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Case Report

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Treatment of Bi-Allelic PRRT-2 Mutation Associated Ataxia and Paroxysmal Dyskinesia

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Abstract

PRRT2 is located on chromosome 16p11.2 and is a transmembrane protein highly expressed in the CNS that has been identified to play a role in epilepsy, movement disorders and hemiplegic migraines. Specifically, variants are identified in families with paroxysmal kinesigenic dyskinesia. Here, we present a patient with a biallelic mutation in PRRT2 leading to a more severe form of the condition who presented with epilepsy, episodic ataxia and dyskinesia in childhood. We demonstrate how oxcarbazepine can reduce the symptoms and allow the child to live without these movement disorders.

Keywords

PRRT2, Paroxysmal kinesigenic dyskinesia, Oxcarbazepine

Case Presentation

A female infant who was born at 34 weeks gestation was first noted to have seizures at 4 months of age. Epilepsy resolved by 6 months of age with phenytoin and levetiracetam treatment which was then transitioned to topiramate. Her seizures were described as generalized tonic-clonic activity that lasted up to 3 minutes.

At 22 months of age, the patient presented with episodic ataxia and episodic dyskinesia. The ataxia was characterized as a loss of balance after waking up in the morning and lasting for 2-3 weeks along with episodes of emesis. She had a broad-based stance when attempting to walk using support (Figure 1). On the other hand, the dyskinesia episodes were 5-15 minutes and occurred several times throughout the day. Her paroxysms consisted of facial spasms and involuntary tongue movements (Figure 2). The orobuccal movements were at times accompanied with dyskinetic movements of the left arm (Figure 3). These movements occurred at rest and also when the patient was engaged with playing or eating. A genetic panel revealed biallelic variants in PRRT2. Although topiramate did not discontinue the episodes, the addition of oxcarbazepine was beneficial. Use of oxcarbazepine alleviated the dyskinesia symptoms; however, the patient was at first vomiting the medication and was given ondansetron to combat this. After receiving oxcarbazepine, the balance impairment was no longer present and she was able to walk and run without support. Moreover, the dyskinetic facial and arm movements had ceased as well (Figure 4 and Figure 5). She is able to live as a healthy child without the paroxysms of ataxia and dyskinesia.

Figure 1: Difficulty maintaining balance without support and a broad-based stance when walking are noted.

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Figure 2: Frequent involuntary orobuccal and jaw movements are noted.

Figure 3: Frequent involuntary orobuccal movements and dyskinetic movements of the left arm and hand are noted.

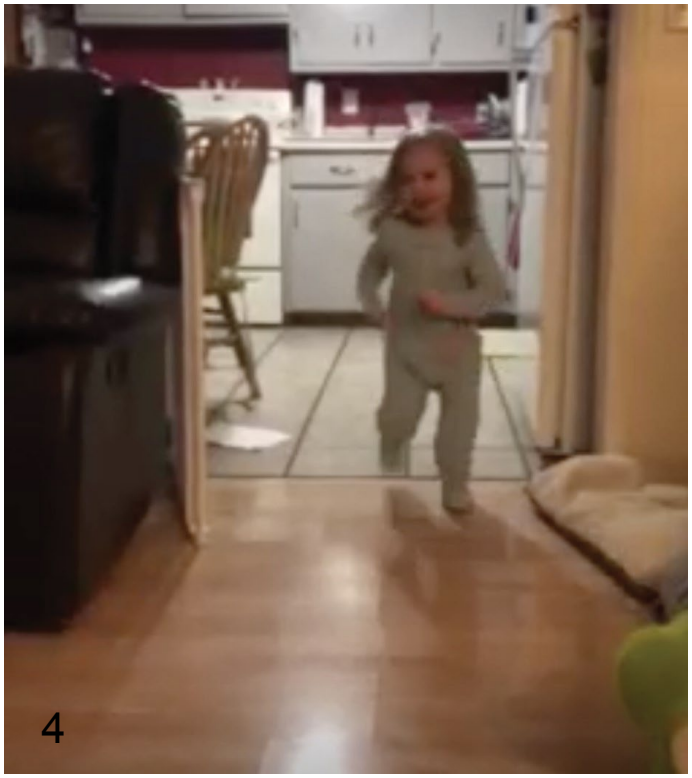

Figure 4 and Figure 5: Obtained on OXC. Balance and movement are noted to be typical. Dyskinetic movements of the arms are not seen. Orobuccal movements are no longer present.

Discussion

PRRT-2 is a transmembrane protein that interacts with SNAP25 and plays a role in exocytosis in neurons [1]. It is primarily expressed in the cerebral cortex, hippocampus, basal ganglia, and cerebellum [2]. Mutations in the PRRT-2 gene are to be shown to present with paroxysmal movement disorders including paroxysmal dyskinesia and episodic ataxia which primarily begin in childhood and adolescence [3]. Episodic ataxia usually lasts from a few seconds to several days and also presents with vertigo, nausea, tremor, or headache. In contrast, paroxysmal kinesigenic dyskinesia lasts a few seconds to a minute is described as dystonia with no change in consciousness [4]. Paroxysmal kinesigenic dyskinesia consists of dystonia, chorea and ballism and is found to be triggered by sudden movements [2]. Upon imaging, the MRI shows no abnormalities and furthermore, there are no morphological changes in autopsy results [4].

Bi-allelic mutations of PRRT2 are associated with more severe disease presentation along with a longer duration of episodes. Moreover, the standard treatment of low-dose anti- seizure medication that are used for paroxysmal kinesigenic dyskinesia may not work because patients with the homozygous mutation have treatment resistance [2,5]. One specific patient with bi-allelic variation in PRRT-2 presented with several episodes of myoclonus and episodic ataxia after minor head trauma. She also had focal cortical dysplasia in the parietal lobe on MRI [6]. Here, we present a case of a patient with bi-allelic pathogenic variants in PRRT2 and demonstrate how her dyskinesia and ataxia improved after treatment with oxcarbazepine.

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