Surgical Removal of an Atypical Macular Epiretinal Membrane in Neurofibromatosis Type 2: Clinicopathologic Correlation and Visual Outcome

Macular epiretinal membranes (ERMs) are common manifestations in children with neurofibromatosis type 2 (NF2). The ERMs in NF2 have been speculated to be hamartomatous in nature. Immunohistochemical techniques have rarely been used to characterize these ERMs. The following case describes the clinical and histologic characteristics of a dense ERM in a case of NF2.

Report of a Case. During a dilated fundus examination, a 2-year-old girl with confirmed NF2 and a history of esotropia and amblyopia in the left eye was noted to have a depigmented macular lesion in her left eye. The patient was undergoing patching therapy for amblyopia and was otherwise healthy. Family history was significant for neurofibromatosis affecting her father and paternal grandmother, the latter of whom had neoplasms of the brain, eyes, and auditory nerves that led to deafness, blindness, and death by age 34 years. On genetic testing, the child and her father were confirmed to have deletion of the NF2 promoter and exon 1, described as c.-854?7?45?del.

Visual acuity was central, steady, and maintained in the right eye and central, steady, and unmaintained in the left eye. There was no afferent pupillary defect. Ocular versions were full with a left esotropia of 30 to 40 prism diopters. Cycloplegic refraction was +3.00 sphere OD and +2.00 sphere OS. Slitlamp examination showed normal anterior segments without cataracts or Lisch iris nodules. Fundus examination of the left eye revealed a gray, flat, macular lesion occupying an area of 2 × 2.5 disc diameters, partially obscuring underlying retinal and perifoveal vasculature (Figure 1A). A clinical diagnosis of a dense macular ERM in the left eye, possibly hamartomatous in etiology and possibly visually significant, was made. A small gray inner retinal opacity was also noted in the perifoveal region of the right eye (not shown). Magnetic resonance imaging of the brain and spine revealed no tumors.

Examination under anesthesia was performed. Spectral-domain optical coherence tomography (Biotigen, Inc) of the left eye demonstrated a thickened ERM and underlying neurosensory retina with evidence of vitreous attachment to the membrane that caused slight elevation at its edges (video, http://www.archophthalmol.com). Fluorescein angiography showed apparent absence of a foveal avascular zone due to perifoveal hyper-vascularity that crossed the horizontal raphe centrally (Figure 1B). The macular ERM showed no intrinsic vascularity. The patient underwent pars plana vitrectomy and ERM stripping in the left eye. The membrane was noted to be densely adherent to the macula but with a definite anatomic plane between the membrane and retina. As the membrane separated, so did a continuous posterior vitreous membrane, presumably a layer of the posterior cortical vitreous. The membrane was submitted for histologic studies. Light microscopy showed a highly cellular membrane with up to 4 layers of cells in some areas. There was weak staining for glial fibrillary acidic protein (Figure 2). There was insufficient specimen for adequate evaluation of periodic acid–Schiff or S-100 protein staining. The cells were of indeterminate origin; no astrocytes were identified in the limited amount of tissue available. Visual acuity was 20/20 OD and 20/125 OS 6 months after vitrectomy and continued refractive and amblyopia management that consisted of part-time occlusion of the right eye. The retinal vasculature in the left macula remained unchanged in appearance without recurrence of ERM.

Video available online at www.archophthalmol.com
Comment. To our knowledge, only 2 previous reports of histologic evaluation of an ERM in NF2 exist. The ERMs in this condition appear clinically distinct from retinal astrocytic hamartomas but may coexist with them, leading to the speculation that they also may be hamartomatous. This speculation is supported by the histologic findings of McLaughlin et al in which staining for glial fibrillary acidic protein and S-100 protein was demonstrated, supporting a glial origin. In our experience, weak staining for glial fibrillary acidic protein as noted in our case may also be observed in the majority of cells in some intracranial astrocytic hamartomas of NF2, although these contain identifiable astrocytes that stain more positively with glial fibrillary acidic protein. Thus, the limited body of evidence in existence suggests an astrocytic and therefore hamartomatous origin for ERMs in NF2.

We were unable to determine whether significant visual improvement resulted from our surgical intervention because of the difficulties in assessing visual function behaviorally in a 2-year-old child. Our enthusiasm for removal of such lesions is tempered by the unchanged anomalous retinal vascular pattern, possibly congenital, that persisted in the macula even after several months and the residual visual impairment observed in our case.

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Central Serous Chorioretinopathy in Myopic Patients

Central serous chorioretinopathy (CSC) is typically seen in hyperopic or emmetropic eyes, most of which have a thickened choroid. We describe 6 eyes of 6 patients with CSC and significant myopia (Table and Figure). All eyes had a thickened choroid relative to their refractive error as measured by enhanced-depth imaging spectral-domain optical coherence tomography (Heidelberg Spectralis HRA + OCT; Heidelberg Engineering, Inc). No patients were receiving steroids.

Methods. The diagnosis of CSC in 6 patients with moderate to high myopia was confirmed by clinical examination, fluorescein angiography, indocyanine green angiography, fundus autofluorescence imaging, and spectral-domain optical coherence tomography. Choroidal thickness was measured subfoveally using enhanced-depth imaging spectral-domain optical coherence tomography.

Results. The clinical information as well as the choroidal thickness measurement and expected choroidal thickness are summarized in the Table. In each of the 3 eyes in which an expected choroidal thickness calculation was appropriate, the expected choroidal thickness was less than the measured thickness.

Comment. In a study of 28 eyes with CSC, the mean (SD) subfoveal choroidal thickness was 505 (124) μm. This contrasts with a mean (SD) subfoveal choroidal thickness of 287 (76) μm in normal eyes. Although choroidal thickness decreases with age in normal eyes, the same pattern may not hold for patients with CSC.

Our 6 eyes with CSC are unusual in that they were all myopic. With the exception of patient 6, the choroidal thickness of our cases would not normally be considered high for emmetropic eyes. However, it is high for myopic eyes. In a study of 31 patients with high myopia (mean refractive error, −11.9 diopeters), the mean subfoveal choroidal thickness was 93.2 μm. A regression analysis suggested a decrease in subfoveal choroidal thickness of 7.84 μm per diopter of myopia in eyes with no history of choroidal neovascularization.

These cases remind us that CSC can occur in myopic eyes. In the absence of a neurosensory detachment, the diagnosis of CSC can be made based on history, fundus appearance, fundus autofluorescence imaging, and measurement of choroidal thickness. In myopic eyes without a neurosensory detachment, CSC may be missed when axial length–related choroidal thickness differences are not considered. Awareness of thin choroids in “normal” myopic patients would allow for the recognition of “thick” choroids relative to refraction in eyes with CSC.

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Table. Clinical Characteristics of Myopic Eyes With Central Serous Chorioretinopathy

<p>| Patient/Sex/| Eye | BCVA | Refraction, D | Subfoveal Choroidal Thickness, μm | Expected Subfoveal Choroidal Thickness, μm* |</p>
<table>
<thead>
<tr>
<th>Age, y</th>
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<tr>
<td>1/M/37</td>
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<td>161</td>
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<tr>
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<td>436</td>
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</tr>
<tr>
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<td>OS</td>
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<tr>
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<td>135</td>
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<tr>
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<td>OS</td>
<td>20/25</td>
<td>−3.50</td>
<td>360</td>
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</tr>
</tbody>
</table>

Abbreviations: BCVA, best-corrected visual acuity; D, diopeters; NA, not applicable (refraction between −3.00 D and −6.00 D).

*a Formula for expected subfoveal choroidal thickness in eyes without central serous chorioretinopathy that have more than 6 D of myopia and no history of choroidal neovascularization is 265.8 μm + 7.84 × (spherical equivalent) − 1.25 × (age in years).