Epiretinal Macular Edema Associated With Thick Epiretinal Membranes

Rishi R. Doshi, MD; Matthew D. Lowrance, DO; Brian T. Kim, MD; Janet L. Davis, MD; Philip J. Rosenfeld, MD, PhD

ABSTRACT: High-resolution imaging with spectral-domain optical coherence tomography has identified an unusual group of epiretinal membranes (ERMs) in the presence of lamellar macular holes. These ERMs are unusually thick. The authors present the case of a patient with age-related macular degeneration who developed edema within a thickened ERM in both eyes after cataract surgery. The edema resolved with anti–vascular endothelial growth factor (VEGF) therapy. The authors propose that the VEGF-responsive fluid within these thick ERMs arose from fibrovascular tissue derived from the retina. Further studies with histopathology will be required to determine whether neovascular tissue is present in all cases of thickened ERMs with epiretinal edema.


INTRODUCTION

Epiretinal membranes (ERMs) are recognized to be a diverse group of proliferations at the vitreoretinal interface involving varying amounts of cells, extracellular stroma, and neovascular tissue. Spectral-domain optical coherence tomography (SD-OCT) has improved our understanding of the different morphologic categories of ERMs, including cellophane maculopathy, tractional, proliferative vitreoretinopathy, and proliferative diabetic retinopathy. However, there are cases imaged with SD-OCT that do not correspond to any of these typical categories. Witkin et al described an unusual form of a thick ERM in 11 of their 19 cases of lamellar macular holes (LMHs) imaged with ultra-high-resolution OCT and hypothesized that these membranes represented either entrapment of vitreous collagen between the ERM and retina or persistent attachment of a thickened posterior hyaloid to the macula. Parolini et al later provided histopathologic correlations to show that these thick ERMs in the setting of LMHs are composed of condensed and remodeled posterior cortical vitreous collagen. In this report, we present a case with a previously undescribed finding of edema within a thick ERM and provide imaging from additional cases to shed light on proposed etiologies for this epiretinal fluid.

CASE REPORT

A 94-year-old man was referred for evaluation of dry age-related macular degeneration (AMD), which was diagnosed 10 years previously. Ocular history included primary open-angle glaucoma treated with topical dorzolamide in both eyes twice daily. Medical history was significant for myocardial infarctions, pacemaker placement, left carotid endarterectomy, hypertension, and hyperlipidemia. Visual acuity at presentation was 20/400 in both eyes. Anterior segment examinations were notable for nuclear sclerotic cataracts in both eyes, and fundus examinations revealed pigmented paravenous retinochoroidal atrophy with patchy geographic atrophy in the maculae. There were no signs of intraocular inflammation. SD-OCT fundus imaging demonstrated an LMH in the right eye and an apparent long-standing full-thickness macular hole in the left eye. A thick ERM was present on the retina in both eyes and appeared to fill in the space created by the full-thickness macular hole in the left eye. Atrophy of the retina, retinal...
pigment epithelium, and choroid was present in both eyes (Figure 1). B-scan ultrasonography confirmed an attached posterior hyaloid in both eyes. The patient was referred for cataract extraction and underwent uncomplicated surgeries in both eyes. He returned 18 weeks after the initial cataract surgery of the left eye with a complaint of metamorphopsia. Visual acuity was unchanged at 20/400, but SD-OCT imaging demonstrated macular edema within both the retina and the ERM (Figure 1). Fluorescein angiography (FA) revealed late leakage in the left macula (Figure 2), and due to the concern that this leakage might represent occult choroidal neovascularization, the patient was treated with intravitreal bevacizumab in the left eye.

One month later, both the intraretinal and epiretinal edema in the left eye resolved, but similar edema had

Figure 1. (A,B) Baseline spectral-domain OCT images of the right and left eye of a patient with age-related macular degeneration and macular hole–associated thick epiretinal membranes (ERM). (C,D) Development of edema within the retina and ERM of the left eye 18 weeks after cataract surgery. (E,F) Resolution of the fluid in the left eye 4 weeks after intravitreal bevacizumab, with interval development of similar intraretinal and epiretinal fluid in the right eye. (G,H) Spectral-domain OCT appearance 4 weeks after intravitreal bevacizumab treatment in the right eye, with no fluid present in either eye.
developed in the right eye, which was treated with an injection of bevacizumab. Both maculae were fluid-free 1 month later, at which time the patient was given bevacizumab injections in both eyes, and the treatment interval was extended (Figure 1). Over the next 12 months of follow-up, there was no evidence of macular fluid in the retina or in the thick ERMs in both eyes, but the patient’s visual acuity did not improve from baseline.

We have observed another case of an LMH in a 90-year-old woman with AMD in which a thick ERM appeared to originate from the outer retina and also had edema (Figure 3). In another case of epiretinal

Figure 2. Color, autofluorescence, and fluorescein angiography images of both eyes 18 weeks after left eye cataract surgery, at which time intraretinal and epiretinal edema was noted in the left eye. (A) The right eye shows late staining of geographic atrophy and pigmented paravenous retinochoroidal atrophy, with no leakage. (B) The left eye demonstrates late leakage in the macula, concerning for occult choroidal neovascularization.

Figure 3. (A) A lamellar macular hole with thick epiretinal membrane and epiretinal fluid in the left eye of a 90-year-old woman with age-related macular degeneration. (B) On an adjacent horizontal cut through the fovea, the membrane appears to be continuous with outer retinal tissue.
macular edema, the left eye of a 75-year-old woman with idiopathic intermediate uveitis showed resolution of the intramembranous fluid in response to topical anti-inflammatory therapy with 1% prednisolone acetate and nepafenac (Figure 4). The inflammatory macular edema in this patient may similarly have originated from the leakage of small capillaries within the ERM.

**DISCUSSION**

This report demonstrates the presence of macular edema within thick ERMs of both eyes in a patient
with AMD after cataract surgery. The fact that the epiretinal edema was responsive to anti–vascular endothelial growth factor (VEGF) therapy suggests the presence of vessels within the ERMs. We propose that expression of VEGF resulted in the leakage of fluid from fibrovascular tissue that composed the ERMs, and that the vascular component of this tissue was derived from the retina. The VEGF-mediated vascular leakage in our patient responded well to bevacizumab injections. While superficial neovascular tissue was not apparent on clinical examination or FA, Snead et al used light microscopy to demonstrate capillaries in a surgically removed ERM that was previously classified on clinical examination as simple cellophane maculopathy, raising the possibility that small capillaries may be present in apparently non-neovascular membranes. The additional cases of thick ERMs associated with LMHs support the concept that such membranes appear to originate from the outer retina, and the associated edema suggests that they may be more than simply entrapped vitreous collagen.

Given the similar SD-OCT appearance of our cases with thick ERMs previously described and the absence of posterior vitreous detachment, it is possible that the epiretinal tissue in our case similarly involved the entrapment of vitreous cortex by glial proliferation. Rather than refer to such membranes as thick or dense ERMs, we propose the term vitreoretinal membranes to correspond with the published histopathology. An alternate hypothesis for the epiretinal edema in our patients may be that the fluid was an extension of the VEGF-responsive intraretinal fluid into the entrapped vitreous space and not the direct result of VEGF acting on neovascular components within the ERMs. While this remains a possibility, the lack of fulminant retinal edema immediately adjacent to the ERMs would make this less likely.

Finally, despite the presence of geographic atrophy characteristic of AMD, the possibility remains that the macular edema in our patient was due to sequential bilateral pseudophakic cystoid macular edema (CME) rather than occult choroidal neovascularization. This seems unlikely given the delayed onset of the macular edema, with the fluid being detected 18 weeks after surgery in the left eye and 12 weeks after surgery in the right eye — uncharacteristically long intervals for pseudophakic CME. However, we do not know the precise time when the fluid first developed. Even if these cases represented postoperative pseudophakic CME, an inflammatory rather than a neovascular process, the edema should be responsive to anti-VEGF therapy, as is typical CME.

In this report, we present edema within thick ERMs that is responsive to anti-VEGF therapy. The membranes in our patients share many SD-OCT characteristics with vitreoretinal membranes that have been previously described but are distinguished by the presence of intramembranous fluid and by the ocular comorbidities in our patients, which may predispose to more complex ERM formation. Further histopathologic studies of these membranes are needed to identify whether a vascular component arises from the retina and is responsible for the bevacizumab-responsive epiretinal fluid.

REFERENCES