

Spinocerebellar Ataxia Type 2 (Sca2) Associated with Retinal Pigmentary Degeneration

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Autosomal dominant spinocerebellar ataxias (SCAs) are a clinical and molecular heterogeneous group of neurodegenerative disorders caused by expansion of an unstable CAG (polyglutamine) trinucleotide repeat. The cloning of the genes responsible and the characterization of the mutation now permit a reliable diagnosis. A wide spectrum of clinical phenotypes has been observed within families with the same genotype, and common pathologic and phenotypic features can be produced by different genetic abnormalities. A new classification based on clinical and molecular findings has recently been proposed [1]. Specific ocular findings contribute to the characterization of different SCA phenotypes and retinal dystrophy is well known to be associated with the SCA7 phenotype [2]. We describe a family with dominant ataxia associated with a SCA2 mutation in which the index case presented with retinal degeneration.

The patient is a 48-year-old woman who presented at 28 years of age with night blindness. At the age of 32 years she began to have gait instability, speech difficulty and hearing loss. She was first admitted to our department at 36 years of age. Neurological examination showed severe gait ataxia, dysarthria, hypotonia and hyperreflexia.

An ocular motility study demonstrated a considerable alteration in the fast component, saccades were slow especially in the vertical plane, pursuit was moderately decreased, and the vestibular ocular reflex was intact. Typical retinitis pigmentosa, optic atrophy and macular changes were observed on funduscopy. Bright flash electroretinogram (ERG) in a full dark-adapted state was not recorded in either eye. A slight sensory neuropathy was evident on EMG. CT scan of the brain showed cerebellar atrophy. Because of the presence of other cases in the family, who had already died, with gait disturbances and not well-defined ocular impairment, hereditary dominant ataxia was diagnosed. Polymerase chain reaction analysis of the CAG repeats of the SCA7 gene was performed, but the alleles were found to be in the normal size range. The SCA2 mutation subsequently tested showed one expanded allele of 41 CAG. Clinical examination and molecular analysis were extended to the other family members: the only younger symptomatic brother and her 2 asymptomatic children. The 45-year-old brother had complained of mild gait instability since the age of 30 years. Neurological examination showed mild ataxia, dysarthria and slow saccades. MRI showed cerebellar atrophy. Slight sensory neuropathy was evident on EMG. Funduscopy was normal. ERG disclosed a slight a and b wave amplitude reduction. Molecular analysis revealed 41 CAG repeats in the SCA2 expanded allele. Neurological examination of both children (a 27-year old female and a 25-year-old male) showed hypotonia, mild instability of gait and slow saccades which was more evident in the son. Normal funduscopy associated with a regular retinal response on ERG and cerebellar atrophy on MRI were observed in both children. Molecular analysis revealed a SCA2 expanded allele of 38 CAG and 43 CAG repeats, respectively.

The ocular involvement in SCA2 is typically characterized by severe impairment of the fast eye component, and saccadic system is much more compromised [3]. Optic atrophy and retinal degeneration are not usually considered part of SCA2 phenotype [4]. The exact mechanism behind retinal dystrophies following SCAs mutations is still unknown, but polyglutamine-related toxicity has been proposed as cause of photoreceptors and ganglion cell damage in the SCA7 phenotype [5, 6]. The presence of retinal dystrophy, associated with hereditary ataxia was suggestive of an underlying common pathogenetic mechanism in the index case. Although evident, retinal pigmentary changes were not seen in the symptomatic brother, a decreased ERG response was suggestive of mild retinal involvement. Further examination should be necessary in all affected members. Babovic-Vuksanovic et al. [7] described retinitis pigmentosa associated with an extreme CAG repeat expansion in an infant with SCA2. ERG alterations have been reported in 6 patients with the SCA1 mutation without retinal changes [8], and optic atrophy has even been reported as an atypical finding in SCA1 patients [9]. In conclusion, our family suggests that: (1) although retinal degeneration is part of the SCA7 phenotype, other SCA mutations should be screened for when the SCA7 molecular investigation is negative, and (2) the clinical heterogeneity within families is often not only related to the CAG expansion size. As recently suggested by Subramony and Filla [10], the specific diagnosis of a SCA subtype on a clinical basis alone is often prone to error.

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