PHENOTYPICAL VARIABILITY OF GNAO1 GENE MUTATIONS

Schteinschnaider A, Alamo R, Chinigioli M, Bracco F, Villanueva M.
Neuropediatric Department, FLENI. Buenos Aires, Argentina.

419

18TH ICNC 2024 Footprints to the future
INTERNATIONAL CHILD NEUROLOGY CONGRESS
Cape Town, South Africa I May 6-10, 2024

INTRODUCTION

The GNAO1 gene encodes the α subunit of G protein-coupled receptors. Its mutation causes a variable spectrum that includes early-onset epileptic encephalopathy, neurodevelopmental delay, and movement disorder.
Genetic functional studies suggest that gain of function is related to a movement disorder phenotype and loss of function is more related to the epileptic phenotype.

OBJECTIVES

To describe 5 pediatric patients with GNAO1 mutations.

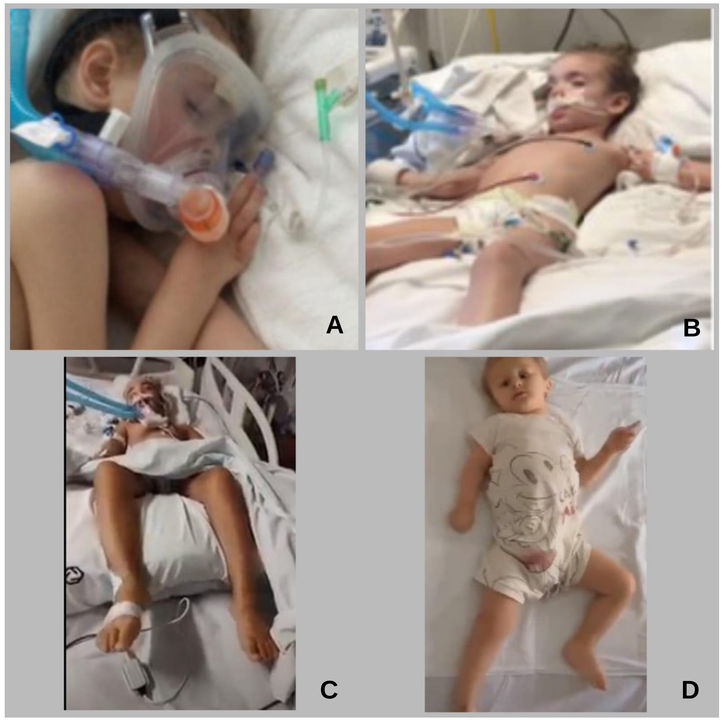
MATERIALS AND METHODS

Phenotype 1: 4 patients, 2 girls and 2 boys, between 16 months and 12 years, who start early with hypotonia and evolve with global developmental delay, without language development but with very good interaction. They added a progressive orolingual dyskinesia and choreic movements. MRI, neurometabolic studies and neurotransmitters were normal. Two received pharmacological treatment while the other two required DBS for refractory choreic status between 6 and 8 years of age. All 4 have molecular confirmation of a pathogenic mutation in the GNA01 gene.

Phenotype 2: A 2 years old boy, with neonatal-onset epileptic encephalopathy. He evolved with global developmental delay, subtle choreic movements and orolingual dyskinesia. Brain MRI and metabolic laboratories were normal. Mutation of the GNAO1 gene is confirmed. He is on plan to start ketogenic therapy.

Patient	1	2	3	4	5
Current age	13 years 5 months	9 years 7 months	2 years 10 months	2 years 10 months	2 years 1 month
Age of onset of symptoms	5 months	3 months	5 months	6 months	7 days
Mutation	c.709 G>A (p.Glu237Lys) Heterozygosis Missense	c.748 C>T (p.Leu250Phe) Heterozygosis Missense	c.709 G>A (p.Glu237Lys) Heterozygosis Missense	c.709 G>A (p.Glu237Lys) Heterozygosis Missense	c.607 G>A (p.Gly203Arg) Heterozygosis Missense
Symptoms	Hypotonia Developmental delay Abnormal movements Language delay	Hypotonia Developmental delay Abnormal movements Language delay	Hypotonia Developmental delay Abnormal movements Language delay	Hypotonia Developmental delay	Seizures Hypotonia Developmental delay Abnormal movements
Current treatment	DBS	Tetrabenazina DBS			AVP TPM Trihexifenidilo

Table 1. Patient summary



Figures A and B Photographs belonging to patient 1.**Figure C** Photographs belonging to patient 2.**Figure D** Photographs belonging to patient 5

CONCLUSIONS

There are two clinical phenotypes with numerous overlaps. In the Epileptic Encephalopathy phenotype there are few guiding elements that allow us to suspect this mutation over other etiologies. But the phenotype of Abnormal Movements is very characteristic, allowing early suspicion and timely intervention with DBS.

Contact: angeles@fleni.org.ar