Immunologic Resistance After Repeated Botulinum Toxin Type A Injections for Facial Rhytides

To the Editor:

Botulinum toxin has become the most common injectable agent used for cosmetic purposes. Although immunity to the botulinum neurotoxin has been reported for other indications, the occurrence of immune-based resistance has neither been reported nor the incidence determined over a long period for cosmetic applications.

A 48-year-old woman received 14 injections of botulinum neurotoxin immunotype A (Botox®, Allergan, Inc., Irvine, CA, U.S.A.) between 1999 and 2005. The desired reduction in dynamic facial lines lasted for 3 to 4 months after each injection cycle. After the 14th exposure, she failed to demonstrate the glabellar muscle weakening effect or effacement of dynamic lines previously attained with the pharmaceutical. Differential injections of botulinum toxin immunotype B (Myobloc®, Solstice Neurosciences, Inc., South San Francisco, CA, U.S.A.) and immunotype A were applied to the glabellar muscular region (frown lines) and the lateral orbicularis region (smile lines), respectively. Immunotype A produced no response, yet immunotype B resulted in contractility and tone suppression in the glabellar region (Fig. 1). Neutralizing antibodies in the patient's sera were found to immunotype A by using a histochemical end point for motor denervation from albino rabbit longissimus dorsi muscle studied for motor denervation.1 Her sera protected against intense staining for acetylcholinesterase and fiber size variability associated with a minimum lethal dose exposure in striated muscle used in this animal model (Fig. 2). A Western blot assay previously validated against neutralizing antibodies proved positive for botulinum toxin type A antibody. ELISA was also positive for botulinum type A antibody.

Given the excellent safety record associated with widespread use of botulinum toxin-based pharmaceuticals as cosmetics, the issue of immunologic resistance rarely is discussed before injecting such patients. As botulinum toxin therapeutics have added substantially to the treatment of many serious medical-neurologic conditions,
Given our experience, resistance can occur with the cosmetic applications of botulinum neurotoxin complex, and both physicians and patients should be aware of this possibility. The incidence of the complications needs further study. The US package insert describes the incidence of this complication as "unknown."

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REFERENCE


lifelong resistance from causal cosmetic use can negatively affect a patient’s future care. Immunity to these agents is usually a lifelong effect.