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Oromandibular and lingual dystonia associated with spinocerebellar ataxia type 8

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The spinocerebellar ataxias (SCAs) are a group of genetically heterogeneous neurodegenerative diseases characterized by limb ataxia with impaired balance, gait and eye movements. Either identified genetic mutations or suspected loci define the specific spinocerebellar ataxia (36 and counting) and each may have additional neurological features including cognitive impairment, seizure or pyramidal signs[1]. Spinocerebellar ataxia type 8 (SCA8) is a dominantly inherited mutation of chromosome 13q21 with a CTG•CAG expansion that is transcribed in both directions causing mutations in both ATXN8 and ATXN8OS (coding for Ataxin-8 and a noncoding sequence respectively). Spinocerebellar ataxia type 8 is an adult onset ataxia characterized by scanning dysarthria, gait and limb ataxia, hyperreflexia and variable eye movement abnormalities[2]. We describe here a patient with prominent oromandibular and lingual dystonia due to spinocerebellar ataxia type 8; these features have not been previously associated with spinocerebellar ataxia type 8. Oromandibular dystonia (OMD) often associated with lingual dystonia is a focal dystonia of either involuntary jaw opening or closure. Oromandibular dystonia especially with the presence of lingual dystonia can lead to dysarthria as well as chewing and swallowing problems. Patients with oromandibular dystonia may have a sensory trick such that placing an item in the mouth like a straw may reduce the involuntary movements thereby improving articulation, chewing or swallowing. Oromandibular dystonia can be a primary focal dystonia or secondary to disorders such as Wilson's disease, neuroacathocytosis, Huntington disease or brainstem and basal ganglia lesions[3].

A 66 year old woman with a twenty year history of gait instability and 18 year history of dysarthria was referred to the Movement Disorders Clinic after four years of markedly worsening speech. Examination revealed dysarthria with excessive jaw opening

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accompanied by tongue protrusions while speaking. Jaw opening and speech improved by placing a dowel rod in her mouth. She also had wide based unstable gait, limb ataxia, hyperreflexia and ocular overshoot with sustained horizontal nystagmus and fine upbeat nystagmus on upgaze. She was much more affected by the oromandibular dystonia than the ataxia (Video). Strength and cognitive function were normal. There was no family history of similar illness or other movement disorders. Investigations including CSF, autoimmune serologies, blood smear and vitamins B12 and E were normal. Brain MRI revealed prominent atrophy of the cerebellar vermis and hemispheres without any other lesion (Figure 1). Genetic testing demonstrated a mutation of ATXN8 with 106 CTG repeats on the abnormal allele and 24 on the normal allele (normal <50). Botulinum toxin A therapy to the bilateral lateral pterygoids, digastric and genioglossus muscles at low doses impaired swallowing while providing minimal benefit for the oromandibular dystonia and lingual dystonia.

The current vignette represents the first report of OMD and lingual dystonia in the context of spinocerebellar ataxia type 8. The prevalence of all dominantly inherited SCAs is 1 per 100,000 [2]. spinocerebellar ataxia type 8 is a rare disorder accounting for 2 – 5% for all autosomal dominant forms of inherited ataxia, with a prevalence of 2 – 5 per 10^7, while the prevalence of OMD is between 1 and 2.8 per 100,000 [4,5]. The probability of these rare diseases occurring together as independent events by chance in a randomly selected person is 2 – 14 per 10^{12}, however the probability of an individual with spinocerebellar ataxia type 8 also having oromandibular dystonia would be between 1 – 2.8 per 100,000.

The development of dystonia in ataxic syndromes with cerebellar degeneration may reflect either direct involvement of basal ganglia-cerebello-thalamo-cortical circuits, dysfunction of those of circuits due to functional connectivity with cerebellar circuits or direct involvement of cerebellar circuits if that may contribute to dystonia. Recent anatomical tract tracing studies have demonstrated the presence of disynaptic projections between the dentate nucleus of the cerebellum and the striatum and between the subthalamic nucleus and the cerebellar cortex[6]. In addition positron emission tomographic studies of hereditary dystonia patients have demonstrated striatal and cerebellar functional abnormalities[7]. Abnormalities in cerebello-thalamo-cortical connectivity may even differentiate disease phenotypes from manifesting carriers in hereditary dystonia[7]. Furthermore, neuropathologic examinations of SCA8 reveal not only cerebellar degeneration with Purkinje cell loss, and loss of pigmented neurons from the substantia nigra pars compacta and loss of inferior olivary neurons[8]. Cerebellar atrophy has also been demonstrated in multiple families with an inherited dystonia phenotype with minimal cerebellar ataxia[9]. Other forms of spinocerebellar ataxias including SCA3, SCA14 and SCA17 have cerebellar pathology and may include dystonic manifestations[1,10]. Examination of additional patients with spinocerebellar ataxia type 8 mutations will determine how commonly dystonia occurs in this disorder. Further, functional imaging in these patients may help to define the underlying connection between ataxic syndromes with cerebellar degeneration and dystonia. We propose that the ATXN8/ ATXN8OS mutations may be implicated in the development of focal dystonia with oromandibular and lingual involvement.

The presence of oromandibular dystonia and lingual dystonia in our patient expands the clinical phenotype of spinocerebellar ataxia type 8.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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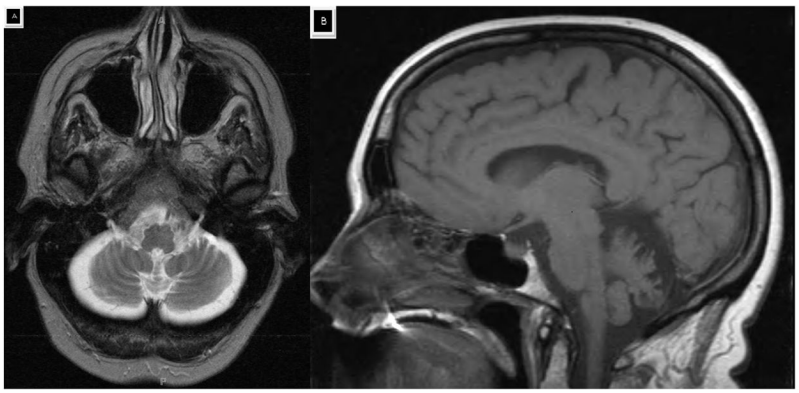

Figure 1.
Axial T2-weighted image (A) and sagittal T1-weighted image (B) demonstrating cerebellar atrophy.