Case Report

Ocular manifestations of a rare case of Miller-Dieker syndrome

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ABSTRACT

We report a rare case of a five-year-old female child who was diagnosed with Miller-Dieker syndrome. She had global developmental delay, seizures, facial dysmorphic features and type 1 lissencephaly on Magnetic resonance imaging of brain. Her ocular manifestations included strabismus, torsional nystagmus, high myopic astigmatism and tortuous retinal vessels.

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1. Introduction

Miller-Dieker syndrome (MDS) is a rare genetic disorder characterised by type I lissencephaly [LIS], typical facial appearance, intellectual disability, developmental delay, hypotonia and feeding difficulties. It is rarely associated with renal, genito-urinary, cardiac abnormalities and ocular manifestations. It is due to a gene deletion involving the 17p13 chromosome on the LIS 1 gene.

2. Case Description

A five-year-old female child presented to the department of Pediatrics of our institute with a history of high-grade fever with rigors of two weeks duration which was diagnosed as urinary tract infection and subsided with appropriate medication. She had a history of myoclonic seizure disorder since one year of age and was under control with multiple antiepileptic drugs. She was the only child of her parents who had a second degree consanguineous marriage. The child’s birth history was not significant and postnatal course uneventful.

Child had features of global developmental delay. Anthropometric measurements revealed growth retardation for age. Head to toe examination revealed closed anterior fontanelle, frontal and parietal bossing, bitemporal hollowing, facial dysmorphic features like elongated forehead, hypertelorism, telecanthus, midfacial flattening, long philtrum and micrognathia and no evidence of neurocutaneous markers [Figure 1]. Her systemic examination was unremarkable. MRI brain showed markedly thickened cerebral cortex with few poorly formed gyri [Pachygryria], a few shallow sulci, shallow sylvian fissure, hypoplasia of corpus callosum giving an hour glass or “figure of 8”
appearance [Figure 2]. It also revealed “C” band heterotopia with diffuse hypomyelination of cerebral white matter-features suggestive of Classical LIS.

Video EEG recording was done using Nihon-Koeden 38 channel digital video EEG system. It recorded multiple flexor spasms [generalized, bi hemispheric] and one complex partial seizure arising from fronto-central region with no lateralization with moderate to severe Encephalopathy. Patient couldn’t get a genetic testing due to financial constraints. She was diagnosed as Miller –Dieker syndrome based on clinical assessment and neuro-imaging.

She was referred to ophthalmology department for ocular examination as a part of syndromic assessment. On Ophthalmological evaluation, she had typical facial dysmorphic features as described above. She was able to fix and follow accommodative targets uniocularly. However, due to cognitive insufficiency, a quantitative visual assessment was not possible. She had an alternating divergent squint of 30 PD on prism alternate cover test performed for distance and near fixation. Child was not able to comprehend sensory and stereopsis tests for assessment of binocular single vision. Ocular motility was normal in both eyes on version and duction testing with normal saccades and pursuits. She had torsional nystagmus with vertical component, moderate frequency and low amplitude in all directions of gaze with no null zone.

Anterior segment examination was normal. Dilated fundus examination was normal except for retinal vascular tortuosity without associated dilatation. Cycloplegic refraction with homatropine 2% eye drops revealed Simple myopic astigmatism of -3.5D at 1800 in both the eyes. She was given spectacle prescription in view of high refractive error and advised to review half-yearly.

Goggle VEP done binocularly could identify NPN complexes but due to poor patient cooperation, superimposition of waveforms and further details could not be elicited [Figure 3].

3. Discussion

(LIS) and agyria-pachgyria are the terms used to describe brain with absent or poor sulcation. Complete LIS is synonymous with agyria whereas incomplete LIS refers to brain with shallow sulci and a relatively smooth surface.2 Macroscopic abnormalities of type I LIS on MR imaging include: agyria, mixed agyria/pachgyria or complete pachgyria, a thick cerebral cortex, incomplete opercularisation resulting in a shallow sylvian fissure and the typical “figure of eight” appearance of the brain, hypoplastic corpus callosum, persistent septum cavum pellucidum and dilatation of the posterior horns of the lateral ventricles [colpocephaly].5 Type II LIS[cobblestone] can be associated with Walker Warburg syndrome, Muscle-eye-brain disease and Fukuyama congenital muscular dystrophy.6 It is associated with severely disorganized cortex, cobblestone appearance of brain, poor myelination, cerebellar vermis hypoplasia and Dandy Walker malformation.7

MDS is a genetic disorder comprising of LIS type 1, facial dysmorphic features and other malformations. It is a rare condition with an incidence of 11.7 per million live births.8 It is associated with severe developmental delay, generalized hypotonia in early life, feeding difficulty, early onset seizure disorder, mental retardation and microcephaly.9 The facial dysmorphic features include prominent forehead, bitemporal hollowing, short nose with upturned nares, midfacial hypoplasia, protuberant upper lip with thin vermilion border and small jaw.10 It can be associated with cardiac, renal and genital abnormalities.

On review of literature of patients with classical LIS, 19.3% of patients had ocular abnormalities.11 Poor visual fixation, tracking, nystagmus, oculomotor apraxia, variable strabismus, corneal clouding, abnormal iris, tortuous retinal vessels12 and delayed visual maturation were reported. In the study by Nabi NU et al., ocular abnormalities were more severe in type 2 compared to type 1 LIS.1 The other ocular abnormalities reported include optic nerve and macular hypoplasia, optic nerve atrophy, refractive errors and cortical visual impairment.13 The rotatory nystagmus found in MDS could be of central vestibular origin or just a type of congenital nystagmus. Our patient with MDS had ocular abnormalities including exotropia, torsional nystagmus, simple myopic astigmatism and tortuous retinal vessels along with facial dysmorphic features.
Fig. 2: T1 and T2 weighted MR images showing paucity of sulci and gyri, thick cerebral cortex and hypoplasia of corpus callosum suggestive of type 1 lissencephaly

Fig. 3: VEP of both eyes showing poorly superimposed waveforms

The differential diagnosis of MDS include other conditions associated with microcephaly, seizures and facial dysmorphism such as Cornelia de Lange syndrome, Smith-Opitz syndrome and Zellweger syndrome. However, none of the above syndromes have associated lissencephaly.

4. Conclusion

The management of patients with MDS is multidisciplinary, symptomatic and supportive. Due to variable incidence of ocular involvement, all patients with lissencephaly should undergo a thorough ophthalmic evaluation.

5. Source of Funding

None.

6. Conflict of Interest

None.

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