E-poster ID:- ePBGC50

Variable Expressivity of *CPLANE1* Variations: A Genotype-Phenotype Correlation in Joubert Syndrome Versus Orofaciodigital Syndrome Type VI

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INTRODUCTION

Joubert Syndrome (JS) and Orofaciodigital Syndrome type VI (OFD6) are rare autosomal-recessive disorders caused by variations in the *CPLANE1* gene. Both conditions present distinct clinical manifestations but share overlapping features due to variable expressivity. This case study investigates the genotype-phenotype correlation in an 18-month-old female with JS, born to consanguineous parents, presenting significant developmental delays, dysmorphic features, and neurological abnormalities. Whole Exome Sequencing (WES) identified a homozygous likely pathogenic variant in the *CPLANE1* gene, confirming the diagnosis

OBJECTIVE

To elucidate the genotype-phenotype correlation in an 18-month-old female diagnosed with Joubert Syndrome (JS) and examine the clinical implications of *CPLANE1* gene variations, highlighting the need for genetic counseling and multidisciplinary management.

CASE PRESENTATION

Proband, an 18-month-old female, born to consanguineous parents, presented with delayed developmental milestones, such as delayed neck holding and sitting with support, unable to pincer grasp, indicating potential developmental delays.

Clinical observations revealed dysmorphic features including dolichocephaly and everted lower lip, which is indicative of underlying genetic abnormalities

Neurological findings, including hypotonia and abnormal MRI brain results showing bilateral basal ganglia hyperintensity, dilated ventricles, and prominent cerebellar peduncles, further complicated her condition, highlighting the multi-systemic nature of her condition.

Other findings included lower respiratory tract infection, Ophthalmological features of deep-set eyes, strabismus, poor visual contact with visual fixation, can recognize her mother, has stranger anxiety with drooling. Blood test- slightly elevated serum potassium (5.29), reduced serum creatinine (0.29), increased lymphocytes

and decreased neutrophils, increased RBC count, PCV,

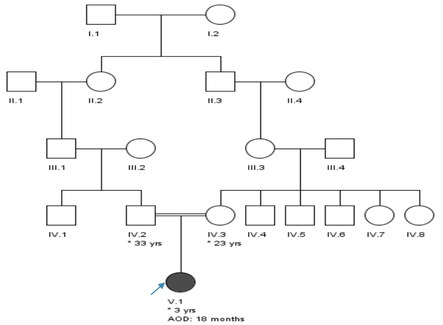
and RDW, decreased MCV and MCH, increased serum

T3 levels, and decreased Vitamin D.

Family History: Proband is born to a fourth-degree

consanguineous parents and there was no significant

family history of similar conditions.



RESULTS

•Whole Exome Sequencing (WES): Homozygous likely pathogenic variant in exon 35 of *CPLANE1* gene (c.7399dupA, p. Arg2467LysfsTer7)
•Parental Testing: Heterozygous carriers of the same variant
•The identification of the genetic variant provides insights into the underlying cause of the child's condition, guiding the approach to medical management and family planning.

CONCLUSIONS

The *CPLANE1* gene, associated with Joubert Syndrome (JS) and Orofaciodigital Syndrome type VI (OFD6), presents distinct clinical manifestations. This case study of an 18-month-old female with JS symptoms, including developmental delays and specific brain MRI findings, confirmed a homozygous likely pathogenic variant in *CPLANE1*. JS is marked by the molar tooth sign and neurological symptoms, while OFD6 affects craniofacial, oral, and limb development.

Comparative studies of *CPLANE1* mutations reveal significant variability in clinical outcomes, highlighting complex genotype-phenotype correlations. Despite overlapping features like the molar tooth sign, the clinical presentation, in this case, did not suggest OFD6, emphasizing the influence of specific mutations and genetic backgrounds.

This case emphasizes the need for comprehensive genetic evaluation and multidisciplinary care to manage JS. Identifying the *CPLANE1* variant guides targeted management strategies and genetic counseling for future family planning. The variable expressivity of *CPLANE1*-related disorders highlights the importance of personalized medical approaches and continuous monitoring to optimize patient outcomes and support families effectively.

REFERENCES

Bonnard, C., Shboul, M., Tonekaboni, S.H., Ng, A.Y.J., Tohari, S., Ghosh, K., Lai, A., Lim, J.Y., Tan, E.C., Devisme, L. and Stichelbout, M., 2018. Novel mutations in the ciliopathy-associated gene CPLANE1 (C5orf42) cause OFD syndrome type VI rather than Joubert syndrome. *European journal of medical genetics*, *61*(10), pp.585-595.