SHORT COMMUNICATION

PHENOTYPIC VARIABILITY IN MABRY SYNDROME: EVIDENCE FOR GENETIC HETEROGENEITY

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The impact of seizures associated with childhood onset metabolic disorders is considerable even though they account for 1% of live births. Like many infantile metabolic storage disorders, hyperphosphatasia with neurologic deficit (Mabry syndrome), has its onset starting in the first year of life – commencing with seizures followed by developmental disability (DD). At first considered rare, Mabry syndrome was originally described in a single family (OMIM#239300) [1970]. In addition to seizures and persistently elevated serum alkaline phosphatase (ALP) levels (from ~1.3 to ~20 times the upper age-adjusted reference limit), our work resulted in the recognition of several other salient features of the disorder including: a characteristic facial dysmorphology (hypertelorism, a broad nasal bridge and a tented mouth), nerve abnormalities (plaques disrupting Schwann cells) and subtle bone abnormalities in the bones of the hand (variable shortening of middle and distal phalanges). The phosphoinositol glycan (PIG) anchor, type V biosynthesis gene was found to be disrupted in eight families. Since approximately 50% of Mabry symptoms patients are not affected by PIGV mutations, however, we decided to commence a search for Mabry syndrome patients without PIGV gene involvement. Since twenty genes are integral to PIG anchor synthesis, we consider these genes candidates genes in some presentations of the disorder. This presentation describes the inborn error of metabolism that underlies Mabry syndrome in the context of the mechanisms that regulate ALP expression/secretion.