http://www.medscidiscovery.com

OPEN ACCESS JOURNAL ISSN: 2148-6832

MSD Medical Science and Discovery
2019; 6(9):221-3

Case Report Article Doi: 10.36472/msd.v6i9.302

Homozygous SCN2A gene mutation causing early infantile epileptic encephalopathy: The second case in literature

Hale Önder Yılmaz [1]*

Abstract

Objective: Early infantile epileptic encephalopathy type11 (EIEE) generally known as an autosomal dominant inherited disease caused by the voltage-gated sodium channel neuronal type 2 alpha subunit (Navα1.2) encoded by the SCN2A gene mutations. The clinic of the disease is variable. Herein we report the second case with a homozygous missense mutation of the SCN2A gene (c.1588 G>T).

Material and methods: NGS gene panel including the SCN2A gene from genomic DNA extracted from peripheral blood using a commercially available kit and quantified using standard methods. Illumina miseq analysis platform was used for this purpose, we performed analysis of coding regions and exon-intron boundaries and the data was analyzed by IGV.

Results: The results confirmed by sanger sequencing show us an SCN2A (NM_001040142) c.1588 G>T homozygote mutation.

Conclusion: This shows us more clinical and molecular studies need for SCN2A associated disease pathogenesis

Keywords: SCN2A, Heretozygote mutation, infantile epilepsy

Introduction

The benign familial infantile seizures type 3 (BFIS3; OMIM: 607745) is the most common clinical presentation of SCN2A defect which is an autosomal dominant neurological disorder. In this syndrome, apnea, cyanosis, and cluster seizures that occur over one or several days can be seen(1). These seizures usually disappeared by the end of the 1 year of life but some patients continue to have seizures through adulthood without neurological abnormality(2, 3). Early infantile epileptic encephalopathy type 11 (EIEE11; OMIM: 61372) is another phenotype associated with SCN2A pathogenesis. This syndrome compromise more severe neurological manifestation than BFIS3 but has a similar inheritance pattern, autosomal dominant. Early-onset of infantile refractory seizures cause an eventual delay in intellectual and motor development in patients with EIEE(4, 5). Patients may firstly present neonatal hypotonia that proceeds to partial and generalized refractory tonic-clonic seizures. Additionally, dysphagia, dysarthria, excessive daytime sleepiness, disturbed visual contact, paralysis can be seen among patients(5-7) Although brain MRI findings of these patients can vary, brain atrophy commonly reported(4, 7, 8)

Case

A five-year-old case came to our clinic because of refractory seizures. She was born as the fifth child of a first cousin parent (Mother age: 37, father age: 40) with an uneventful pregnancy(Figure 1). At birth, she was 50 cm (10th-25th centile), 3.3 kg (10th-25th centile), head circumference (HC) of 35 cm (10th-25th centile). After birth, she had stayed in an intensive care unit because of respiratory distress in a period of 12 days. Her head-neck control started during the third month of her life. When she was six months old, her afebrile myoclonic seizures started.

On physical examination, She was 94 cm(97th centile) and 15 kg (10th-25th centile). Her head circumstance was 50 cm. She has a flat nose, upslanting palpebral fissure, high palate, bilateral epicanthal folds, rotatuar nystagmus (Figure 2). Pes equinovarus, joint laxity, negative Babinski and clonus reflexes are the other findings (could not taken a photo because of agitation of the case). She was hypotonic, she can not walk and speak. Her mental cooperation was negative. Her eye and hearing examination was normal. In laboratory findings there in not any abnormalities and her metabolic scannings were normal. Her abdominal USG result was normal.

Received 26-08-2019 **Accepted** 24-09-2019 **Available Online** 25-09-2019 **Published** 30-09-2019
1 Kahramanmaraş Necip Fazıl City Hospital, Dept of Medical Genetics, Kahramanmaraş, TR
*** Corresponding Author:** Hale Önder Yılmaz **E-mail:** drhaleonder@hotmail.com **Phone:** +90 (344) 228 28 00

http://dx.doi.org/10.36472/msd.v6i9.302

Her MR result showed mild vermis hypoplasia, corpus callosum hypoplasia and right temporal region cortical thickness.

Her peripheral blood chromosome analysis result was normal also the array-CGH result was normal. Because of her clinical presentation, we studied an early infantile epilepsy custom NGS gene panel including the SCN2A gene from genomic DNA extracted from peripheral blood using a commercially available kit and quantified using standard methods.

Illumina miseq analysis platform was used for this purpose, we performed analysis of coding regions and exon-intron boundaries and the data was analyzed by IGV.

The results confirmed by sanger sequencing show us an SCN2A (NM_001040142) c.1588 G>T homozygote mutation. After that, we performed carrier analysis to parents. Both parents were carriers in terms of SCN2A c.1588 G>T. This change has not been shown before

Discussion

We describe the second documented homozygous SCN2A mutation causing EIEE in autosomal recessive inheritance, the first case was published three months before(9). All previous patients were reported having a heterozygous SCN2A variant in either dominant or de novo fashion. The variant was evaluated by MutationTaster and Varsome databases as pathogenic. Epileptic phenotypes seen in patients with de novo or dominant heterozygous SCN2A gene mutations so, it is not surprising that homozygous SCN2A mutation carriers also have similar epileptic phenotype. There are two main facts that should take into account by clinicians in terms of SCN2A mutations after our case. First, SCN2A gene defects in any patient presenting with seizures without family history may be an indicator of an autosomal recessive or autosomal dominant pattern. Another fact is that autosomal recessive patterns may lead to more severe clinical presentation, such as early neonatal epileptic encephalopathy rather than other phenotypes (ataxia or autism) in heterozygous mutation carriers.

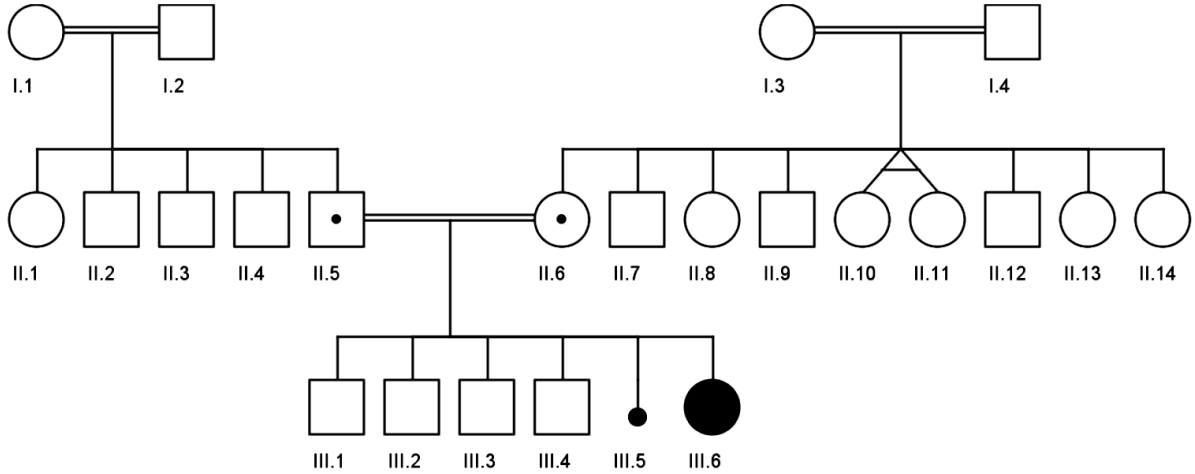

Figure 1: Pedigree of the family (III.6 is the case, II.6 is the mother and II.5 is the father)

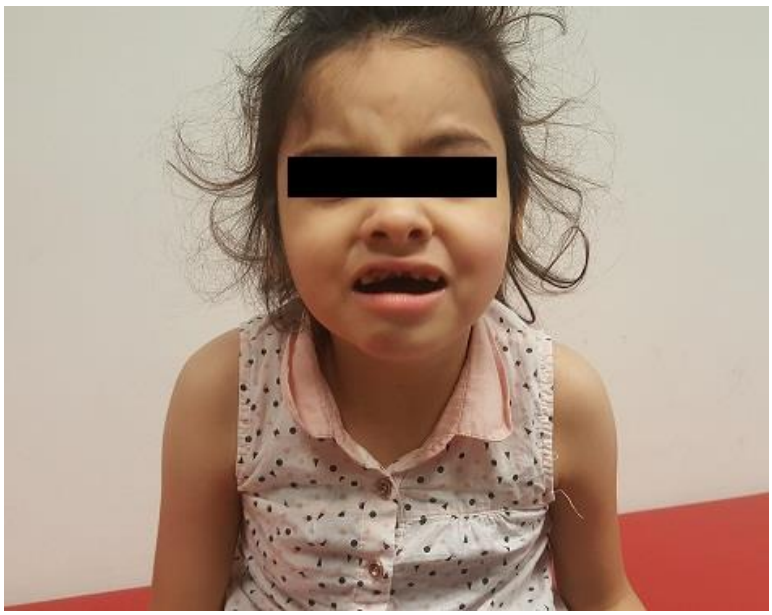

Figure 2: The case.

Conclusion

Being the second case described in her family and literature is the main limitation of the current study. Therefore, further homozygous reported cases with similar phenotypes are necessary to confirm such a conclusion. We report the second case of a homozygous SCN2A gene mutation in a female patient from Turkey. In addition, we describe a novel mutation that can help to increase the mutational spectrum of SCN2A-associated disease pathogenesis. We hope our findings will open new insights for the molecular and inheritance spectrum of SCN2A gene defects.

Acknowledgments: None

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: HÖY; Research concept and design, Patient examinations, Genetic Analyzes, Research the literature, preparation of the article **HÖY;** Revision of the article.

References

1. Shevell MI, Sinclair D, Metrakos K. Benign familial neonatal seizures: clinical and electroencephalographic characteristics. Pediatric neurology. 1986;2(5):272-5.

2. Berkovic SF, Heron SE, Giordano L, Marini C, Guerrini R, Kaplan RE, et al. Benign familial neonatal - infantile seizures: characterization of a new sodium channelopathy. Annals of neurology. 2004;55(4):550-7.

3. Kaplan RE, Lacey DJ, Opitz JM. Benign familial neonatal - infantile seizures. American journal of medical genetics. 1983;16(4):595-9.

4. Kamiya K, Kaneda M, Sugawara T, Mazaki E, Okamura N, Montal M, et al. A nonsense mutation of the sodium channel gene SCN2A in a patient with intractable epilepsy and mental decline. Journal of Neuroscience. 2004;24(11):2690-8.

5. Ogiwara I, Ito K, Sawaishi Y, Osaka H, Mazaki E, Inoue I, et al. De novo mutations of voltage-gated sodium channel αII gene SCN2A in intractable epilepsies. Neurology. 2009;73(13):1046-53.

6. Liao Y, Anttonen A-K, Liukkonen E, Gaily E, Maljevic S, Schubert S, et al. SCN2A mutation associated with neonatal epilepsy, late-onset episodic ataxia, myoclonus, and pain. Neurology. 2010;75(16):1454-8.

7. Hackenberg A, Baumer A, Sticht H, Schmitt B, Kroell-Seger J, Wille D, et al. Infantile epileptic encephalopathy, transient choreoathetotic movements, and hypersomnia due to a De Novo missense mutation in the SCN2A gene. Neuropediatrics. 2014;45(04):261-4.

8. Baasch AL, Hüning I, Gilissen C, Klepper J, Veltman JA, Gillessen - Kaesbach G, et al. Exome sequencing identifies a de novo SCN 2 A mutation in a patient with intractable seizures, severe intellectual disability, optic atrophy, muscular hypotonia, and brain abnormalities. Epilepsia. 2014;55(4):e25-e9.

9. AlSaif S, Umair M, Alfadhel M. Biallelic SCN2A Gene Mutation Causing Early Infantile Epileptic Encephalopathy: Case Report and Review. Journal of central nervous system disease. 2019;11:1179573519849938.

Copyright © 2019 The Author(s); This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), (CC BY NC) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. International journal of Medical Science and Discovery.