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CASE REPORT

A Case Report of a Novel Isovaleryl-CoA Dehydrogenase Gene Mutation in a Chinese Family with Isovaleric Acidemia

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SUMMARY

Background: **Isovaleric acidemia (IVA) is a rare autosomal-recessive metabolic disorder caused by a genetic deficiency of isovaleryl-CoA dehydrogenase (IVD). Deficiency of IVD leads to the accumulation of organic acids; however, the genotype–phenotype relationship has not been well established.**
Methods: **Two brothers with acute neonatal IVA in a Chinese family were reported, and their clinical manifestations and examination were described. MS/MS and GCMS were used to perform organic acid analysis of blood samples and urine samples, and the patient's blood was sequenced by NGS and Sanger sequencing of the *ivd* gene.**
Results: **Sequence analysis of the *ivd* gene identified compound heterozygous mutations in the patient, the c.250T>C (p.W84R) missense mutation (novel) and the c.466-3_466-2 delCAinsGG splicing mutation, which were inherited from their parents. Various bioinformatics prediction algorithms suggest that the p.W84R missense mutation may destabilize the IVD monomer and reduce its ability to bind to substrates.**
Conclusions: **Both the clinical and genetic features of this family will help us to further expand the knowledge of IVA.**
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Supplementary Data

Table S1. Predictions using bioinformatics tools.

Bioinformatics tools	ΔΔG for p.W84R (kcal/mol) †	Pathogenic ‡
CUPSAT	-3.89	
I-Mutant v2.0	-2.06	
MuPRO	-1.32	
SDM	-1.00	
Dezyme	-2.45	
FoldX	-2.43	
BeAtMuSic	-0.85	
PolyPhen2		probably damaging
PhD-SNP		disease
MutPred2		pathogenic
PROVEAN		deleterious
MutationTaster		disease causing

Table note: † - ΔΔG < 0: destabilizing mutations, ΔΔG > 0 - stabilizing mutations, ‡ - Although criteria and conclusive terms vary in bioinformatics tools, all results indicate the mutation is pathogenic.