A Novel Missense Mutation in the Spectrin Beta Nonerythrocytic 2 Gene Likely Associated with Spinocerebellar Ataxia Type 5

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To the Editor: Spinocerebellar ataxia type 5 (SCA5) is a rare autosomal dominant spinocerebellar ataxia. Mutations in the spectrin beta nonerythrocytic 2 gene (*SPTBN2*) are known to cause SCA5, six of which have been reported, including three missense mutations and three deletion mutations.[1]

The patient was a 19-year-old Chinese girl presenting with progressive unsteady gait while running from the age of 11 years. She was not concerned by the symptoms until a fever at the age of 18 years made her imbalance more evident. Downbeat nystagmus on bilateral gaze that was not suppressed by visual fixation was noted. Her gait was wide. The heel-knee-shin test was inaccurate and unsteady. Bilateral rebound tests were positive. Brain magnetic resonance imaging (MRI) showed marked atrophy of the cerebellar hemisphere and vermis with no evidence of abnormalities in supratentorial and brainstem structures [Figure 1].

Based on gene sequencing, one likely candidate mutation was found in the *SPTBN2* gene, a heterozygous A > G transition at nucleotide position 833 (c. 833A > G) altering codon 278, substituting arginine for histidine (p.H278R). The p.H278R variant was not found in any database of normal sequence variation. Sorts intolerant from tolerant predicted that this mutation was damaging with a score of 0.001 where less than 0.05 is considered harmful.[2] Polymorphism phenotyping v2 predicted that it was possibly damaging with a score of 0.85. A value close to 1 is suggestive that the mutation is damaging.[3]

We presented a case of SCA5 with a missense mutation in the *SPTBN2* gene, which is a rare case reported worldwide. Her symptoms started at the age of eleven, which was earlier than the onset of symptoms in the German kindred, which ranged from 15 to 50 years (mean 32.8 ± 12.7 years, median 37.0 years).[4] The parents of our

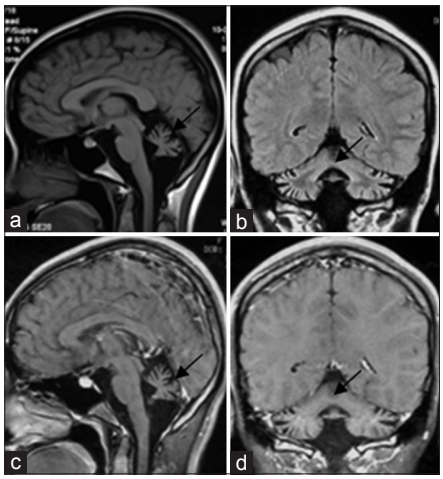

Figure 1: Brain MRIs: Atrophy of the cerebellar hemispheres sparing the brainstem and supratentorial structures is evident (a and c; arrows). Atrophy of the cerebellar vermis is apparent (b and d; arrows). MRI: Magnetic resonance imaging.

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patient were normal clinically and based on genetic tests. Without further functional studies, we cannot confirm whether it is truly pathogenic. However, the patient experiences clinically supported spinocerebellar ataxia. In clinically appropriate patients lacking previously reported mutations, a novel missense mutation (p.H278R) in *SPTBN2* should be considered.

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Conflicts of interest

There are no conflicts of interest.

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