Two siblings with combined oxidative phosphorylation defect 11 with a novel mutation in the RMND1 gen

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INTRODUCTION

Mutations in the RMND1 gene have recently been linked to infantile onset mitochondrial disease characterized by multiple mitochondrial respiratory chain defects named as combined oxidative phosphorylation defect 11 (COXPD11). The clinical phenotypes and prognoses of RMND1-related COXPD11 are heterogeneous and the main clinical features are congenital sensorineural deafness, central hypotonia, developmental delay, seizures, lactic academia and renal disease. The number of cases reported in the literature is quite low, and to the best of our knowledge, no case has been reported from Turkey so far.

OBJECTIVES

Herein, we present two sibling cases with RMND1-related COXPD11 with a novel homozygous mutation as the first report from Turkey.

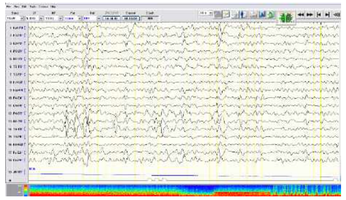

Figure 1: The EEG of the first patient

Case 1

Case 1, 11-year-old, female patient

Complaint:

- Developmental and speech delay
- At 7 years, resistant dialepctic and generalized tonic-clonic seizures
- Congenital hearing loss
- Hyperactivity

History:

- Difficult birth
- Consanguineous parents
- Mental retardation and hearing loss in her three cousins and brother

Examination:

- Mental retardation
- Long facial structure
- Anteriorly rotated ears
- Axial hypotonia, increased deep brisk tendon reflexes, and peripheral spasticity
- Mild pes cavus deformity

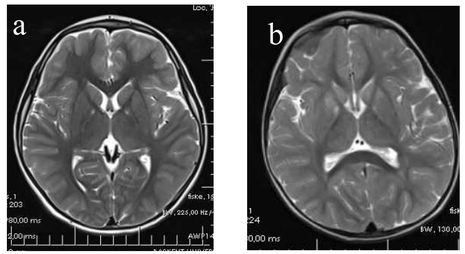

Figure 2: The brain MRI of the patients (a: case1, b:case 2); Axial T2 weighted imaging shows the abnormal symmetrical signal intensity of bilateral lentiform nuclei

CASES

Investigations:

- High plasma lactate levels:(lactic acid:32.3 mg/dl, pyruvic acid: 1.2 mg/dl, lactate/pyruvate (L:P) ratio: 26)
- EEG: Active multifocal epileptic disorder (Figure 1)
- Brain MRI: Symmetrical signal increase in bilateral lentiform nuclei (Figure 2)
- MR spect: Normal
- Karyotype and microarray analysis were normal.
- WES: A novel *homozygous c.791T>A (p.V264E) mutation in the RMND1 gene* (NM_017909.4)
- Heterozygous mutation in her parent and the other sibling

Case 2, 8- year-old, male patient

- Hearing loss at 2 years old, mild learning disability
- Pes planus, DTR increased
- He was diagnosed during genetic counseling
- *A homozygous c.791T>A (p.V264E) mutation in the RMND1 gene*

DISCUSSION

- RMND1 plays a vital role in mitochondrial translation by anchoring or stabilizing the mitochondrial ribosome near the site of mRNA maturation.
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- In 2012, it was first reported that mutations in the RMND1 gene caused COXPD11 as related to infantile encephalopathy.
- The clinical phenotypes and prognoses associated with RMND1 mutations are heterogeneous ranging from mild growth retardation, hypotonia, and hearing loss to severe infantile encephalopathy with lactic acidosis, and cases with a fatal course have also been reported.
- While our index case is characterized by resistant epilepsy, hearing loss and severe mental motor retardation, his brother with the same mutation has no findings other than mild mental motor retardation and hearing loss. No renal involvement has been detected in both siblings so far. RMND1 mutations have been observed to cause different organ involvement in different individuals. It is not yet clear why a particular RMND1 mutation can cause different signs and symptoms, even within the same family.

CONCLUSIONS

Herein, we described the first two Turkish siblings with a novel homozygous mutation of the RMND1 gene with different phenotypes.

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