Coexistence of Megaconal Congenital Muscular Dystrophy and Cystinuria: Mimicking Hypotonia—Cystinuria Syndrome

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Introduction

✓ Hypotonia-cystinuria syndrome (HCS) is an autosomal recessive contiguous gene deletion syndrome that occurs in the event of deletions of different sizes from chromosome 2p21. The syndrome is characterized by marked hypotonia-nutritional problems in the neonatal and infantile period, developmental delay, growth hormone deficiency, short stature and cystinuria type A (cystine stones).
✓ Cystinuria is a cystine metabolism disorder caused by SLC3A1 (chromosome 2p21) or SLC7A9 (chromosome 19q12) gene mutations that lead to cystine stone formation.
✓ Megaconal congenital muscular dystrophy (CMD) is characterized by mildly elevated serum creatin kinase levels, proximal weakness, early-onset hypotonia, muscle wastage, intellectual disability, delay in gross motor developmental milestones, ichthyosis skin changes such as problems, and is a result of a mutation in the choline kinase beta gene (CHKB).
✓ We present here a case with clinical findings of HCS, but who was diagnosed with coexisting cystinuria and megaconal CMD following a whole exome sequencing (WES) analysis.

Case

✓ 16-month-old male patient was admitted to our center with complaints of restlessness, body laxity and growth retardation. The patient was born to consanguineous parents at a gestational age of 34 weeks (birth weight-length was normal for age). It was stated that hypotonia and growth retardation were detected at the age of 2 months, and that there was a family history of nephrolithiasis.
✓ Physical examination revealed growth retardation [weight 8100 gr (SDS: -2.54), length 70 cm (SDS: -3.25), head circumference 46 cm (3rd-10th percentile)]. The patient was hypotonic. He had slightly long facial appearance, deep sunken eyes, slightly drooping ears. Brief eye contact was possible. He had global developmental delay. Other system examinations were unremarkable. Serum creatinine kinase (CK) was moderately high [335 U/L (range<171)]. Other laboratory examination and basal metabolic tests normal range, urinary- brain- cardiac imaging were normal. Urine amino acids analysis revealed elevated dibasic amino acids [cystine: 2611 µmol/crea (range<160), ornithine: 435.5 µmol/crea (range<250), arginine: 304.2µmol/crea (range<100), lysine: 3710µmol/crea (range<200)].
✓ HCS was considered as a differential diagnosis, and genetic analysis was performed.
✓ Genetic Analysis: Chromosomal microarray analyses (CMA) revealed no deletion in 2p21. Whole exome sequencing analysis was performed to explain clinical and laboratory findings. As a result, heterozygous mutation of c.1266_1267delGT in SLC7A9 gene and a novel homozygous c.225-2A>T pathogenic variant in CHKB gene were found (Fig.1). Co-occurrence of megaconal congenital muscular dystrophy and cystinuria which mimicked hypotonia-cystinuria syndrome was detected.

Conclusion

Different rare diseases, which are more common in countries with a high incidence of consanguineous marriage, can sometimes coexist in the same person. Whole exome sequencing analysis is a reliable diagnostic method to reveal coexistence of rare disorders.

References