Spinocerebellar Ataxia Type 7 Sans Retinal Degeneration: A Phenotypic Variability

Sir,

Spinocerebellar ataxias (SCAs) are the hereditary neurodegenerative ataxia of autosomal dominant inheritance characterized by the progressive dysfunction of the cerebellum, basal ganglia, brain stem, cerebral cortex, spinal cord, and peripheral nerves.[1] With the advance in the human molecular genetics, SCA currently includes SCA1–36. The unique feature of SCA7 is the occurrence of pigmentary retinal degeneration along with degeneration of the cerebellum, brain stem, and the cervical spinal cord. Hereby, we report a middle-aged lady of African descent with SCA7 without retinal degeneration for 5 years.

A 45-year-old lady of African descent presented with the complaints of gait unsteadiness of 5-year duration. The unsteadiness was insidious in onset and slowly progressive over 5 years. She is able to ambulate on her own without support. There are no cognitive disturbance, visual disturbance, dysarthria, motor weakness, sensory symptoms, upper-limb incoordination, seizures, or myoclonus. None of the family members had similar complaints. On neurological examination, her higher mental functions were normal. Speech was normal. Fundus examination was normal. Cranial nerves, motor, and sensory examination were normal. There was mild incoordination of both upper limbs with prominent gait ataxia. Plantar responses were flexor. Complete hemogram, and renal, thyroid, and liver function tests were normal. Vitamin B12 and E and folate were normal. Brain magnetic resonance imaging (MRI) showed pontocerebellar atrophy [Figure 1]. Nerve conduction studies were normal. Visual-evoked potential and optical coherence tomography were normal. Genetic analysis for SCA1, -2, -3, -6, -7, and -12 was done. Pathological cytosine–adenine–guanine (CAG) repeat expansion (repeat number-43) in the SCA7 gene was detected.

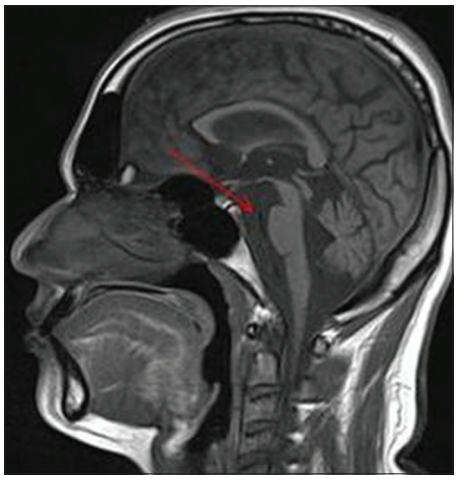

Figure 1: Brain magnetic resonance imaging sagittal T1 view showing pontocerebellar atrophy (red arrow)

Autosomal dominant cerebellar ataxia (ADCA) was classified into Type I, Type II, and Type III, based on the clinical phenotypes by Harding. ADCA Type I presents with both cerebellar and noncerebellar signs and includes SCA1–SCA4, SCA8, SCA10, SCA12-SCA23, SCA25, SCA27, SCA28, and SCA32–SCA36. ADCA Type II consists of syndromes in association with pigmentary retinopathies and includes SCA7. ADCA Type III includes mostly pure cerebellar syndromes and includes SCA5, SCA6, SCA11, SCA26, SCA30, and SCA31.[2] Now, ADCA has been replaced by SCA. SCA7 belongs to ADCA Type II phenotype. SCA7 is caused by the expansion of CAG trinucleotide repeats in exon 3 of *ATXN7* gene on the chromosome 3p12–21.1. The gene encodes for the protein ataxin-7. Ataxin-7 is an 892-amino acid nuclear protein of unknown function. The polyglutamine expansion in the N-terminal segment of ataxin-7 exerts a toxic effect on the cerebellar Purkinje cells. In the healthy individuals, CAG repeats range from 4 to 19. The repeat length of 28–33 is regarded as mutable normal alleles. Repeats of 34 and 35 are alleles with reduced penetrance. Repeats above 37 are the pathogenic full-penetrance alleles.[3] The prevalence of SCA7 has been reported to be the highest in South Africa and Scandinavian region. The age of onset can be early (<25 years) or late (>40 years) onset. The phenotypic abnormalities are dependent on the repeat lengths. Cerebellar ataxia is seen in all age onsets. Retinal degeneration precedes cerebellar ataxia with higher repeat length and in early onset and vice versa with lower repeat sizes and in late onset. This is due to early-onset toxicity in the retinal tissue than in cerebellum from higher length of a pathogenic polyglutamine stretch in ataxin-7 protein.

Our patient had pure cerebellar syndrome without retinal degeneration. The CAG repeat length was 43. A study by Faruq *et al*., on nine families with SCA7 reported a mean CAG repeats of 45 in patients who presented with initial ataxia followed by vision loss and a mean CAG repeats of 53 in patients who presented with initial vision loss followed by ataxia.[4] Kim *et al*. reported a 60-year-old man with SCA7 without retinal degeneration for 8 years. His repeat lengths were 42.[5] Similarly, our patient with CAG repeats of 43 had only ataxia without vision loss even at 5-year follow-up. This suggests phenotypic variability in SCA7.

Phenotypic variability occurs in different types of SCA including SCA7. The absence of retinal degeneration should

not preclude the diagnosis of SCA7 as it depends on the repeat length.

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Conflicts of interest

There are no conflicts of interest.

Rohan R. Mahale, Anish Mehta, Abhishek Miryala, Rangasetty Srinivasa

Department of Neurology, MS Ramaiah Medical College and Hospital, Bengaluru, Karnataka, India

Address for correspondence: Dr. Rohan R. Mahale, Department of Neurology, MS Ramaiah Medical College and Hospital, Bengaluru - 560 054, Karnataka, India.
E-mail: rohanmahale83@gmail.com

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