that begins within 5 years of the onset of motor symptoms. Thus, the presence or absence of neuropsychiatric features is not a reliable way of discriminating neuroferritinopathy from Huntington’s disease, in which psychiatric symptoms usually precede involuntary movements.\(^7\) Our results also showed the defects in verbal fluency on ACE-R, and verbal learning and language with neuropsychometry were similar to other neurodegenerative movement disorders such as progressive supranuclear palsy and corticobasal degeneration,\(^8\) demonstrating the importance of an accurate assessment of motor and cognitive symptoms to reach a diagnosis. These findings redefine the phenotype of neuroferritinopathy and highlight the importance of assessing and monitoring nonmotor symptoms in patients following diagnosis.

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References


PRRT2 Gene Mutations in Familial and Sporadic Paroxysmal Kinesigenic Dyskinesia Cases

Paroxysmal kinesigenic dyskinesia (PKD) is a well-known paroxysmal movement disorder. It is often triggered by sudden voluntary movements and acts as brief attacks of dystonia or chorea movements. Some patients from families with PKD have additional neurologic disorders such as benign familial infantile convulsions (BFICs) or infantile convulsions and parkinsonism or choreothetosis. More than 60% of the patients with primary PKD have a family history of a similar disorder, and PKD is commonly transmitted via an autosomal-dominant mode of inheritance.\(^1\)

Recently, PRRT2 has been reported as the causative gene of PKD.\(^2–5\) Results for determination of the frequency of PRRT2 mutations in patients with PKD have supported the notion that PRRT2 mutations are responsible for most familial and some sporadic PKD cases.\(^5,7\) In this study, we screened for PRRT2 mutations in a cohort of PKD patients from China.

We sequenced all the exons and flanking introns of the PRRT2 gene of 8 familial PKD patients from 3 families and 6 sporadic PKD patients. The mean onset age for our cohort was 14.5±3.4 years. The proband of family B presented with BFICs, whereas his father had PKD; all the other patients had pure PKD.

We detected a truncating mutation, c.649dupC (p.Arg217fsX7), in all the familial PKD cases and in 2 of the 6 sporadic cases. We also identified 1 heterozygous synonymous mutation, c.1011C/T (p.Gly337Gly), in a sporadic case. Further testing for mutations in both parents of the 3 PRRT2 mutation–positive patients with sporadic PKD showed that the c.649dupC and c.1011C/T mutations occurred de novo. No PRRT2 gene mutations were identified in the remaining 3 patients with sporadic PKD, and neither of the 2 mutations was detected in any of the 198 healthy controls. Haplotype analysis of the 3 families carrying the c.649dupC mutation revealed 3 different haplotypes (Fig. 1).

The PRRT2 protein has 2 transmembrane domains. Because PKD is considered an ionic channelopathy, PRRT2 may regulate key properties of ion channels.\(^4\) In this study, we found PRRT2 mutations in a majority of the familial and sporadic PKD cases (11 of 14). Similar to previous studies,\(^2–5\) our study showed that the c.649dupC (p.R217Fs*7) mutation was the most frequent mutation in familial PKD cases. Further, cosegregation analysis for sporadic PKD cases indicated that this mutation might have occurred in a de novo manner, as also suggested by previous results.\(^6,7\)

The synonymous c.1011C/T (p.G337G) mutation was detected in 1 sporadic PKD case and was proved to be de novo. This mutation was also detected in 1 sporadic PKD case in a previous study.\(^6\) Because this mutation is located very close to the exon–intron junction, it may affect splicing.
and result in haploinsufficiency. However, more evidence is required to elucidate the pathogenicity of this mutation. In conclusion, along with previous studies, this study further supports the idea that \textit{PRRT2} is the main causative gene for PKD in Chinese people. Further functional studies are needed to understand the underlying pathogenic mechanisms associated with \textit{PRRT2} mutations.

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