Table 2. Cox Proportional Hazards Model Results for First Diagnosis of Age-Related Macular Degeneration During Follow-up in Matched Vitamin D– and Non–Vitamin D–Deficient Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonneovascular</th>
<th>Neovascular AMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D deficiency</td>
<td>1.023 (0.904-1.157)</td>
<td>1.058 (0.770-1.453)</td>
</tr>
<tr>
<td>Age</td>
<td>1.044 (1.031-1.056)</td>
<td>1.039 (1.010-1.069)</td>
</tr>
<tr>
<td>Male</td>
<td>0.793 (0.681-0.924)</td>
<td>1.173 (0.824-1.672)</td>
</tr>
<tr>
<td>Black</td>
<td>0.472 (0.360-0.620)</td>
<td>0.273 (0.111-0.670)</td>
</tr>
<tr>
<td>Other race</td>
<td>0.708 (0.497-1.008)</td>
<td>0.832 (0.366-1.889)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.946 (0.809-1.105)</td>
<td>0.745 (0.499-1.111)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.942 (0.776-1.143)</td>
<td>0.987 (0.579-1.686)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.043 (0.854-1.247)</td>
<td>0.974 (0.591-1.665)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1.149 (0.971-1.359)</td>
<td>1.349 (0.934-1.948)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.124 (0.964-1.311)</td>
<td>0.701 (0.465-1.056)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.278 (1.075-1.519)</td>
<td>0.983 (0.645-1.497)</td>
</tr>
<tr>
<td>History of smoking counseling</td>
<td>1.216 (1.018-1.453)</td>
<td>1.499 (0.976-1.081)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index score</td>
<td>0.976 (0.955-0.998)</td>
<td>1.027 (0.976-1.081)</td>
</tr>
</tbody>
</table>

Abbreviation: AMD, age-related macular degeneration.

Although more research is needed, our study did not find a statistically significant association between vitamin D deficiency and subsequent diagnosis of either nonneovascular or neovascular AMD.

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Familial adenomatous polyposis (FAP; OMIM #175100) is an autosomal dominant condition with multiple (>100) adenomatous colonic polyps developing at a mean age of 16 years.1 Colorectal carcinoma is inevitable without prophylactic colorectal surgery. Familial adenomatous polyposis is caused by germline mutation in the adenomatous polyposis coli gene (APC; GenBank NC_000005) at chromosome 5q21. These mutations are almost 100% penetrant. Familial adenomatous polyposis is associated with well-demarcated, cometi


Epiretinal Membrane and Retinal Pigment Epithelial Lesions in a Young Child and Detection of De Novo APC Mutation

A 17-month-old healthy boy had exotropia of the left eye. Family history was negative for gastrointestinal cancer. Ophthalmic examination revealed age-appropriate visual responses and central, steady, and maintained fixation in both eyes. A comitant, left exotropia of 15 prism dipters was noted. Ocular motility and anterior segment examination findings were normal in both eyes. Ophthalmoscopy revealed 4 RPE lesions smaller than 200 µm in diameter in the right eye and 6 RPE lesions 300 µm to 3.0 mm in diameter in the left eye. The lesions were round to cometioid in shape, and the larger lesions had a nonpigmented halo (Figure). A translucent, gray ERM causing mild vascular dragging and foveal distortion was noted in the left eye (Figure).

The RPE lesions in both eyes suggested a possibility of FAP, and sequencing of APC was performed with the parents' informed consent. This revealed a frameshift mutation (3793G>T), predicted to result in a truncated APC protein at amino acid position 1265 of APC. Mutations in this region of the gene are associated with polyposis.4 Both parents (father aged 36 years and mother aged 34 years) had normal testing results, implying de novo mutation in the child. Screening for gastrointestinal polyps has been recommended to begin when the child is 8 to 10 years old.
Comment. Familial adenomatous polyposis, attenuated FAP (<100 polyps), Gardner syndrome (FAP and extraintestinal osteomas and fibromas), and Turcot syndrome (FAP and medulloblastoma) are hereditary, precancerous, adenomatous polyposis syndromes caused by mutations in \(\text{APC}\). Early detection is the key to reducing mortality from colorectal cancer in these conditions. Ophthalmoscopy of at-risk children is recommended for early detection of \(\text{FAP}\) gene carrier status, and screening colonoscopy is recommended from age 10 years, although intestinal polyps have been reported as early as age 7 years.

Ethical concerns have been raised about presymptomatic genetic testing at an age when no intervention would be indicated. Kodish\(^5\) refers to the rule of earliest onset when testing children for cancer genes. We justify genetic testing in our patient because finding the mutation not only serves to emphasize the need for later gastrointestinal screening in the proband but also helps in determining the \(\text{APC}\) mutation status in first-degree relatives, who may not otherwise know they are at risk for colon cancer.

Epiretinal membrane, a degenerative condition most often detected in adults, is hypothesized to arise from fibrocytic transformation of RPE cells dispersed in the vitreous.\(^6\) In young patients, ERM is uniquely rare but can be found in inflammatory conditions and tumors such as combined hamartoma of the retina and RPE and neurofibromatosis type 2. To our knowledge, ERM has not been previously reported with FAP. Liou et al.\(^7\) found that the \(\text{APC}\) protein plays an important role in cell-cycle cessation and regulates the potential for RPE cells to migrate and proliferate. In a study of human and murine RPE, they noted that downregulation of \(\text{APC}\) resulted in RPE proliferation and differentiation into the RPE-like cells of ERM.\(^6\) We speculate that the ERM in our young patient could be related to the \(\text{APC}\) mutation and might have led to the left exotropia. We have no reason to explain its occurrence other than as hypothesized. Epiretinal membrane might be another, albeit uncommon, ophthalmic feature of FAP. We suggest that patients with RPE lesions consistent with FAP and patients known to have \(\text{APC}\) mutations be carefully screened for ERM.

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Figure. Fundus photographs from the initial visit show multiple, scattered, hyperplastic retinal pigment epithelial lesions (white arrows) that are small (<200-µm diameter) in the right eye (A) and small to medium sized (300-µm to 3-mm diameter) in the left eye (B) as well as an epiretinal membrane, causing minimal vascular dragging and foveal distortion, in the left eye (black arrow) (B). Fluorescein angiography confirmed these findings without related edema in the right (C) and left (D) eyes.
Intravitreal Bevacizumab for Peripapillary Choroidal Neovascular Membranes

Peripapillary choroidal neovascularization (PCNV) can result in significant vision loss due to extension of blood or fluid into the macula.1,2 Treatment options for PCNV have included laser photocoagulation, subretinal surgery, and photodynamic therapy.1,3,4 More recently, the use of intravitreal anti–vascular endothelial growth factor antibodies has emerged as the optimal treatment for macular CNV due to age-related macular degeneration, presumed ocular histoplasmosis, myopia, angioid streaks, and traumatic choroidal rupture,5,6 but clinical trials almost exclusively included patients with subfoveal CNV. The purpose of this study was to review cases of PCNV treated with intravitreal bevacizumab.

Methods. Institutional review board approval was obtained. The Institutional Review Board for Human Subjects Research, University of Iowa, waived informed consent for this retrospective record study. The study was compliant with the Health Insurance Portability and Accountability Act of 1996 and adhered to the tenets of the Declaration of Helsinki. Data from records of patients who received 1.25-mg intravitreal bevacizumab injections at the University of Iowa between September 12, 2008, and March 21, 2011, were retrospectively reviewed. Patients were included if they demonstrated a new, previously untreated PCNV confirmed by fluorescein angiography and subretinal or intraretinal fluid on optical coherence tomography (OCT) and had at least 6 months of follow-up. Patients with vision loss from other non-PCNV causes were excluded. Resolution of PCNV was determined by the absence of intraretinal or subretinal fluid on examination and OCT. Recurrence was defined as new subretinal or intraretinal fluid detected by OCT or hemorrhage detected by ophthalmoscopy.

Results. Twenty eyes from 19 patients met the inclusion criteria. The average patient age was 70.6 years (range, 26-94 years). Causes of PCNV included AMD in 12 eyes, presumed ocular histoplasmosis in 6 eyes, traumatic choroidal rupture in 1 eye, and idiopathic PCNV in 1 eye. Fifteen of 20 eyes had peripapillary fluid on OCT within 1 disc area from the disc without any subfoveal fluid. Only 5 eyes had subfoveal fluid. Sixteen had peripapillary fluid located temporal to the optic nerve, 3 had it located superiorly, and 1 had it located inferiorly. The follow-up averaged 13.5 months (range, 6-32 months).

An average of 5.6 total injections (range, 2-14 injections) were performed. Complete resolution of intraretinal and subretinal fluid on OCT was achieved in 17 of 20 eyes (85%) after an average of 2.4 intravitreal injections (range, 1-5 intravitreal injections) (Figure). Subsequently, there were an average of 2.7 injections (range, 0-10 injections) (Figure). Although some of these were given for maintenance therapy, 5 of 17 eyes developed recurrent fluid on OCT at an average of 8.3 months following the last injection (range, 4.5-15 months). The recurrent cases included 4 eyes with AMD and 1 eye with presumed ocular histoplasmosis. The fluid did not resolve completely in 3 of 20 eyes (15%). Six of 8 non-AMD cases remained dry after treatment throughout follow-up (Figure).

The preinjection visual acuity averaged 20/40 (range, 20/20-20/100). The postinjection visual acuity averaged 20/30 (range, 20/15-20/60). In eyes with sustained fluid or recurrent fluid, vision at the final follow-up examination remained stable compared with their baseline visual acuity. Of the 112 total injections given, there were no adverse events related to treatment. The injection visual acuity averaged 20/40 (range, 20/20-20/100). The postinjection visual acuity averaged 20/30 (range, 20/15-20/60). In eyes with sustained fluid or recurrent fluid, vision at the final follow-up examination remained stable compared with their baseline visual acuity. Of the 112 total injections given, there were no adverse events related to treatment.

Comment. In our study, 17 of 20 eyes (85%) achieved resolution of the fluid after an average of 2.4 intravitreal injections of bevacizumab, and 5 of these had recurrent fluid. Visual acuities improved by an average of 5 letters or 1 line of Snellen visual acuity after an average of 13.5 months of follow-up, and only 1 patient lost vision limited to 1 line (Table).

Overall, it is our impression that PCNV responds to intravitreal bevacizumab with reduction of retinal fluid and improvement or preservation of vision comparable to other treatment modalities.1 However, our results are limited by the relatively short term of the study. In PCNV cases of recurrent or incomplete fluid resolution, intravitreal bevacizumab may still shrink lesions prior to other treatment. Further prospective and comparative studies...