Novel FKRP mutations in a Japanese MDC1C sibship clinically diagnosed with Fukuyama congenital muscular dystrophy.

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Abstract

INTRODUCTION: Fukuyama congenital muscular dystrophy (FCMD), caused by fukutin mutations, is the most common form of Japanese CMD. We followed a Japanese CMD sibship without fukutin mutation, and herein identified new FKRP mutations causing MDC1C rarely reported in Oriental countries.

PATIENTS: Two affected siblings, individuals 1 (I-1, male) and 2 (I-2, female), were born uneventfully to unaffected, non-consanguineous parents. Severe hypotonia was soon apparent and serum CK levels were elevated: I-1: 1025 IU/L (normal range <130 IU/L) and I-2: 5350 IU/L. I-1 had neither shown head control, nor said any words until he died of pneumonia at the age of 23months. I-2 learned to sit at 4years and 10months and spoke sentences at 6years and 5months. She had received respiratory support since 9years of age and died at 22years. Both showed a low-density area in the cerebral white matter on CT. MRI of I-2 revealed diffuse hyperintensity in the cerebral white matter on T2-WI, polymicrogyria over the frontal and parietal lobes, and disorganized folia and cysts in the cerebellum.

METHODS AND RESULTS: Next generation and Sanger sequencing were performed for I-2. Heterozygous FKRP mutations were identified in exon 4: c.1167_1168delGC, p.Gly391Leufs*72 and c.501_502GT>CC, p.Arg167Ser, p.Cys168Arg.

DISCUSSION: Recently, fukutin and FKRP were identified as sequentially acting ribitol 5-phosphate transferases involved in the post-translational modification of α-dystroglycan. This may explain the clinical similarities between the two disorders.

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KEYWORDS: FKRP; Fukutin; Fukuyama congenital muscular dystrophy; MDC1C; Next generation and Sanger
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