Case Report

A novel mutation in the GRIN2A gene associated with autism spectrum disorder

Oguz Guvenmez¹, Serkan Gunes², Muhammed Furkan Kanca³

¹Independent Researcher, Adana, Turkey
²Department of Child and Adolescent Psychiatry, Hatay State Hospital, Hatay, Turkey
³Cukurova University Medical Faculty, Adana, Turkey

Received: 01 December 2019 / Accepted: 16 December 2019

Abstract

Autism spectrum disorders (ASD) are neurodevelopmental disorders with multiple symptoms including social communication/interaction deficits and restrictive/repetitive behaviors. Several genetic mutations have been reported to be associated with ASD. Here, we present a case report of 4-year-old boy with a novel mutation in the GRIN2A gene and ASD.

Keywords: autism, gene, mutation

Introduction

Autism spectrum disorders (ASD) are neuropsychiatric developmental disorders characterized by impairments of social communication and interaction and restrictive/repetitive behaviors [1]. Genetic mutations, including GRIN2A located on chromosome 16p, are reported as a potential cause of ASD. The GRIN2A gene encodes Glun2A which is a transmembrane ligand-gated ion channel and a subunit of the N-methyl D-aspartate receptor (NMDAR) [2,3]. Glun2A is responsible for neural development, synaptic plasticity, learning and memory. The association between GRIN2A and Huntington disease, Parkinson disease, epilepsy, autism and schizophrenia has been reported [2]. In this paper, a 4-year-old boy with a novel mutation in the GRIN2A gene and ASD will be discussed.

Case

A 4-year-old boy was consulted from the pediatric neurology clinic for the complaints of delayed speech and social interaction deficits. Prenatal, natal and postnatal histories were unremarkable. At 8 months of age, seizures consisting of tonic/clonic movements of the extremities began. He was started levetiracetam 50 mg/kg and clonazepam 1 mg/kg. On clinical examination, no dysmorphic features were observed. He had no eye contact and joint attention. Impairments in social interaction and verbal and non-verbal communication were evident. He also showed stereotyped interests and behaviors.

Address for Correspondence: Serkan Gunes, Department of Child and Adolescent Psychiatry, Hatay State Hospital, Hatay, Turkey.
E-mail: dr_sgunes@hotmail.com

DOI: 10.5455/im.302645125
This is an Open Access article under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/)
Denver-II test showed delays in personal/social and language developmental areas. Childhood autism rating scale total score was 43. The ophthalmic evaluation and brainstem evoked response audiometry test were normal. Common blood and biochemical tests, metabolic parameters (e.g. ammonia, lactate, tandem-mass, urine organic acid), chromosomal analysis, microarray results and brain magnetic resonance imaging were also normal. Whole-exome sequencing showed a heterozygote NM_001134407.3:C.3299A>G (p.E1100G) (p.Glu1100Gly) mutation in the GRIN2A gene. In silico analysis was made with SIFT, Mutation Taster and Provean programs and variant was predicted as pathogenic. The patient was diagnosed with ASD, according to the DSM-5, accompanied with a novel mutation in the GRIN2A gene.

Discussion
NMDARs have been reported to have different roles in synaptic plasticity and excitotoxicity. In this context, the dysfunction of NMDA signaling has emerged in a wide variety of neurological and neurodevelopmental disorders [4]. In ASD, possible causative mutations in NMDAR genes have been suggested [5–7] and ASD in animal models are related to NMDA abnormalities [4]. Furthermore, disturbance in the balance between excitation and inhibition is a widely recommended disease mechanism for ASD [8]. In a study, memantine which is an NMDAR antagonist has been shown to improve ASD symptoms [9]. Advanced techniques in molecular genetics can let the recognition of responsible genes in children with neurodevelopmental disorders [2]. Genes encoding NMDAR subtypes were first identified in 1993 [10]. Endele et al reported cases of developmental disorders, learning disabilities and seizures with heterozygous mutations in the area encoding the GRIN2A gene [11]. Further studies of GRIN2A mutations have often revealed intellectual disability and intractable epilepsy. Venkateswaran et al reported a 4-year-old girl with de novo GRIN2A mutation, severe global developmental delay, visual defect and refractory seizures [3]. In a recent case presentation, Sarigecili et al reported a heterozygote NM_001134407.2:C.3299A>G (p.Glu1100Gly) mutation in the GRIN2A gene, which has not been reported previously, in a 2.5-year-old boy with global developmental delay, hypotonia, nystagmus and refractory seizures [2]. However, the patient was not diagnosed with ASD. Our case did not have motor deficits or nystagmus and showed predominantly social interaction and communication problems. To our knowledge, this is the first report that suggests the novel mutation in GRIN2A gene may be associated with ASD.

In conclusion, this case study illustrates the clinical presentation of GRIN2A mutations and the role of a novel mutation in the GRIN2A gene in ASD. Further studies should be performed to clarify the association.

Conflict of interest
The authors declare no conflict of interest.

Funding
No financial support was provided for this study by any sponsoring organization or any for-profit product companies.

References