

Myaesthesia gravis exacerbation caused by axillary injection of botulinum toxin-A for treatment of hyperhidrosis

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We present a 17 year old with congenital myasthenia gravis treated with pyridostigmine and 3,4-diaminopyridine who had severe hyperhidrosis of the axillae that had a profound psychosocial and occupational impact. Antiperspirants proved ineffective, aluminium hydroxide preparations were irritant and iontophoresis was not available for this body site.

Following careful consideration, half the typical botulinum toxin (BTX) cumulative dose was delivered intradermally; 50 units (Dysport) per axilla followed by 72 hours inpatient observation. There was no evidence of worsening myasthenic symptoms and significant improvement in hyperhidrosis at four months. A second treatment with 25 units (Xeomin) per axilla was delivered, this resulted in intermittent diplopia and persistent muscle weakness at six months. 3, 4 – diaminopyridine dose was increased, treatment with BTX was discontinued and hyperhidrosis gradually recurred.

Primary focal hyperhidrosis is a result of neurogenic over-activity of the eccrine sweat glands and is usually idiopathic. It can considerably impact quality of life; leaving individuals feeling socially debilitated. First line treatment includes topical metal salts in aqueous or ethenolic solution such as aluminium chloride. When these fail, iontophoresis or Botulinum toxin may be indicated.

BTX inhibits the release of acetylcholine (ACh) from presynaptic cholinergic neurons leading to inactivity of the muscles or glands innervated. For localised hyperhidrosis, serotype A of the botulinum toxin (BTX-A) is most frequently used. It is available as Onabotulinumtoxin (Botox), Abotoulinumtoxin (Dysport) and Incobotulinumtoxin A (Xeomin). These preparations are not bioequivalent. The conversion ratios are approximately Dysport 4

units: Xeomin 1 unit: Botox 1 unit.^{1,2} BTX is injected intradermally, divided into aliquots covering the area affected. Anhidrotic effects are temporary and repeat treatments are often required every 4-6 months. There is a lack of evidence for involution of sweat glands with repeated treatments and theoretically, antibody formation can lead to ineffectiveness.

The congenital myasthenic syndromes are heterogeneous disorders of neuromuscular transmission caused by defects in presynaptic, synaptic, and postsynaptic proteins of the neuromuscular junction. In this case, the underlying mutation is a compound heterozygote mutations (N88K and delK373) in the *RAPSN* gene encoding rapsyn (43-kd receptor-associated protein of the synapse). Mutations in rapsyn prevent clustering of the nicotinic acetylcholine receptors (AChR) in the postsynaptic membrane at the neuromuscular junction and there is loss of signalling at the post-synaptic folds.³ It is interesting that the defective rapsyn mediated clustering had little effect on the sweating in this case, despite sympathetic innervation of sweat glands that is dominantly regulated by cholinergic signalling; this suggest that rapsyn clustering may not be required for sweat gland cholinergic signalling.

Therapy for CMG involves increasing ACh release (3,4 diaminopyridine) and reducing synaptic metabolism of ACh with anticholinesterase agents (pyridostigmine) (Figure1). Inhibition of synaptic release of ACh in the setting of a congenital deficiency of ACh receptors raises a major concern that myaesthesia exacerbation could be precipitated by BTX. Compound heterozygotes with a K373 deletion suffer more severe myaesthetic disease⁴ and this may explain the acute sensitivity to BTX in this case.

Although previous reports suggest the effect of BTX-A may be graded by varying the dose and frequency of administration⁵, this has not specifically been explored for hyperhidrosis. We suspect that prolonged effects of BTX on muscle in this case (6 months) was mediated by the underlying myasthenic syndrome. It is also possible that the switch from Dysport to Xeomin resulted in a different biofunctional availability of the neurotoxin, however, this is controversial.

Our case highlights that extreme caution is needed when considering BTX in individuals with impaired neuromuscular signalling, and in individuals with significant muscular weakness following BTX, the possibility that BTX has unmasked a subclinical myasthenia should be considered.⁶

References

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Figure legends

Figure 1. The neuromuscular junction and the effects of 3,4 diaminopyridine in increasing ACh release and pyridostigmine in reducing synaptic metabolism of ACh .

Questions

Q1. What is the most frequently used serotype of botulinum toxin in localised hyperhidrosis?

- a. Serotype A
- b. Serotype B
- c. Serotype C
- d. Serotype D
- e. Serotype E

Answer

- a. Correct. Botulinum toxin serotype A is the most frequently used serotype in localised hyperhidrosis.
- b. Incorrect. Botulinum toxin serotype B is not the most frequently used serotype in localised hyperhidrosis.
- c. Incorrect. Botulinum toxin serotype C is not the most frequently used serotype in localised hyperhidrosis.
- d. Incorrect. Botulinum toxin serotype D is not the most frequently used serotype in localised hyperhidrosis.
- e. Incorrect. Botulinum toxin serotype E is not the most frequently used serotype in localised hyperhidrosis.

Q2. What is the approximate conversion ratios for botulinum toxin A preparations?

- a. Dysport 4 units: Xeomin 1 unit: Botox 1 unit
- b. Dysport 1 units: Xeomin 1 unit: Botox 1 unit.
- c. Dysport 2 units: Xeomin 1 unit: Botox 2 units.
- d. Dysport 1 units: Xeomin 2 unit: Botox 2 units.
- e. Dysport 6 units: Xeomin 1 unit: Botox 1 unit.

Answer

- a. Correct. The approximate conversion ratios are Dysport 4 units: Xeomin 1 unit: Botox 1 unit.
- b. Incorrect. The approximate conversion ratios are not Dysport 1 units: Xeomin 1 unit: Botox 1 unit.
- c. Incorrect. The approximate conversion ratios are not Dysport 2 units: Xeomin 1 unit: Botox 2 units.
- d. Incorrect. The approximate conversion ratios are not Dysport 1 units: Xeomin 2 unit: Botox 2 units.
- e. Incorrect. The approximate conversion ratios are not Dysport 6 units: Xeomin 1 unit: Botox 1 unit.