Second Turkish case with MICU1 mutation-related myopathy and extrapyramidal findings

Elif Perihan Öncel[1] , İlknur Erol[1] , Şeyda Besen[1] , Leman Tekin Orgun[1] , İbrahim Boğa[2], Atıl Bişgin[2]

[1]Baskent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Department of Pediatric Neurology
[2]Cukurova University AGENTEM (Adana Genetic Diseases Diagnosis and Treatment Center) and Medical Genetics Department of Medical Faculty

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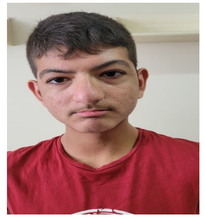
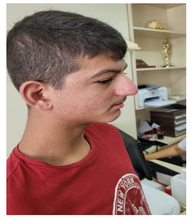
INTRODUCTION

Mitochondrial Ca^{+2} homeostasis is the most important signaling pathway for cell death and survival. Decrease in mitochondrial calcium uptake protein 1 (MICU1) causes changes in calcium signaling in mitochondria, leading to myopathy with extrapyramidal manifestations with autosomal recessive inheritance. Proximal myopathy, learning difficulties, developmental delay and progressive extrapyramidal movement are characteristic clinical findings. Ataxia, microcephaly, ophthalmoplegia and optic atrophy can also be seen.

OBJECTIVES

Here in we present the second case of MICU1 mutation-related myopathy with extrapyramidal findings from Turkey. We also described *a novel homozygous c.1027A>T (p.K343*) mutation in MICU1 gene.*





MATERIALS & METHODS

13-year-old male patient

Complaint:

- Gait disturbance
- Frequent falls

History:

- Cerebral palsy
- Autism spectrum disorder
- Developmental delay
- Parents are consanguineous

Examination:

- Global developmental delay
- Bilateral ptosis, epicanthus, protruding eyebrow arch
- Borderline low ear, short philtrum, prominent chin, thin upper lip
- Spasticity in lower extremities, tense Achilles
- Dystonic-choreiform movements
- DTR are brisk
- Tiptoe walking normal , difficulty on walking heels, mild ataxia

Investigations:

- CK: 588 IU/L
- Brain and spinal MRI: Normal
- ENMG: Compatible with proximal myopathy
- WES: A homozygous *c.1027A>T (p.K343*)* mutation in *MICU gene*
- The same heterozygous mutation was found in the mother and brother

DISCUSSION

- Myopathy with extrapyramidal findings is OR inherited and results from a mutation in the MICU1 gene located on chromosome 10q22.1
- Clinical features may vary depending on the effects of changes in calcium homeostasis on mitochondrial metabolism and characterize nonprogressive proximal muscle weakness, delayed motor development, learning difficulties, and progressive extrapyramidal motor signs including chorea, dystonia and tremor like our patient.

CONTACT

Prof. Dr. İlknur EROL
e-mail: ilknur_erol@yahoo.com
Phone: +905053837661

DISCUSSION

- Limited information and case examples are available in the literature.
- Blood lactate levels may be normal and CK levels may be slightly increased.
- **Here, we reported *the first variant, c.1027A>T (p.K343*) of MICU1* in a 13-year-old Turkish boy.**
- 39 of 44 patients reported with MICU1 mutations carrying homozygous and 5 of them carrying compound heterozygous variants in the literature.
- Most of the cases were from the Middle East where consanguineous marriage is ranging from 20 to 70%. Our patient is from the Eastern Mediterranean region of Turkey and he was also born to consanguineous parents.

CONCLUSIONS

MICU1 mutation must be considered in the differential diagnosis of children and adolescents presenting with nonprogressive proximal muscle weakness, delayed motor development, learning difficulties, and progressive extrapyramidal motor signs especially in countries where consanguineous marriage is high.

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