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Tremor and Other Hyperkinetic Movements

Case Report

Childhood-Onset Spinocerebellar Ataxia 3: Tongue Dystonia as an Early Manifestation

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Abstract

Background: Dystonia is a relatively common feature of spinocerebellar ataxia 3 (SCA3). Childhood onset of SCA3 is rare and typically associated with either relatively large, or homozygous, CAG repeat expansions.

Case report: We describe a 10-year-old girl with SCA3, who presented with tongue dystonia in addition to limb dystonia and gait ataxia due to a heterozygous expansion of 84 repeats in *ATXN3*.

Discussion: Diagnosis of the SCAs can be challenging, and even more so in children. Tongue dystonia has not previously been documented in SCA3.

Keywords: Spinocerebellar ataxia type 3, childhood onset, tongue dystonia, lingual dystonia, polyglutamine tract expansion disorder

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Introduction

There are hundreds of different forms of hereditary ataxia,[1] and more than 40 types of spinocerebellar ataxia (SCA), each caused by mutation at a different genetic locus.[2,3] The clinical features of the various SCAs are heterogeneous,[4] and can vary considerably even within the same family.[5] Diagnosis of the specific SCA is required for establishing prognosis, genetic counseling, management, and potential treatment.

Spinocerebellar ataxia type 3 (SCA3) is caused by a pathogenic expansion of an unstable CAG trinucleotide repeat in exon 10 of the *ATXN3* gene.[6,7] The onset age of SCA3 is inversely related to the size of expansion of this CAG tract.[8] Most SCA3 cases occur in adults and symptoms typically manifest in the 30s.[9] Some patients with very long repeat expansions may exhibit symptoms at a very early age.[10,11] Homozygous CAG repeat expansions in *ATXN3* have also been reported in childhood or young-onset SCA3.[12,13] In addition to the predominant effect of CAG expansion size, other modifier loci are under investigation for their effects on SCA3-onset age.[14–17] The CAG triplet repeat lengths in various other genes associated with ataxia also seem to affect age of onset.[18]

The most consistent clinical manifestation of SCA3 is ataxia. Other features are reflective of progressive brainstem degeneration, and include dysfunction of oculomotor systems, pyramidal and extrapyramidal pathways, motor neurons, and peripheral nerves.[19] Movement disorders are not unusual in SCA3, and can include parkinsonism and frequently dystonia.[20–22]

Oromandibular dystonia and dysarthria have been noted in previous reports of people with SCA3; however, tongue dystonia has not, to our knowledge, been explicitly reported. In general, tongue dystonia is an uncommon clinical feature, and in most cases is due to tardive dyskinesia or it is idiopathic.[23,24] This symptom is often overlooked or misdiagnosed in clinical settings, resulting in low reported prevalence and limited

treatment options.[25] Childhood, or young-onset, tongue dystonia is even more unusual. Here we present a girl with childhood-onset SCA3 who presented with tongue dystonia in addition to ataxia.

Methods

Neurological evaluations were performed at a *pro bono* movement disorders clinic. The parents of the patient provided written informed consent for genetic testing, release of clinical history, and publication of video documentation of the movement disorder. Assent was also obtained from the patient. Due to the small population size of the Caribbean island where our patient and family reside (less than 100,000 residents), our IRB has requested that we do not reveal their precise nationality or geographic locations.

DNA was isolated from whole blood using Qiagen Puregene (Venlo, the Netherlands). The CAG repeat region of the *ATXN3* gene was analyzed by PCR amplification followed by capillary electrophoresis with internal standards as previously described.[26,27]

Case report

An 11-year-old Afro-Caribbean girl presented with a 1-year history of dysarthria, dysphagia, hand clumsiness, leg pain, and progressive gait disturbance with toe-walking, stumbling, and falling. Detailed family history was not available. There was no indication of cognitive dysfunction and she was attending classes appropriate for her age, apart from physical education. Plain radiography of hips and spine showed mild scoliosis. Routine laboratory investigations were noncontributory. Soon after her initial neurological examination, she had been given haloperidol, 2.5 mg at bedtime, for the tongue dystonia and other dystonic movements; this was discontinued after 3 days due to sedation and lack of clinical efficacy. Brain MRI scan, although limited by movement artifact, was grossly normal (Figure 1).

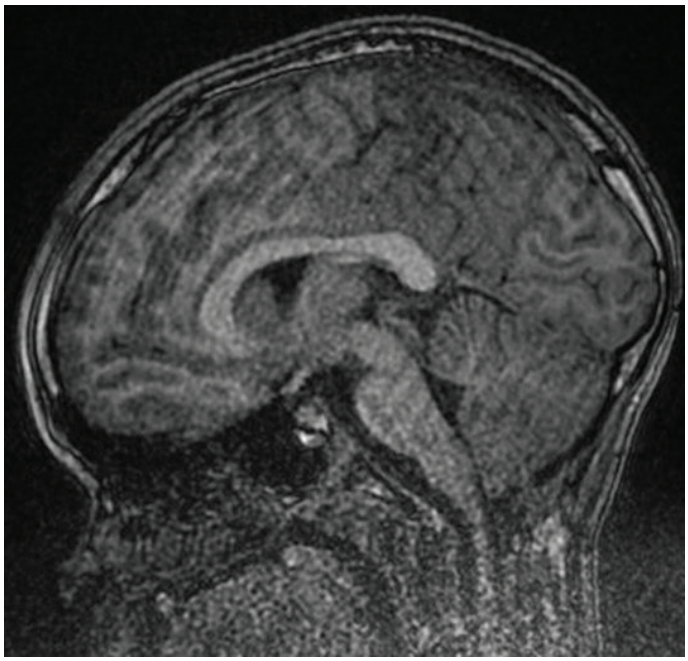

Figure 1. **Brain Imaging of Patient.** Cerebellum and other brain structures appear normal by MRI.

Neurological examination revealed moderate nystagmus on lateral gaze. Speech was dysarthric; her tongue was hypertrophic with involuntarily movements and abnormal posturing (Video). There was dystonic finger posturing, which increased with repetitive finger movements. On finger-to-nose testing there was a slight tremor and mild ataxia. She had dystonic posturing of both feet with plantar flexion and spontaneous extension of the big toes. She walked on her toes with a wide-based gait and was unable to perform tandem gait. She also had a positive Romberg's sign and reflexes were pathologically increased in all extremities. Genetic testing showed 84 and 22 CAG repeats of the alleles of the *ATXN3* gene. Management was focused upon dietary advice to manage dysphagia and weight loss. Nutritional supplementation with pureed foods, thick liquids, and high-calorie/high-protein drinks was recommended.

Discussion

Tongue dystonia is more likely to be seen in adults than in children; the most frequent etiology is tardive dyskinesia.[25] Although our patient had been given haloperidol, the tongue dystonia was clearly present before this treatment, so we do not believe that this was the cause. Tongue dystonia may be part of the clinical spectrum of rare neurodegenerative disorders such as chorea-acanthocytosis and McLeod syndrome.[28] In these disorders, it typically consists of tongue protrusion and can be precipitated by eating. In childhood or adolescence, tongue dystonia can be a feature of pantothenate kinase-associated neurodegeneration.[25] Tongue dystonia has also been reported as a symptom of other disorders, including Wilson's disease, Lesch-Nyhan syndrome, and stroke, although in many patients it appears to be idiopathic.[23–25,29–31]

Only a small number of childhood-onset cases of SCA3 are documented in the medical literature. As observed in our patient, normal brain MRI imaging has been reported even after symptom onset.[12,13] Features of childhood-onset SCA3 are similar to the adult onset form, but appear to be more rapidly progressive.[11] A range of movement disorders, including dystonia, has been reported in SCA3 and some of the other inherited ataxias,[21] leading to support for the hypothesis that the cerebellum might play a role in the generation of dystonia.[32] Dystonia has been reported as a feature in childhood-onset SCAs,[11,12] but to our knowledge, tongue dystonia in SCA3 has never been documented.

Treatment of tongue dystonia can be challenging. When the movements consist of tongue protrusion, injections of botulinum toxin into the genioglossus, which protrudes the tongue, have been reported to be effective.[33] When other muscles are involved, this treatment is not appropriate due to the risk of causing airway obstruction.[34] However, we were not able to offer the botulinum toxin option to our patient as we do not have the support of a full-time neurologist and the drug is not available in our community.[35,36] Treatment otherwise consists of the usual strategies employed in dystonia.[24]

Video segment **1. Features of the Neurological Examination.** In the initial segment, the patient has some dystonia of the fingers which increases with repetitive movements. There is slight clumsiness with pronation/supination of the hands. Finger-to-nose testing appears relatively normal apart from a mild end-point tremor. Speech appears mildly dysarthric. She has a normal range of eye movements with moderate nystagmus on smooth pursuit, especially on left lateral gaze. Her gait is mild-moderately wide-based with dystonic posturing of both feet with plantar flexion and extension of the big toes. She has difficulty performing tandem gait. On examination 1 year later, the spontaneous extension of her big toes is clearly seen, along with a Babinski sign. With arms extended there is dystonic posturing of her fingers. Her tongue is hypertrophic and demonstrates involuntarily movements with abnormal posturing; this is evident when her mouth is open and when she voluntarily moves the tongue from side to side.

Conclusion

Tongue dystonia is an extremely rare disorder in childhood, and to our knowledge, this finding has not been reported as a feature of SCA3. Here, we document tongue dystonia in a child who presented with manifestations of SCA3 at 10 years of age.

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