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Epidemiology of Epiretinal Membrane in a Large Cohort of Patients with Uveitis

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Objective: To identify clinical characteristics associated with the presence of epiretinal membrane (ERM) in patients with uveitis.

Design: Case-control study.

Participants and Controls: Five hundred ninety-eight subjects seen in a single tertiary referral clinic between January 1, 2008, and December 31, 2011, who were diagnosed with uveitis.

Methods: Spectral-domain optical coherence tomography (SD OCT) images of all subjects were reviewed to assess for ERM. A multivariate logistic regression analysis was performed to compare characteristics of subjects with ERM (cases) with characteristics of subjects without ERM (controls). A second multivariate analysis assessed the relationship between ERM and visual acuity. Fundus photographs were reviewed to compare SD OCT ascertainment of ERM with photographic ascertainment.

Main Outcome Measures: Presence or absence of ERM on OCT imaging.

Results: Of 598 uveitic participants, 246 (41%) were found to have ERM in at least 1 eye on SD OCT imaging. The prevalence of ERM by Standardization of Uveitis Nomenclature anatomic subtype was 28.1% for anterior uveitis, 57.0% for intermediate uveitis, and 43.4% for posterior uveitis and panuveitis. Multivariate analysis showed that the following clinical factors were associated significantly with ERM: older age (3% increased risk per year of age; 95% confidence interval [CI], 1.02−1.05), intermediate uveitis (odds ratio [OR], 3.41; 95% CI, 1.67−6.96), posterior uveitis and panuveitis (OR, 1.81; 95% CI, 1.09−3.01), male sex (OR, 1.59; 95% CI, 1.05−2.42), and history of cataract surgery (OR, 1.78; 95% CI, 1.13−2.79). When adjusted for covariates, eyes with ERM had a mean logarithm of the minimum angle of resolution visual acuity of 0.58 (20/76) versus 0.48 (20/60) in non-ERM eyes ($P = 0.039$). Of OCT-defined ERMs in this cohort, 38% were not detectable on fundus photographs.

Conclusions: Epiretinal membrane is a common complication of uveitis that is associated with patient age, intermediate uveitis, posterior uveitis, panuveitis, male sex, and previous cataract surgery. It can contribute independently to vision loss in uveitic eyes. In uveitis, OCT is more sensitive than fundus photography for identification of ERM. *Ophthalmology 2014;121:2393-2398 © 2014 by the American Academy of Ophthalmology*

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Epiretinal membrane (ERM) is common in uveitis,[1] and it can cause loss of visual acuity, metamorphopsia, and micropsia. Large studies of ERM to date predominantly address idiopathic ERM, a condition associated with aging and posterior vitreous detachment.[2] Epiretinal membranes that are associated specifically with uveitis seem to differ from idiopathic ERM in cellular composition, suggesting that they may emerge through a different pathogenic mechanism.[3] Nazari and Rao[4] and Nazari et al[5] reported that most uveitic eyes with ERM did not lose vision over 1 to 2 years of follow-up and that thinner ERMs are associated with better visual acuity.

Studies of ERM traditionally have relied on gradings of color fundus photographs for the identification and characterization of ERM.[2,6–9] In fact, some recent epidemiologic studies of ERM have maintained this approach.[10,11] However, it has been reported that optical coherence tomography (OCT) may be more sensitive for detection of ERM than color fundus photography.[12] The use of OCT for ERM detection and characterization may have additional advantages in studying uveitic ERMs because of the high prevalence of media opacities that can prevent clear visualization of fundus features on color photography.

In the current study, we used an OCT-based definition of ERM to examine the prevalence of ERM in uveitis and to evaluate clinical characteristics that may be associated with its presence, including patient age, duration of uveitis, anatomic classification of uveitis based on Standardization of Uveitis Nomenclature criteria,[13] and lens status.

Methods

The National Eye Institute electronic medical records were queried for the signatures of physicians who treat uveitis patients to compile a database of all patients with uveitis seen between January 1, 2008, and December 31, 2011. Each patient chart

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was reviewed by the investigators to confirm the diagnosis of uveitis. Masquerade syndromes, including primary intraocular lymphoma, were excluded. The Cirrus spectral-domain (SD) OCT (Carl Zeiss Meditec, Jena, Germany) database then was reviewed for each patient to assess for the presence of ERM, and subjects without SD OCT data were excluded. Cases of ERM and controls thereby were identified, and a retrospective case-control study was conducted. The study was carried out under an institutional review board-approved clinical research protocol, and chart review was conducted in accordance with the Health Insurance Portability and Accountability Act and the Declaration of Helsinki.

Epiretinal membrane was diagnosed based exclusively on SD OCT findings. Epiretinal membrane was defined as follows: hyperreflective signal at the inner retinal surface and evidence of contractility. Therefore, a hyperreflective signal that conformed to the natural contour of the inner retina did not qualify as ERM (Fig 1A). Evidence of contractility included any distortion, corrugation, or flattening of the inner retina (Fig 1B).

All ERMs were within the macula. The macula for the purposes of this study was defined as the full extent of the Cirrus 512×128 (6×6 mm) macular cube. The full cube scan was reviewed for each eye. If the cube was decentered or captured the arcuate nerve fiber layer at the arcades, ERM that involved only nonmacular portions of the scan were not included. Reviewers could refer to raster scans for additional data in the event of poor signal strength on the cube scan or to confirm signs of contractility. Reviewers were masked to the patient's chart and therefore to prior clinical assessment of patient features.

The National Eye Institute electronic medical record of each subject was reviewed for several parameters to assess for suspected risk factors for ERM in uveitis: age, sex, race, anatomic classification of uveitis, etiologic diagnosis, duration of uveitis, best-corrected visual acuity, presence of diabetes mellitus, systemic corticosteroid use, steroid-sparing drug use, activity of intraocular inflammation on the date of the OCT, and lens status. Several additional parameters were recorded for subjects with ERM: OCT central retinal thickness, OCT macular volume, presence or absence of cystoid macular edema, presence or absence of chorioretinal scarring on color photographs, history of vitrectomy or other intraocular surgery, history of proliferative diabetic retinopathy, history of intraocular and periocular injections, and history of retinal laser treatment. All central retinal thickness and macular volume values were verified by the OCT graders, and manual segmentation was performed when automated segmentation was inadequate.

Statistical Analysis

A multivariate logistic regression analysis was performed to assess for clinical characteristics associated with ERM. In this model, characteristics of subjects with ERM (cases) were compared with characteristics of subjects without ERM (controls). Variables for the model were chosen based on an exploratory age- and sex-adjusted logistic regression analysis of 26 characteristics.

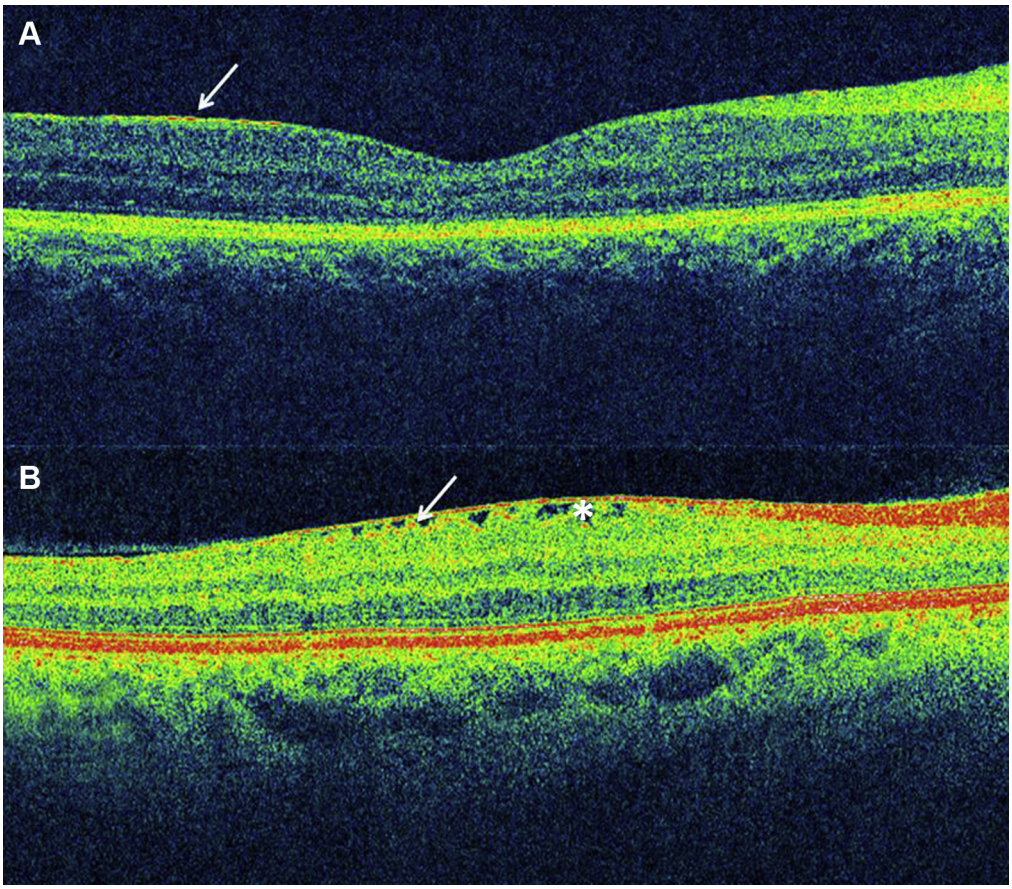

Figure 1. Optical coherence tomography images used to define epiretinal membrane. **A**, Hyperreflective inner retinal signal (arrow) conforms strictly to the natural contour of the inner retina. This finding did not meet our definition of epiretinal membrane. **B**, To meet our definition, evidence of contractility was required, such as distortion of the inner retinal contour (arrow) and spanning of gaps in the inner retinal contour (asterisk).