



A novel TRPM6 variant (c.3179T>A) causing Familial Hypomagnesemia with Secondary Hypocalcemia

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INTRODUCTION

Familial hypomagnesemia with secondary hypocalcemia (FHS) is a rare autosomal recessive disorder (*OMIM# 602014*) caused by mutations in the gene encoding TRPM6 (Transient receptor potential melastatin 6) on chromosome 9q22.

Fewer than 100 cases have been reported in literature

CLINICAL DESCRIPTION

A four year old girl had presented to us with tetany lasting for 30 minutes. Detailed history revealed that she had repeated episodes of convulsions, the first being when she was 3 days old, tetany like episodes consequently were observed at the age of 1 yr and 3 yrs. All the previous episodes subsided with intravenous calcium gluconate. She was developmentally normal and there was no family history of similar episodes or consanguinity. General and Systemic examination was essentially normal

GENETIC EVALUATION

Clinical Exome Sequencing was done which revealed a homozygous nonsense variation in exon 17 of the TRPM6 gene that results in a stop codon and premature truncation of the protein at codon 717.

Our case revealed a novel TRPM6 gene variant c.3179T>A (p.Arg717Ter). As far as we know this homozygous variant has not been reported in the 1000 genomes database and has a minor allele frequency of 0.0007% in the gnomAD database. The *in silico* prediction of the variant is damaging by MutationTaster2. With this information we considered the variant found in the patient to be pathogenic, especially associated with the clinical manifestations at presentation.

PARAMETER	VALUE	NORMAL RANGE
SERUM CALCIUM (mg/dl)	7.1	8.8-10.8
SERUM MAGNESIUM (mg/dl)	0.5	1.7-2.3
FRACTIONAL EXCRETION OF MAGNESIUM	<1.4%	2-4%
SERUM PARATHORMONE (pg/ml)	54.2	12.0-65

TREATMENT

In view of the severe hypomagnesemia, magnesium sulphate infusion and intravenous calcium gluconate was started. On Day 2 of treatment serum magnesium levels increased to 1.4 mg/dl and serum calcium levels normalized.

She was discharged on 20mg/kg/day of oral magnesium supplements and at the end of a six month follow up maintains a magnesium level at the lower end of normal range. She remains normal clinically and developmentally.

CONCLUSION

Although rare, FHS should be considered in any child presenting with refractory hypocalcemic seizures and severe hypomagnesemia, as early diagnosis and treatment can result in a normal physical and neurological development.

REFERENCES

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