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Iatrogenic botulism

SHORT CASE REPORT

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This case study describes severe iatrogenic botulism following treatment with a botulinum toxin injection at a private clinic abroad.

A woman in her forties was urgently admitted to the medical department of a Norwegian hospital due to increasing pharyngoplegia, neck muscle weakness, constipation, dry mouth, headache, fatigue, ptosis and blurred vision over the preceding five days. In the three days prior to admission, she had not consumed any liquids or solid food, and her head needed support when she tried to sit up.

It was revealed that 15 days earlier, she had been injected with botulinum toxin type A for migraines during a stay abroad. Due to chronic migraines, she had previously received several injections in the forehead, temples, back of the head and neck in Norway. At the clinic abroad, injections were administered in the front and back of the neck and the upper part of the chest. The toxin used is not approved in Norway.

On admission, the patient had stable respiration and circulation, and was afebrile with normal blood gas and normal results from initial blood tests. Apart from bilateral ptosis and paresis of the neck, face and pharynx, the neurological examination showed normal findings. Supplementary flexible endoscopy to evaluate pharyngeal function confirmed moderate dysphagia and pronounced pharyngeal weakness. A nasogastric tube was inserted due to a high risk of aspiration.

Local adverse effects of botulinum toxin A injections were considered the likely cause of the paresis. Headache, fatigue, constipation, dry mouth, ptosis and blurred vision were diagnosed as possible systematic adverse effects, and the Norwegian Institute of Public Health was contacted to discuss treatment with antitoxin. Blood samples were sent to the Food Safety Unit in the Faculty of Veterinary Medicine, Norwegian University of Life Sciences (NTNU), where three mice were injected with the patient's serum (mouse test). One of the three mice developed symptoms of botulism within four days, and the test was considered inconclusive for free botulinum toxin. Following an overall assessment, treatment with antitoxin was ruled out due to the duration of symptoms, uncertainty about the adverse effects and efficacy of antitoxin, and the mild improvement in the patient's symptoms.

After ten days in hospital, the patient was discharged with follow-up from home care services. Her general condition had improved and she had normal vision and no headache. Her pharyngeal function was still reduced, requiring tube feeding, but she could now consume liquids and pureed food in an upright sitting position. At the three-month check-up, she was still reliant on the feeding tube for sufficient nutrition.

Discussion

Low-dose botulinum toxin is widely used as a cosmetic treatment and for various medical conditions, such as muscle spasticity, cervical dystonia and chronic migraines. The toxin is produced by the Gram-positive, anaerobic, rod-shaped bacterium *Clostridium botulinum* and ranks among the most potent natural toxins. Paralysis occurs in high doses, which can lead to respiratory failure and death. Seven serotypes (types A–G) have been identified, with A, B, E and F capable of causing botulism in humans (1).

From 1977 to 2022, 81 cases of botulism were reported in the Norwegian Surveillance System for Communicable Diseases. Of these, 37 were foodborne, 26 were wound botulism associated with subcutaneous drug use, and 8 were cases of infant botulism. The mode of transmission was not recorded for the remaining cases (2). A common cause of botulism in Norway is the

consumption of contaminated *rakfisk* (a salted and fermented fish dish) or cured meat, where patients typically develop abdominal pain, vomiting and diarrhoea within 12–36 hours, accompanied by dry mouth, ptosis, diplopia, speech problems, paresis and constipation (2).

Botulism as a complication of medical and cosmetic injections is less known and often associated with incorrect administration or overdosing (3). In February and March 2023, 87 cases of botulism were reported following intragastric injections for weight management treatment in Turkey (4). Some patients exhibited severe symptoms, and several required intensive care and antitoxin treatment (4). In a European prospective study, preliminary data were recorded on 22 German patients who developed botulism after such treatment in Turkey. This included injections with 1000–2500 units of botulinum toxin A, which is much higher than the maximum dosage of 500 units per treatment recommended for the most widely sold botulinum toxin A preparations in Norway (5, 6). It is uncertain what dose our patient received, as no information on dosage was available.

Botulinum toxin can be indirectly detected by inoculating mice (mouse test) with the patient's serum. New promising tests that are more sensitive and do not involve animals are not available in Norway (7). Among the first 12 German patients, all with a negative mouse test, toxin was detected in nine using an Endopep-MS assay. The available test methods are thus not sensitive enough, and a negative mouse test does not rule out botulism if clinical findings are consistent (5).

In cases of suspected wound or foodborne botulism, the recommended treatment is rapid (within 48 hours) infusion of heptavalent antitoxin produced in an immunised horse and supplied by the Norwegian Institute of Public Health. Antitoxin treatment has shown better survival rates in animal experiments, while data and clinical experience with iatrogenic botulism are limited (5, 8). In a Chinese observational study of 86 patients with iatrogenic botulism after receiving cosmetic botulinum toxin A injections, dosages ranged from 6 to 1000 units. Symptoms developed within 0 to 36 days, with the most common being headache, dizziness, fatigue, blurred vision, ptosis and dysphagia. All received antitoxin treatment, which was reported to be effective and without serious adverse effects (9).

The mouse test indicated that free toxin might be present in our patient. It is unclear whether the clinical deterioration beyond one week after injection was due to effects in neurons from initial toxin binding, or if free toxin was still present (3). In a more recent case study, a patient with progressing paralysis was treated 15 days after receiving a botulinum toxin A injection, with observed improvement (10).

Systemic distribution and the efficacy of antitoxin treatment are under-researched, but due to the increasing trend of 'beauty and health tourism' abroad, we are likely to see more cases of iatrogenic botulism where antitoxin treatment needs to be considered.

The patient has consented to publication of this article.

Authors Nakstad and Koht treat patients with a medical indication for botox.

The article has been peer-reviewed.

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