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DELAYED ABDOMINAL PAIN FOLLOWING BOTOX® BLADDER INJECTION MIMICS EXERCISE-INDUCEDTRANSIENT ABDOMINAL PAIN: A CASE REPORT

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Background: Overactive bladder and associated incontinence are increasingly treated with onabotulinumtoxinA (Botox®) intradetrusor injections. An observed but poorly understood side effect is generalized abdominal pain that simulates cramps.

Case Report: Here, we describe a patient with lower left quadrant abdominal pain beginning 16 days after treatment that worsened in severity over several days and persisted for an additional 5 weeks before abating over 3 more weeks. The unique pain symptoms mimicked the acute condition known as exercise-induced transient abdominal pain (ETAP), rendering the patient's exertion and supine position intolerant due to pain intensity.

Conclusions: The hypothesis is that the Botox spread from bladder injection sites impacts the same ill-defined visceral-somatic abdominal neuronal-muscular circuitry underlying the ETAP phenomenon or complex regional pain syndromes.

Key words: Abdominal pain, intradetrusor injection, Botox spread, exercise-induced transient abdominal pain, overactive bladder

BACKGROUND

Overactive bladder (OAB) generates a pathological syndrome of increasing urinary urgency that can lead to incontinence, nocturia, and reduced quality of life (1). It affects approximately 15% of men and women equally, although urgency incontinence is almost 2 times more common in women (1,2). An effective and prevalent treatment strategy involves intradetrusor injection of botulinum toxin A as onabotulinumtoxinA (Botox®, Allergan, Irvine, CA, United States). The recommended dosage is 100-200 U injected across an evenly spaced grid of 30 sites across the inner bladder wall (3). With respect to more worrisome side effects, the manufacturer states intradetrusor injection of 200 U at one time in patients followed over 44 weeks was associated with autonomic dysreflexia (1.5%), muscle weakness (4%), and muscle spasm (2%) (3). The US Food and Drug Administration required a black box warning for this product in 2009 because the toxin can spread outside the immediate area of injection over hours and even weeks, leading to life-threatening and serious adverse events in a small percentage of patients (3,4). Studies (5,6) in animals

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have shown that Botox can spread beyond the area of injection by diffusion through the intracellular space and into lymphatics and capillary networks or by traveling through peripheral nerves.

CASE PRESENTATION

Here, we report a 58-year-old man with chronic OAB and a history of 4 previous treatment sessions of 100 U with Botox, who was treated again on June 19, 2025, although this time with 200 U that were given in 30 separate injections across the bladder, 1 mL each. The patient had no other significant comorbidities and was otherwise healthy and exercised routinely. The current treatment was uneventful, yet the patient reported greater hematuria for 3 days compared with past sessions. However, within 16 days, the patient reported the beginning of general lower left quadrant abdominal pain that over the next 2 days became fulminant and highly exertion-dependent, which persisted for the next ~5 weeks before gradually subsiding over the next 3 weeks.

The pain was Carnett's negative, suggesting a more visceral etiology. At peak symptomology, the patient reported unbearable pain within 1 minute of mild exercise or 2 minutes of brisk walking, or when resting in the supine position or left lateral recumbent position. Near complete relief of pain occurred at rest in the sitting position or in the right recumbent position. Given the extreme and progressive pain and its positional dependence, the patient sought medical attention and received 2 separate computed tomography scans over 2 days at 2 different health systems (2 different radiology reports), the latter of which included vascular contrast imaging. However, the radiology reports were uniformly unremarkable across the abdomen, pelvis, and lower chest cavity, which, in conjunction with comprehensive blood and metabolic analysis, failed to identify an obvious cause for the pain. Consultation with a gastroenterologist supported the lack of disease within the entire gastrointestinal tract or related tissues. The patient reported mild and transient nausea at peak pain, although vomiting was absent and bowel movements were unremarkable without hematochezia. The patient data also ruled out the urogenital system as causative, and the pain symptoms also ruled out anterior cutaneous nerve entrapment syndrome or median arcuate ligament syndrome as potential underlying etiologies. Consultation with a pain physician also supported the absence of a definable medical cause for the symptoms. Importantly, the patient was completely free of the pain symptomatology ~10 weeks after the initial intradetrusor Botox injections, a time course consistent with gradual dissipation of side effects due to Botox spreading (3,4).

DISCUSSION

The patient had also experienced the same, albeit less severe pain symptoms with a previous intradetrusor Botox injection approximately 7 months earlier (100 U) that lasted for 2-3 weeks and had a similar 2-week onset delay. With the latest 200 U injections, the patient described a unique pain syndrome he described as a debilitating "side-stitch" that mimics the same overwhelming abdominal pain response reported with extreme exercising postprandial, which in sports medicine is referred to as exercise-related transient abdominal pain (ETAP) (7).

To this day, the reason for ETAP remains unknown and is characterized by a sharp, stabbing pain in the left or right side of the abdomen that can be momentarily debilitating for athletes, although it typically resolves within minutes of exercise cessation (7). Theories to the origin of ETAP include ischemia of the diaphragm or generalized gastrointestinal system, with or without compression of one or more supply arteries, stress on visceral ligaments or abdominal muscles, or irritation of the spinal nerves and parietal peritoneum (7). Interestingly, ETAP is even reported in individuals during horseback riding, suggesting a nonischemic mechanism of pain (7). During its peak, the patient was nonetheless pain free at rest while sitting, as well as during the first 20 seconds of walking, after which the pain intensified until cessation of activity. Interestingly, the abdominal pain from continuous exertion required 2-4 minutes of inactivity in the sitting position before abating completely. This collective temporal manifestation of pain symptoms is suggestive of a toxin "sensitized" response that impacts the visceral-somatic neuronal sensing systems in the lower abdomen that could underlie the mysterious ETAP response, although in this case, the Botox spread from the intradetrusor injection region likely impacted these same pathways. Alternatively, it is also possible that the Botox spread caused weakening of select abdominal or pelvic floor muscles that then promoted overcompensation of unaffected regional muscles during physical activity to induce the temporary pain response.

CONCLUSIONS

Our case report highlights the hypothesis that the well-known "side-stitch" phenomenon referred to as ETAP from extreme exercise (often after eating), could involve the same neurogenic or visceral-somatic abdominal pain response that can occur with diffuse intraabdominal Botox spreading after intradetrusor or pelvic floor injection procedures, as observed in some patients.

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