B3GALNT2-Related Dystroglycanopathy: Expansion of the Phenotype with Novel Mutation Associated with Muscle-Eye-Brain Disease, Walker-Warburg Syndrome, Epileptic Encephalopathy-West Syndrome, and Sensorineural Hearing Loss.

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Abstract
Mutations in B3GALNT2, encoding a glycosyltransferase enzyme involved in α-dystroglycan glycosylation, have been recently associated with dystroglycanopathy, a well-recognized subtype of congenital muscular dystrophy (CMD). Only a few cases have been reported with B3GALNT2-related dystroglycanopathy with variable severity ranging from mild CMD to severe muscle-eye-brain disease. Here, we describe a child with a novel homozygous nonsense mutation in B3GALNT2. The affected child has severe neurological disease since birth, including muscle disease manifested as hypotonia, muscle weakness, and wasting with elevated creatine kinase, eye disease including microphthalmia and blindness, brain disease with extensive brain malformations including massive hydrocephalus, diffuse cobblestone-lissencephaly, deformed craniocervical junction, and pontocerebellar hypoplasia. The clinical and radiologic findings are compatible with a diagnosis of severe muscle-eye-brain disease and more specifically Walker-Warburg syndrome. A more distinct aspect of the clinical phenotype in this child is the presence of refractory epilepsy in the form of epileptic spasms, epileptic encephalopathy, and West syndrome, as well as sensorineural hearing loss. These findings could expand the phenotype of B3GALNT2-related dystroglycanopathy. In this report, we also provide a detailed review of previously reported cases with B3GALNT2-related dystroglycanopathy and compare them to our reported child. In addition, we study the genotype-phenotype correlation in these cases.

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Conflict of interest statement