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Successful treatment of tardive lingual dystonia with botulinum toxin: Case report and review of the literature☆

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Abstract

Tardive dyskinesia (TD) is a dreaded side effect of antipsychotic medication. Recommended treatments for TD may provide reliable improvement but can be, in turn, associated with additional adverse reactions. Recently, several reports have suggested that botulinum toxin A (BTX-A) injection in affected muscles may significantly improve TD. Here, we report a case of severe tongue protrusion dystonia secondary to an antipsychotic medication in a young man. Several approaches including clozapine, amisulpride, aripiprazole, ziprasidone, tiapride and clonazepam failed to improve the symptoms. Injection of 50 U of BTX-A (Dysport®, Ipsen, Ettlingen, Germany) into each genioglossal muscle dramatically improved tongue protrusion within few days with a sustained effect. If reasonable precautions are taken, the application seems to be well tolerated with only minor side effects. A review of the literature that is part of this article adverts BTX-A injection as a potential beneficial approach of various kinds of TD.

Keywords: Botulinum toxin; Neuroleptics; Tardive dyskinesia; Tardive dystonia; Tongue protrusion

1. Introduction

Antipsychotic agents (neuroleptics) are effective drugs in the treatment of psychotic symptoms in various psychiatric disorders. They can be life-saving and prescription is often devoid of alternatives. On the other hand, especially classical (first generation) antipsychotics, but also so-called "atypical" (second generation) neuroleptics may be afflicted with serious adverse reactions, mainly potentially irreversible movement disorders such as tardive dyskinesia (TD). In severe cases such as protrusion of the tongue, TD can even cause unintelligible speech and respiratory distress.

Still, none of diverse treatment regimes for TD have yet proven to be effective in a major part of the affected patients, but harbours the risk of serious additional side effects (Kiriakakis et al., 1998; Margolese et al., 2005; Soares-Weiser and Fernandez, 2007). Various other disorders associated with uncontrolled muscle activity such as primary cervical dystonia, on the other hand, have been treated successfully for years by local injection of botulinum toxin (Jankovic, 2004). We report a case of TD with severe tongue protrusion dystonia which was dramatically improved with a sustained effect by local injection of botulinum toxin A (BTX-A) in the genioglossal muscles. In addition, we review the literature on BTX-A in the treatment of TD and discuss its potential for this indication.

Abbreviations: BTX-A, botulinum toxin A; OMD, oromandibular dystonia; PKAN, pantothenate kinase-associated neurodegeneration; TD, tardive dyskinesia; U, units.

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2. Case report

At the age of 23, a 28-year old patient with schizoaffective disorder had been treated with a single dose of haloperidol which caused severe early dyskinesia of the throat, neck and both upper extremities. Haloperidol was stopped and a treatment with flupentixol (20 mg intramuscularly every 2 weeks) in combination with biperiden was established for about 1 year, upon which the patient developed within several months tardive dystonia of the tongue characterized by involuntary protrusion of the tongue. As a consequence of his impairment, the patient lost all his social contacts and could not find a job for years. In the following 4 years, TD persisted despite several trials to improve its symptoms by using amisulpride (300 mg), olanzapine (2.5 mg) and ziprasidone (120 mg). Symptoms of TD even worsened with aripiprazole (10 mg). Two attempts using clozapine in low dosages for several months were not tolerated because of severe hypotension associated with syncopes.

At admission, the patient suffered from involuntary protrusion of the tongue each time he started to speak. Furthermore, the mouth was mainly kept open during speech to prevent tongue biting. The speech rate was markedly reduced and he was hardly intelligible. Routine laboratory parameters, serum coeruloplasmin, serum and urine copper content, electroencephalogram and magnetic resonance imaging were normal. We identified a CYP2D6 poor metabolizer phenotype, assessed with the dextromethorphan test (Streetman et al., 2000), as possible origin of the substantial intolerance of our patient to both conventional and atypical antipsychotics.

Following unsuccessful attempts using quetiapine (500 mg) or tiapride (800 mg) as well as clonazepam and lorazepam in various dosages, we offered the patient a trial with local injection of BTX-A for the treatment of tardive tongue protrusion dystonia. We injected 50 U of BTX-A (Dysport®) in each genioglossal muscle via a transdermal access (total dose of 100 U) as described previously (Charles et al., 1997). The puncture was guided by ultrasound (Figs. 1 and 2) and simultaneous recording of the electromyogram using a combined injection needle (35 mm; 27 G; Ambu, Ballerup, Denmark). Local anaesthesia was not necessary and the procedure was well tolerated by the patient. Tongue protrusion improved dramatically within 3 days. The effect lasted for about 10 weeks when speech began to slightly worsen again. The major side effect was transient mild swallowing difficulties and flu-like symptoms that disappeared within 3 weeks. The patient decided to continue the treatment with BTX-A and a second injection was administered 16 weeks later with a slightly lower dose (total dose of 80 U). This time virtually none side effects occurred whereas clinical improvement was the same, lasting stable for about 3.5 months.

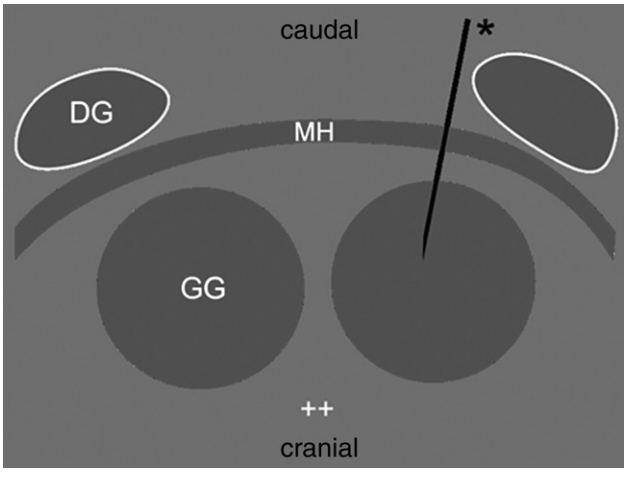

Fig. 1. Schematic view of the floor of mouth muscles and submandibular approach to the genioglossus muscle. A combined injection needle (asterisk) is transdermically introduced and guided under ultrasound and electromyographic control into the genioglossus muscle (GG). Digastric muscle (DG), mylohyoid muscle (MH), intrinsic muscles of the tongue (crosses).

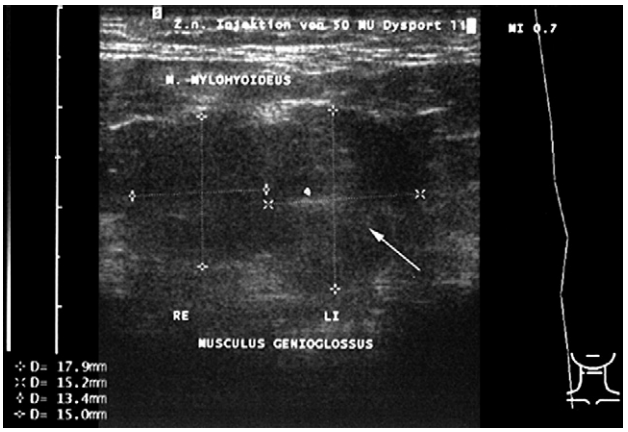

Fig. 2. Ultrasonic presentation of the floor of mouth muscles. 50 U BTX-A is injected into the left genioglossus muscle (white arrow).

3. Discussion

TD may not only occur after years of treatment with antipsychotics but may develop even in the very disabling form of tongue protrusion dystonia already after a relatively short period of use of classical neuroleptics. TD develops under conventional antipsychotics in about 5–29% per year (Jeste, 2004). Although the annual incidence of TD under atypical agents adds up to only 0.5–6.8% (Kane, 2004), long-term treatment – as often necessary – is still associated with an important cumulated risk over the years. CYP2D6 poor metabolizer status that occurs with a frequency of 5–10% in the European Caucasian population, may be a contributing factor in the development of TD (Andreassen et al., 1997). Still, the exact pathophysiological mechanisms underlying the induction of TD are not elucidated and a causal therapy is lacking. Hitherto treatment regimes for TD have been heterogeneous and mainly suggest reduction of antipsychotic doses and switching antipsychotic treatment from classical to atypical agents including clozapine. In some cases, a so-called ‘suppressive therapy’ with conventional antipsychotics or tetrabenazine may be effective (Margolese et al., 2005). More experimental treatments include amongst others melatonin, donepezil, benzodiazepines, branched chain amino acids,