Subsequent genetic testing revealed a POMGnTI mutation, consistent with MEB disease. Specifically, the mutation was in POMGnTI intron 17. This resulted in a DNA substitution of c1539 + 1 G>A, which is a common founder mutation in Finnish patients. Mutations in POMGnTI 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 choroidal 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 pe-
The child also received craniospinal radiation. With CSF becoming free of tumor cells and the optic nerve size reverting to normal (Figure 2C), enucleation of the right eye was performed. Histopathological examination of the globe revealed retinoblastoma cells diffusely infiltrating the retina and the optic nerve (Figure 2D). The cut end of the optic nerve and choroid were free of tumor cells.

The child was followed up at monthly intervals and has since received 3 cycles of systemic and intrathecal chemotherapy. Cytological analysis of the CSF after 6 months of radiation and chemotherapy showed no malignant cells.

Comment. Diffuse infiltrating retinoblastoma poses a diagnostic challenge. Any interventional procedure such as a diagnostic tap is contraindicated while a diagnosis of retinoblastoma is being considered, and therapeutic decisions have to be made based on clinical diagnosis. In our patient, retinoblastoma was not on the initial list of potential diagnoses. It was only after referral to the oncology service that the diagnosis of retinoblastoma with CSF spread was made. Although the CSF was clear after systemic treatment, owing to the possibility of live tumor in the eye, enucleation and examination of the cut end of the optic nerve were considered essential.

Metastasis to the CSF in retinoblastoma is difficult to treat. Intensive chemotherapy has been reported to be successful in obtaining a cure; however, metastatic retinoblastoma shows multidrug resistance and the blood-brain and blood-retinal barriers impede access to tumor cells. Orbital and craniospinal radiation is often resorted to in these patients. The cut end of the optic nerve in our patient was found to be free of tumor cells. However, the possibility of residual tumor cells in the central nervous system cannot be ruled out. Our patient continues to receive chemotherapy and is under close follow-up.
To our knowledge, diffuse infiltrating retinoblastoma with central nervous system spread at the initial visit has not been previously reported.

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Topical Timolol for Periocular Hemangioma: Report of Further Study

Childhood superficial capillary hemangiomas of the eyelid may lead to amblyopia or anisometropia.1,2 Although benign, such tumors can cause irreversible visual loss if not treated promptly. Treatment options for infantile hemangioma include both systemic...