Short communication

Botulinum toxin A for treating muscular contractures in cephalic tetanus

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Abstract

Objective: This study reports the use of botulinum toxin for treatment of muscle contractures in a patient with cephalic tetanus.
Method: Case report.
Results: An 80-year-old woman was diagnosed with cephalic tetanus, with contractures of the masseter, sternocleidomastoid, trapezius, and levator scapulae muscles. After one month of conventional treatment good recovery was observed, but with persistence of the contractures of the sternocleidomastoid, trapezius and levator scapulae. These contractures were treated with botulinum toxin A (75 IU in the right sternocleidomastoid, 25 IU in the right trapezius; one month later 50 IU in the left levator scapulae, 50 IU in the right levator scapulae, 75 IU in the left sternocleidomastoid; two months later 25 IU in the left trapezius). Full recovery was observed.
Conclusions: Local infiltration with botulinum toxin A appears to be an effective treatment for persistent muscle contracture in cephalic tetanus.

Keywords: Tetanus; Cephalic tetanus; Tetanus toxin; Botulinum toxin; Pain

Summary

We report the use of botulinum toxin A to treat persistent contractures of the sternocleidomastoid, trapezius, and levator scapulae in an 80-year-old woman diagnosed as having cephalic tetanus. She responded well, and eventually made a full recovery.

Clostridium tetani usually enters the body through an open wound and is commonly found in the soil and in manure; it may also be present in the human intestine among other places. Local tetanus is characterised by rigidity and spasms near a lesion through which C. tetani has entered. Cephalic tetanus is a rare variant, which accounts for about 1–3% of reported cases, and typically involves several cranial nerves.1,2

The ability of botulinum toxin to disrupt neurotransmission, often for prolonged periods, has been exploited for use in several ways, and these toxins, now licensed pharmaceutical products, are the treatment of choice for several neuromuscular conditions, including oromandibular and other focal dystonias,3 strabismus, chronic anal fissure,4 and management of pain in some soft tissue syndromes.5

In 1994, Andrade and Brucki1 described a case of cephalic tetanus that was successfully treated with botulinum toxin A. This is the only report that we know of to date of the use of
botulinum toxin A to treat it. Here we report a case in which botulinum toxin A was used to treat muscular contractures in a patient with cephalic tetanus.

Clinical report

An 80-year-old woman presented with throat pain, dysphonia, and inability to swallow solid food. During the subsequent two weeks she developed gradually increasing muscle contractures and neck rigidity, which by 15 days had led to severe contracture of both masseters with complete inability to open the mouth, and contracture of both the sternocleidomastoid and trapezius muscles. Examination showed no surface wounds, skin infections, or tumours in the head and neck region. Detailed intraoral examination was prevented by trismus. Panoramic radiography indicated that she was edentulous with no associated conditions. She was taking no medication, but her tetanus vaccination history was not clear. She was admitted to hospital. Computed tomography of the brain and neck showed no abnormalities. Laboratory analyses were within reference ranges (notably, white cell count 7.9 × 10⁹/L, serum calcium concentration and creatine phosphokinase (CPK) activity within reference ranges). Electromyography indicated dystonia of the masseter, sternocleidomastoid, and trapezius muscles; as noted, she had taken no drugs that might explain this. She also had no obvious lesions or septic foci in the oral cavity through which C. tetani might have entered. Nevertheless, after ruling out other possibilities, we made a diagnosis of cephalic tetanus, and started treatment with metronidazole (Flagyl, Aventis Pharma, Madrid, Spain; 1 g intravenously every 12 h for 10 days), antitetanus gamma globulin (Gama Antibiotico Tetanos Grifols, Instituto Grifols, Barcelona, Spain; single intramuscular dose of 6000 IU), and diazepam (50 mg every 12 h). In view of her general condition and the cephalic site of the muscle contractures, the possibility of treatment with curare-type peripheral neuromuscular blockade was ruled out.

During her hospital stay she made good progress, though the contractures of the sternocleidomastoid, trapezius, and levator scapulae persisted for 8 weeks. We then opted for treatment of the contractures by local infiltration with botulinum toxin A (Botox, Allergan, Irvine, CA, USA): 75 IU in the right sternocleidomastoid, and 25 IU in the right trapezius. She responded well, so we treated the remaining muscles: 50 IU in the left levator scapulae, 50 IU in the right levator scapulae, and 75 IU in the left sternocleidomastoid. Two months later, she had pain only in the left trapezius, which was again infiltrated with 50 IU of toxin, after which she made a full recovery.

Doses of botulinum toxin were calculated according to the length and width of the contracted muscle, the degree of contracture, and the required effect (relaxation of the muscle, as opposed to full paralysis).

Discussion

The neuroparalytic syndromes of tetanus and botulism are caused by neurotoxins that are produced by bacteria of the genus Clostridium, C. tetani, and C. botulinum, which are both Gram-positive, spore-forming, rod-shaped, anaerobic bacteria. C. tetani can enter human tissues through wounds (including surgical wounds), burns, ulcers, compound fractures, or injection sites. If the environment in the tissue is anaerobic, the spores will germinate and multiply to produce the tetanus neurotoxin, which affects nerve transmission and therefore muscular activity.

The neurotoxins produced by C. tetani and C. botulinum are 150 kDa proteins consisting of three domains, endowed with different functions: neurospecific binding, membrane translocation, and specific proteolysis of three key components of the neuroexcytotic apparatus. After binding to the presynaptic membrane of a motoneuron, the neurotoxin is internalised and transported retroaxonally to the spinal cord, where it blocks release of neurotransmitters from spinal inhibitory interneurons (Fig. 1). In contrast, the seven botulinum neurotoxins act at the periphery and inhibit release of acetylcholine from peripheral cholinergic nerve terminals. Tetanus neurotoxin and botulinum neurotoxins B, D, F, and G specifically cleave the membrane protein VAMP/synaptobrevin, associated with small synaptic vesicles, at single but different peptide bonds. Botulinum neurotoxins A, C, and E cleave sensory nerve action potential —25 at different locations within the carboxyl terminus, and type C also cleaves syntaxin. Botulinum neurotoxins are increasingly used in medicine for the treatment of human diseases involving hyperfunction of cholinergic terminals.

Clinically, tetanus has been classified into four types: neonatal, local, cephalic, and generalised. Cephalic tetanus is a rare variant of local tetanus (about 1–3% of reported cases).
cases) that may involve any of several cranial nerves. It may follow an injury such as laceration, abrasion, or a puncture wound, or it may be associated with a head injury or middle ear infection. Two-thirds of cases of cephalic tetanus progress to generalised disease that can gradually involve the muscles of the limbs and trunk. The commonest presenting symptom is trismus. Other symptoms include dysfunction of one or more cranial nerves (often the VIIth nerve), facial pain, dysphagia, dysarthria, risus sardonicus (spasms of the face and jaw), stiffness of the neck and back, opisthotonos (head and neck arched back), spasms, voiding difficulties, abdominal pain and gastrointestinal problems, and mental and emotional problems. Other presenting symptoms may be fever, nystagmus, diplopia, cardiac disorders, and general malaise.

The diagnosis of tetanus is based entirely on clinical findings: laboratory tests are not helpful. Serum creatine phosphokinese activity may be increased in some cases, but is not pathognomonic. It is of interest that C. tetani can be isolated from wounds of patients without tetanus, and often cannot be isolated from wounds of patients with tetanus. Diagnosis is thus based on clinical manifestations. Differential diagnosis should consider strychnine poisoning, generalised convulsive seizures, extrapyramidal reaction, hypocalcemic tetany, black widow spider bite, rabies, meningitis, subarachnoid haemorrhage, sepsis, progressive fluctuating muscular rigidity (stiff-man syndrome), peritonitis, drug withdrawal, and conversion reaction. Various uncommon systemic infections may present with head and neck manifestations either initially or during the course of the disease.

Treatment of tetanus includes antibiotics (preferably penicillin, tetracycline, and metronidazole), as well as passive immunotherapy with a single intramuscular dose of 3000–6000 IU of antitoxin, which is given to neutralise circulating and unbound toxin in the wound. Muscle relaxants and analgesics may also be required. Prompt supportive intensive care is also required, which may include respiratory support, intubation, and tracheostomy to preserve the airway and diazepam intravenously.

In the patient described in the present report, cephalic tetanus was diagnosed after other possible causes of trismus and contracture of the neck muscles had been ruled out. The fact that we did not detect a portal of entry of C. tetani in the facial region is consistent with the diagnosis, as non-detection of the presumed portal of entry is common in tetanus.

Our patient showed altered motoneuron function in the trigeminal nerves (masticatory musculature), accessory nerves (sternocleidomastoid and trapezius muscles), and branchial plexus (levator scapulae). The activity of the muscles dependent on the trigeminal nerve recovered spontaneously within about a month of the onset of symptoms. However, contractures persisted in the sternocleidomastoid and trapezius muscles (dependent on the accessory nerve) and in the levator scapulae muscles (dependent on the branchial plexus), so we opted for treatment with botulinum toxin.

Botulinum toxin is used for the treatment of muscle contractures in disorders such as oromandibular dystonia, other focal dystonias, and strabismus. In 1994, Andrade and Brucki described a patient with cephalic tetanus who they treated successfully with botulinum toxin A. Botox is a commercial formulation of botulinum toxin type A, which is not expected to be present in the bloodstream in measurable concentrations after treatment with the recommended dose, and typically remains in the injected muscle, although it may spread to adjacent muscle.

The treatment of tetanus by infiltration of the affected muscles with botulinum toxin is a palliative measure, as it does not eliminate the toxin or block its mechanism of action. However, the resulting neuromuscular block relaxes the muscles until the tetanus toxin is eliminated, which greatly increases the patient’s comfort and well-being.

References