PCGF2 Related Syndrome

https://pubmed.ncbi.nlm.nih.gov/36408521/

Objective:

To analyze the genotypes and phenotypes of mosaic male patients with

PCDH19

-related epilepsy (

PCDH19

-RE) and explore the correlation between genotype, variant allele frequency (VAF), and phenotypic severity.

Methods:

Clinical data and peripheral blood samples of 11 male mosaic patients were collected and analyzed in our study. The VAF of the

PCDH19

gene from peripheral blood was quantified using amplicon-based deep sequencing. Additional 20

mosaic male patients with

PCDH19

-RE were collected from the published literature, with 10 patients whose VAFs of the

PCDH19

gene were available for analytic purposes.

Results:

In our cohort of 11 patients, 10 variants were identified, and four were novel. The VAF of the

PCDH19

gene from peripheral blood ranged from 27 to 90%. The median seizure onset age was 6 months (range: 4-9 months). Clinical manifestations included cluster seizures (100%), fever sensitivity (73%), focal seizures (91%), developmental delay/intellectual disability (DD/ID, 82%), and autistic features (45%). Thirty-one mosaic male patients collected from our cohort and the literature developed seizures mostly (87%) within one year of age. Variant types included missense variants (42%), truncating variants (52%), splice variants (3%), and whole

PCDH19

deletion (3%). Among 21 patients with a definite VAF from our cohort and the literature, nine had a low VAF (≤ 50%) and 12 had a high VAF (> 50%). Seventy-five percent of variants from the high VAF group were missense, whereas 89% of those from the low VAF group were truncations.

The median seizure onset age was 6 months in the low VAF group and 9 months in the high VAF group ($p = 0.018$). Forty-four percent (4/9) of patients from the low VAF group achieved seizure-free for ≥1 year, whereas none of the 12 patients from the high VAF group did ($p = 0.021$). DD/ID was present in 83% (10/12) of the high VAF group and 56% (5/9) of the low VAF group ($p = 0.331$).

Conclusion:

The predominant variant types were truncating and missense variants. Missense variants tended to have higher VAFs. Patients with a high VAF were more likely to have a more severe epileptic phenotype. Our findings shed light on the phenotypic implications of VAF in mosaic males with *PCDH19*-RE.