MEHMO SYNDROME

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Background: MEHMO syndrome is an X-linked rare genetic syndrome associated with mutations in the EIF2S3 gene, and characterized by mental retardation, epilepsy, hypogonadism, microcephaly, and obesity. Only 15 patients with MEHMO syndrome have been reported in the literature. MEHMO syndrome has been previously described in association with various endocrine manifestations including short stature, growth hormone deficiency, hypoglycemia, hyperglycemia, hypogonadism, and delayed puberty.

Materials/Methods: We describe 6 patients with MEHMO syndrome with a special focus on their endocrine phenotype. All patients are members of the same family. Clinical data were obtained through medical record review.

Results: We identified 6 male patients with MEMHMO syndrome. The patients include a set of 2 brothers, their maternal cousins (a set of 3 brothers), and their maternal uncle. The children's mean (±SD) age is 12.6 years old +/- 3.9 years; the maternal uncle is 35 years old. All 5 children and their mothers had an identical hemizygous missense mutation c.428C>T; p.A143V identified in the EIF2S3 gene on the X chromosome by targeted Sanger sequencing. The 6th patient (maternal uncle) did not have genetic testing - the diagnosis was made clinically. This missense mutation c.428C>T; p.A143V in the EIF2S3 gene is a novel mutation that has not been previously described. Age at diagnosis ranged from 2 to 12 years old. The most common symptoms at presentation were small for gestational age, microcephaly, failure to thrive, developmental delay, and epilepsy. Endocrine manifestations included: hypogonadism, hypoglycemia, diabetes, growth hormone deficiency, and adrenal insufficiency. The children of this cohort have been followed longitudinally for the past 14 years. The natural history of their endocrinopathies and response to treatment is described in detail.

Conclusions: MEHMO syndrome is frequently associated with endocrinopathies, most commonly with glucose dysregulation, hypogonadism, and growth hormone deficiency. However, other endocrine disorders including adrenal insufficiency can be seen. A baseline evaluation for endocrinopathies is important for all MEHMO cases. Surveillance studies are also useful although the appropriate surveillance schedule requires more study.

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