Oculodigital Sign: A Clinical Clue for Diagnosis

Sir,

A one-and-half-year-old boy, second born to a third-degree consanguineous couple, was brought for the evaluation of poor tracking of objects noticed since early infancy. Mother's antenatal period and neonatal transition were uneventful. There was history of mild delay in attaining milestones since infancy. Child had one episode of left focal motor seizures in the second week of life and was treated elsewhere with phenobarbitone. Deep-set eyes, vertical nystagmus, and bilateral alternate divergent squint were observed. Prolonged pressing of eyes with thumb [Figure 1] and repetitive eye-poking were observed. The child had poor eye contact and did not fix and follow the light. Menace reflex was absent. Pupils were dilated and sluggishly reacting to light. Fundus examination was normal. Motor system examination was also normal. Hand and leg flapping stereotypies were observed. Differentials of visual impairment due to hypoglycemic brain injury, intrauterine infection, and inherited retinal diseases were considered. Brain MRI did not reveal any structural abnormality. Visual evoked potentials (VEPs) were absent. Clinical exome revealed a homozygous nonsense variation, c.2952C>A in the exon 16 of the *GUCY2D* gene [ENST00000254854.5; genome assembly: GRCh37.p13; rs1395017892] that results in a stop codon and premature truncation of the protein at codon 984 (p.Cys984Ter). The p.Cys984Ter variant has not been reported in the 1000 genomes, and ExAC databases. The in silico prediction

Figure 1: Photograph of the child depicting oculodigital sign

of the variant is damaging by Mutation Taster 2. Based on the ACMG guidelines, this *GUCY2D* variant has been classified as a pathogenic variant, confirming the diagnosis of Leber congenital amaurosis (LCA-1). Another variant of uncertain significance was detected in exon 11 of the *CRB1* gene which is likely to be a polymorphism.

LCA is a rare inherited retinal disease characterized by early infantile-onset vision loss, poor pupillary responses to light, nystagmus, oculodigital sign, abnormal visual evoked potentials (VEPs) and abnormal electroretinogram (ERG).[1,2] The prevalence of LCA has been estimated as 1:33,000–1:81,000.[1] Oculodigital sign of Franceschetti refers to repeated poking, pressing, and rubbing of eyes.[2] During this self-stimulatory phenomenon, the child perceives a flash of light due to the generation of action potentials in retina or optic nerve by digital compression of the eyes.[3] Our patient had cardinal clinical features of LCA with oculodigital sign and absent VEP. Ocular auto-stimulation or oculodigital phenomenon has been described in children with LCA, retinopathy of prematurity, congenital rubella syndrome, Norrie's disease, and severe vision impairment due to congenital causes such as cataract, glaucoma, corneal leucoma, and retinal degeneration.[4] Eye poking behavior may also be observed in children with severe intellectual disability despite the absence of vision impairment.[3] Oculodigital sign is observed frequently in young children with severe vision impairment of the above mentioned causes and disappears during adolescence.[2] The consequences of oculodigital phenomenon are enophthalmos and corneal ectasia.[3,5]

Though many genes have been identified to cause LCA, mutations in some of the genes expressed in the retina, including Guanylate Cyclase 2D, Membrane (*GUCY2D*), nicotinamide nucleotide adenylyltransferase 1 (NMNAT1), centrosomal protein, 290-KD (*CEP290*), and aryl hydrocarbon-interacting receptor protein-like 1 (*AIPL1*) genes, are frequently encountered.[1] Our patient with *GUCY2D*-associated LCA had visual impairment, nystagmus, normal fundus, typical oculodigital sign, deep-set eyes, and motor stereotypies. *GUCY2D*-associated LCA is characterized by substantial preservation of rod function and relatively normal fundus in contrast to retinal disease caused by mutation in other genes.[1] Fundus examination findings described in patients with LCA are disc pallor, peripheral pigmentary retinopathy, optic drusen, nummular pigmentation, and flecked retina.[1]

Ocular auto stimulation may be difficult to control with physical restraints or negative reinforcement. It often tends to decrease with advancing age and may be controlled by engaging in play activities that keep the hands occupied.[3] Oculodigital sign in children must alert the clinicians to search for vision impairment of varied etiology.

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Conflicts of interest

There are no conflicts of interest.

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