A case of a ADPRHL2 Mutation; Stress-induced childhood-onset neurodegeneration with variable ataxia and seizures

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Introduction

ADPRHL2 is thought to function in the pathway of ADP ribosylation, which is a reversible posttranslational modification used to regulate key cellular processes such as transcription, DNA repair, translation, and apoptosis. Loss-of-function mutations in the ADPRHL2 gene result Neurodegeneration with Developmental Delay, Ataxia, and Axonal Neuropathy. Here we report of an individual diagnosed Neurodegeneration with Developmental Delay, Ataxia, and Axonal Neuropathy.

Case Report

14-year-old girl was consulted from the orthopedics clinic to pediatric neurology clinic due to preoperative consultation before scoliosis surgery. Her prenatal and natal history was unremarkable and was born to healthy consanguineous parents. Her early development was normal. She was diagnosed epilepsy and seizures were controlled with valproate therapy. She had moderate mental retardation. Her neurological exam revealed distal weakness in upper and lower extremities, pes cavus and hammer toes were noted. EMG was found to be consistent with axonal polyneuropathy. Cranial magnetic resonance imaging and electroencephalograph was normal. Whole exome sequencing (WES) study was done and a mutation in the ADPRHL2 c.235A>C gene was detected.

Discussion

Pediatric neurodegenerative diseases are progressive conditions typically associated with severe disability or even death in early infancy. Patients with ADPRHL2 mutation had stress-induced episodes leading neurodegeneration which were triggered by several factors such as febrile infections, surgery, minor head trauma, and even by emotional stress. In this individual scoliosis surgery was planned but after the diagnose of ADPRLH2 mutation surgery plan was cancelled.

In animal models, inhibition of poly (ADP-ribosylation) leads to improved neuronal regeneration after axonal injury. The prevention of excessive PAR accumulation with its detrimental downstream effects culminating in cell death could evolve as a potential therapeutic target in selected neurodegenerative disease entities in humans. Selective PARP1 inhibitors can be good candidates for slowing down the progression of neurodegeneration in patients with ADPRHL2 disorders. The possibility of a potential treatment with PARP1 inhibitors accentuates the importance of early diagnosis in the patients and prevention of stress induced neurodegeneration.

Key words: ADPRHL2, Developmental Delay, Scoliosis

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