Conclusions: This case highlights the complexities of managing adverse reactions to Botox and raises considerations for alternative treatments, such as atropine, or concurrent neostigmine treatment with glycopyrrolate.

Key words: Botox, botulinum, dropped head syndrome, chronic migraine, migraine, multiple sclerosis

BACKGROUND

Chronic migraines are defined as experiencing headache symptoms on 15 or more days per month for over 3 months. (1) Diagnosis relies on patient-reported symptoms and may include a neurological examination. Typically, nonsteroidal anti-inflammatory drugs or triptans are used to treat migraines (1). In 2010, botulinum toxin (or Botox) (now known as onabotulinumtoxinA [OBTA]) was approved as an effective preventative therapy for chronic migraines, demonstrated by the randomized double-blind placebo-controlled and Phase III Research Evaluating Migraine Prophylaxis Therapy trials (2). OBTA, when injected, blocks neurotransmitter release in the extracellular space (2,3) (Fig. 1).

CASE PRESENTATION

The patient, with a past medical history of multiple sclerosis (MS) (diagnosed approximately 5 years ago), and chronic migraines presented to the emergency department complaining of progressively worsening neck stiffness, face droop, and leftward-oriented facial rotation. She stated that it started the day after she had received Botox injections for chronic migraines, and had been worsening , which prompted her to seek emergency care.

On further evaluation and questioning, the patient stated that her neck became stiffened, and her face slowly dropped. She also endorsed some right upper extremity weakness that is abnormal from her baseline, and due to the orientation of her head and neck has made ambulation increasingly difficult, even with the assistance of a 4-wheel walker. She also stated that she has had worsening dysphagia due to her facial orientation over this time period that has made it difficult to eat

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Patient consent for publication: Patient was lost to follow-up, all patient identifiers are removed to ensure confidentiality.
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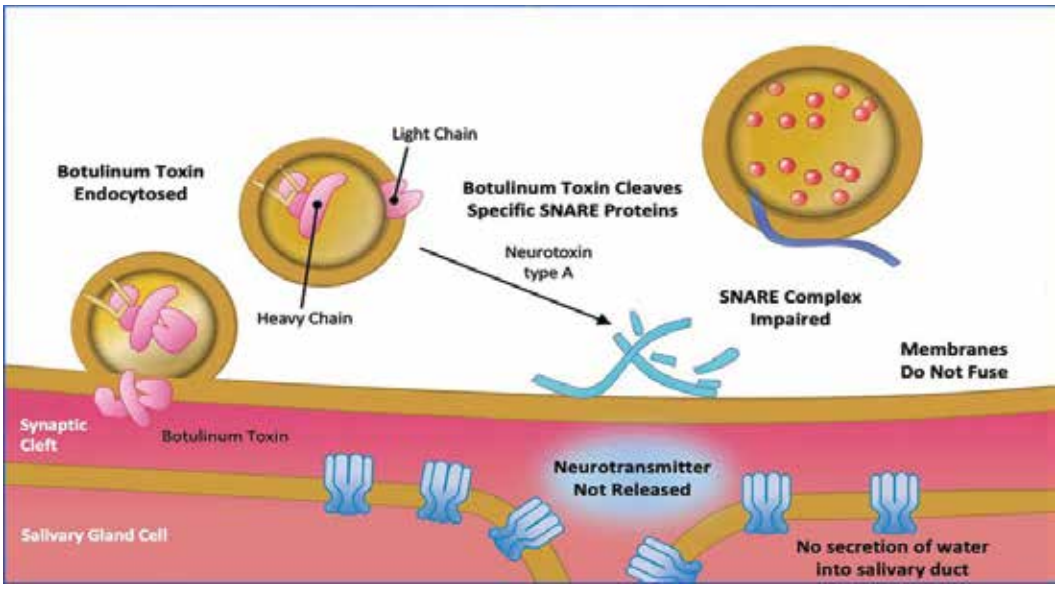

Fig. 1. Mechanism of Action of OBTA (Botox) at neuromuscular junction.

food. The patient denied any vision changes, headaches, bladder, or bowel dysfunction, or recent falls/trauma. When inquiring about her Botox injections, the patient states that she has received Botox injections for years for chronic migraines, and repeats the procedure every 3 months with the same provider. To her knowledge, the injections were in the same standardized locations (Fig. 2) and she was unaware if any different formulation was given (4).

Upon physical exam of the patient, the patient's head was forward flexed, with leftward rotation, and side bending. She was unable to extend her neck posteriorly, passively, or actively. Additionally, she presented with good neck strength but resisted rightward head rotation. A neurologic exam was conducted; CN II-CN XII appeared intact, with observed flattening of the forehead creases (likely secondary to Botox injections at this location). Right upper extremity pronator drift was observed, the patient was able to flex the right shoulder to 90°, abduct to 45°, and sensation appeared intact of the right lateral deltoid. Right elbow flexion/extension 5/5 strength and wrist flexion and extension 5/5 strength.

A computed tomography angiogram of the head and neck was completed due to concern for a vascular lesion, aneurysm, or a mass effect due to the right-sided pronator drift and presenting right upper extremity weakness; however, imaging was unremarkable.

After consultation with the pharmacy, dropped head syndrome secondary to botulinum toxicity was considered and trial treatment with neostigmine was discussed with the patient. After administration, subsequently, the patient was able to extend her neck, and while monitoring the patient, began to exhibit profuse secretions, blurry vision, and lacrimation. Collectively, the decision was then made to administer glycopyrrolate, which resolved the symptoms. With resolution of neck stiffness and facial droop via medication administration, the patient was advised by Neurology to be admitted for magnetic resonance imaging to rule out acute MS lesions or cerebrovascular accident; however, the patient left the emergency department against medical advice, and was advised to follow-up with her neurologist.

DISCUSSION

Botulinum toxicity prevents neurotransmitter release into the neuromuscular junction. In our case presentation, it prevented our patient from neck extension, and also caused a leftward rotation (likely due to inhibition of the contralateral [right] sternocleidomastoid muscle). The combined symptoms contributed to dysphagia that had brought the patient to the emergency department. To counteract this toxicity at the junction, we attempted to use neostigmine as a treatment.

Neostigmine inhibits the enzyme acetylcholinesterase and increases acetylcholine at the neuromuscular junction. By doing so, it increases the neurotransmitter quantity, and reverses the effect of OBTA (5). However,

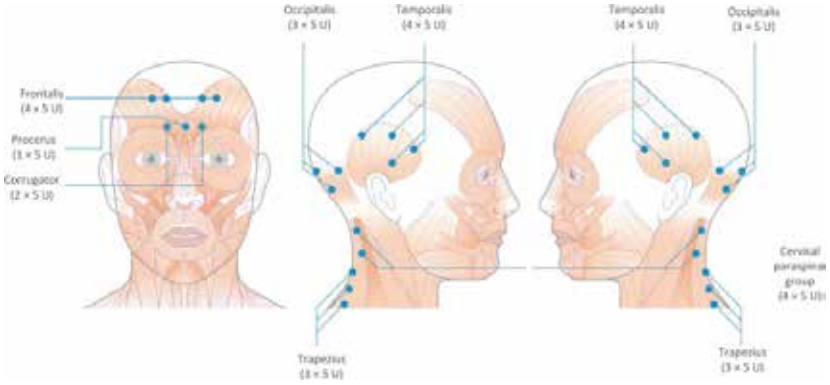

Fig. 2. OBTA (Botox) injection sites used for for chronic migraine patients.

in our patient, we encountered an unforeseen complication. By increasing the acetylcholine at the junction, our patient experienced cholinergic toxicity and exhibited profuse secretions, which were subsequently treated with glycopyrrolate with a responsive resolution of symptoms. In hindsight, atropine may have been a better option as the mechanism of action would block acetylcholine and the patient may not have developed secretions as an adverse effect of the medication (6). Or alternatively, it may have been prudent to prophylactically use glycopyrrolate in combination with neostigmine to avoid adverse effects (7). Regardless, the use of these medications in patients should be closely monitored due to additional side effects, such as cardiac toxicity (8). Unfortunately, as our patient left without a complete workup, we cannot say definitively Botox was the cause; however, very likely due to her clinical presentation and response to treatment.

It is crucial to be vigilant and observe patients' reactions during and after treatment to monitor for unforeseen adverse effects for prompt treatment of adverse reactions. We encountered unforeseen complications when administering neostigmine, and the patient subsequently developed cholinergic toxicity, highlighting the importance of anticipating and promptly addressing such reactions. This emphasizes our role as health care providers to know our treatments holistically, including their complications to ensure swift and effective management. Additionally, as each patient is unique, their responses to treatment may be unique as well. It becomes imperative to be well-knowledgeable providers for a comprehensive patient-centered approach to care.

CONCLUSIONS

In conclusion, our case underscores the unpredictable challenges inherent in OBTA for chronic migraines. The unexpected emergence of cholinergic toxicity following neostigmine administration emphasizes the critical need for vigilant monitoring and adaptable approaches to patient care. The intricacies of individual responses highlight the ongoing imperative for research to better comprehend the nuanced interactions of OBTA, particularly in patients with concurrent neurological conditions like MS. This case prompts a reconsideration of therapeutic strategies, advocating for a more nuanced and individualized approach that anticipates and addresses potential complications, thereby optimizing patient outcomes.

Moreover, our experience invites contemplation of alternative treatments for botulinum toxicity, such as the potential efficacy of atropine in mitigating cholinergic toxicity. Hindsight suggests that atropine, with its acetylcholine-blocking mechanism, might have offered a more favorable outcome in our patient. As we navigate the complexities of rare presentations, this case serves as a reminder of the essential role of interdisciplinary collaboration, with insights from pharmacy and neurology, to ensure comprehensive patient care. Overall, this scenario contributes to the evolving landscape of medical knowledge, reinforcing the importance of adaptability and collective expertise in managing the intricate challenges posed by innovative therapeutic interventions.

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