Multiple Retinal Holes and Peripheral Nonperfusion in Muscle-Eye-Brain Disease

Muscle-eye-brain (MEB) disease is a rare congenital autosomal recessive disorder with around 30 reported cases in the literature.\(^1,2\) It is 1 of 3 types of congenital muscular dystrophy with severe defects in organogenesis and neuronal migration, and, along with Walker-Warburg syndrome, is associated with ocular abnormalities.\(^3\) Usually, the retina in MEB disease and Walker-Warburg syndrome is described as dysplastic.\(^4\) A detailed histopathologic description has been given,\(^5\) but a clinical description of retinal findings, especially in early disease, is lacking. Herein, we describe detailed retinal findings in a neonate with the diagnosis of MEB disease confirmed by genetic testing.

**Report of a Case.** A 12-day-old girl who was born full term was referred owing to a suspected retinal detachment in the right eye noted soon after birth. Her neonatal history was significant for an endoscopic third ventriculostomy at 1 day of life for hydrocephalus after magnetic resonance imaging revealed severe brain and brainstem malformation with an absent corpus callosum, cortical gyral thickening, cerebellar vermian hypoplasia, and markedly enlarged lateral and third ventricles (Figure 1). Examination under anesthesia disclosed unremarkable anterior segment examination results in both eyes. Posterior segment examination of the right eye revealed a retinal detachment that obscured the optic nerve and fovea, but with a bullous elevation in a nearby macular area and superior elevated fibrosis (Figure 2A). Closer examination of the peripheral detachment revealed an avascular retina with multiple lacunae and full-thickness holes (Figure 2B). Posterior examination of the left eye revealed moderate optic nerve hypoplasia, an indistinct but attached fovea, and an anomalous distribution of vessels with very reduced caliber to vessels coursing superiorly, which appeared to terminate in the equatorial zone (Figure 3). The periphery of the left eye was featureless with poor pigmentation and an impressive extent of visible choroidal vasculature.
Fluorescein angiography of the right eye revealed leakage from the fibrosis, indicative of extraretinal fibrovascular proliferation (Figure 4). Fluorescein angiography of the left eye showed a hypoplastic retina with prominent choroidal flush and anomalous vasculature that terminated in the equatorial zone (Figure 5). Prophylactic laser treatment was performed in each eye in areas of nonperfusion, and pars plana vitrectomy, lensectomy, and silicone oil placement were performed in the right eye.
Subsequent genetic testing revealed a POMGnT1 mutation, consistent with MEB disease. Specifically, the mutation was in POMGnT1 intron 17. This resulted in a DNA substitution of c1539 + 1 G>A, which is a common founder mutation in Finnish patients. Mutations in POMGnT1 near the 5’ terminus, as is the case with c1539 + 1 G>A, have been suggested to correlate with more severe cerebral malformations.

Comment. Both MEB disease and Walker-Warburg syndrome have underlying deficiencies in posttranslational glycosylation of α-dystroglycan that lead to severe defects in organogenesis and neuronal migration. Brain and eye phenotypes in MEB disease and Walker-Warburg syndrome likely involve defective glycosylation in proteins other than α-dystroglycan since chimeric mice deficient in α-dystroglycan develop congenital muscular dystrophy but not brain or eye phenotypes of MEB disease or Walker-Warburg syndrome. In both diseases, there can be hypoplasia of the retina, choroid, optic nerve, and iris. Specifically, Zervos et al performed a histopathologic examination of 2 siblings with MEB disease and found loss of the inner nuclear layer, thinning of the outer nuclear layer, absence of rod and cone outer segments in midperipheral portions of the retina, and localized nerve fiber layer schisis nasal to the optic nerve head. They also noted focally atrophic retinal pigment epithelium and diffuse chorioidal atrophy.

In our patient, with genetic testing results supportive of an MEB disease diagnosis, we describe the previously unreported clinical findings in early disease. A peripheral avascular retina led to extraretinal fibrovascular proliferation with subsequent contracture and combined tractional and rhegmatogenous retinal detachment with multiple perforating holes in the right eye. The underlying defect in glycosylation in MEB disease, which results in a severe defect in neuronal migration and possibly in hypoplasia of various structures, may be the cause of these retinal findings.

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Diffuse Infiltrating Retinoblastoma With Central Nervous System Metastasis

A diffuse infiltrating pattern of growth seen in 1% to 2% of retinoblastomas is associated with horizontal growth of tumor cells along the retinal tissue as well as retinal thickening. Vitreous and anterior segment seeding simulate uveitis. We describe a child who developed acute onset of headache and vomiting followed by visual loss in his right eye. Findings on clinical examination led to a diagnosis of diffuse infiltrating retinoblastoma with central nervous system involvement, which was confirmed following discovery of malignant cells in the cerebrospinal fluid (CSF).

Report of a Case. A 10-year-old boy visited the pediatric emergency department with headache, vomiting, and altered sensorium of 3 days’ duration. There was no history of fever or upper respiratory tract infection. The next day, he developed acute, painless diminution of vision in the right eye. Systemic examination results were unremarkable. Full blood cell count and workup for infectious diseases yielded negative results. Magnetic resonance imaging of the brain and orbit showed diffuse thickening and enhancement of the right optic nerve and meninges (Figure 1A and B). Lumbar puncture revealed normal opening pressure; CSF analysis showed low glucose and high protein content. With a tentative diagnosis of right optic neuritis with meningoencephalitis, the child was referred for ophthalmic examination. Findings on examination of the right eye showed visual acuity of no light perception, anterior chamber flare 1+, clumps of vitreous cells, a swollen optic disc, and a thickened superonasal retina (Figure 1C and D). B-scan ultrasonography of the right eye revealed medium-amplitude vitreous echoes, disc swelling, and thickened retina (Figure 2A). Repeated lumbar puncture showed clumps of malignant cells (Figure 2B), confirming the clinical suspicion of diffuse infiltrating retinoblastoma with CSF metastasis. The child was referred to the p-