Pyridoxal phosphate-responsive seizures in a patient with cerebral folate deficiency (CFD) and congenital deafness with labyrinthine aplasia, microtia and microdontia (LAMM)

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We present an 8-year-old boy with folate receptor alpha (FR?) defect and congenital deafness with labyrinthine aplasia, microtia and microdontia (LAMM syndrome). Both conditions are exceptionally rare autosomal recessive inherited diseases mapped to 11q13. Our patient was found to have novel homozygous nonsense mutations in the FOLR1 gene (p.R204X), and FGF3 gene (p.C50X). While the FR? defect is a disorder of brain-specific folate transport accompanied with cerebral folate deficiency (CFD) causing progressive neurological symptoms, LAMM syndrome is a solely malformative condition, with normal physical growth and cognitive development. Our patient presented with congenital deafness, hypotonia, dysphygia and ataxia in early childhood. At the age of 6 years he developed intractable epilepsy, and deteriorated clinically with respiratory arrest and severe hypercapnea at the age of 8 years. In contrast to the previously published patients with a FOLR1 gene defect, our patient presented with an abnormal l-dopa metabolism in CSF and high 3-O-methyl-dopa. Upon oral treatment with folinic acid the boy regained consciousness while the epilepsy could be successfully managed only with additional pyridoxal 5'-phosphate (PLP). This report pinpoints the importance of CSF folate investigations in children with unexplained progressive neurological presentations, even if a malformative syndrome is obviously present, and suggests a trial with PLP in folinic acid-unresponsive seizures.

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