ABSTRACT

Cerebrotendinous xanthomatosis (CTX) is an inherited metabolic disease characterized by an inability to form specific bile acids. Bile acid precursors and cholesterol accumulate in various tissues, resulting in multiple neurologic sequelae. We report a case of a young woman who developed oromandibular dystonia (OMD) due to CTX. Chemodenervation of the affected muscles with botulinum toxin type A (BTX) resulted in a significant improvement in her symptoms. This is the first report of CTX associated dystonias treated with BTX.

INTRODUCTION

Cerebrotendinous xanthomatosis (CTX) is a rare, inherited lipid-storage disease caused by mutations in the sterol 27-hydroxylase gene CYP27A1. This defect in bile acid synthesis results in the accumulation of cholestanol and cholesterol in all tissues, especially the tendons, brain, and lungs. CTX is characterized clinically by premature bilateral cataracts, tendon xanthomas, premature atherosclerosis, chronic diarrhea, osteoporosis, low intelligence, psychiatric disorders, and progressive neurological dysfunction. The neurologic sequelae of this disease include cerebellar ataxia, systemic spinal cord involvement, peripheral neuropathy, seizures, and a pseudobulbar phase leading to death. The diagnosis is made by demonstrating elevated serum cholestanol1,2. Treatment with chenodeoxycholic acid (CDCA) and statin medications may arrest the progression of the disease, although reversal of the clinical manifestations has not been observed3.

Case Report

A 38 year-old female with CTX, diagnosed in 2002, developed involuntary jaw thrusting and opening, as well as, tongue posturing. Progressing over a seven-month period, these dyskinesias prevented normal speaking, mastication, and swallowing. Despite five months of speech therapy, dysphagia secondary to oral incompetence and discoordination of tongue movements resulted in a 15 lb weight loss. She had no episodes of aspiration pneumonia. Although she could tolerate small amounts of a modified diet, her weight loss necessitated PEG placement for nutritional support. Her medications include CDCA, trihexyphenidyl, and tolterodine. She had previously undergone bilateral cataract removal in 1989.

Physical examination revealed severe dysarthria due to an open-jaw posture and frequent tongue posturing characterized by curling and lateral displacement (Figures 1 & 2). She was unable to move the tongue independently of the mandible. However, she had developed a “sensory trick” which decreased the jaw dyskinesias by placing a plastic needle guard between her teeth. She subsequently learned to reduce her tongue dyskinesia and improve her speech intelligibility by holding her mandible in a closed position (Figures 3 & 4). In addition, manual pressure applied to a “trigger point” on the right cheek helped to facilitate mandible closure.

Examination of the pharynx and larynx revealed symmetric palate elevation without myoclonic movements, and the gag reflex was intact. Fiberoptic nasopharyngolaryngoscopy revealed no velopharyngeal insufficiency, and full vocal fold motion with normal phonation, despite occasional laryngeal dyscoordination. Complete glottic closure was achieved during swallowing.

She was treated with speech therapy and serial titrated electromyography-guided BTX injections (Figure 5). A maximum of 15 units of BTX were administered to each of the external pterygoid muscles and 5 units of toxin were administered to each anterior belly of the digastric muscles. Following chemodenervation of these muscles, the patient experienced decreased frequency, intensity, and duration of the dyskinesias. Her speech articulation and fluency improved. Her ability to masticate and swallow both solids and liquids improved, although she remained PEG dependent. She is currently working with a nutritionist to maximize her oral caloric intake, with the goal of reducing or eliminating her PEG dependence.

DISCUSSION

Oromandibular dystonia (OMD) is a neurologic disorder characterized by involuntary movements of the masticatory, lingual, and pharyngeal muscles. Oral pharmacologic agents have limited efficacy in alleviating the symptoms of OMD. OMD complicated by recurrent temporomandibular joint dislocation has previously been described in a patient with CTX4. BTX is a safe and effective treatment for OMD5. In addition to directly weakening the affected muscles, some authors suggest that BTX also modulates inhibitory and excitatory intracortical pathways6.

Jaw-opening dystonias are primarily related to spasms of the external pterygoids and the muscles of the submental region. Due to the close proximity of the submental musculature to the intrinsic tongue musculature, injection of botulinum toxin is limited to the anterior digastic muscle. Direct injection of the intrinsic tongue musculature may result in increased dysarthria and dysphagia due to lingual hypofunction. EMG guided administration of standard starting doses of botulinum toxin7 were used to significantly improve this patient’s symptoms.

CONCLUSIONS

CTX is a rare inherited lipid storage disease with multiple neurological manifestations, including OMD. EMG-guided administration of BTX is an effective treatment for the symptoms of OMD in the setting of CTX.

REFERENCES