Age-Related Choroidal Atrophy

RICHARD F. SPAIDE

• PURPOSE: To report the clinical characteristics of a newly defined entity, age-related choroidal atrophy.
• DESIGN: Retrospective, observational case series.
• METHODS: The choroidal thickness was measured in images obtained by positioning a spectral-domain optical coherence tomography device close enough to the eye to acquire an inverted image. Seven sections each comprised of 100 averaged scans were obtained within a 5 × 15-degree or larger rectangle to encompass the macula and temporal juxtapapillary retina. The choroidal thickness of patients less than 125 μm in thickness were included, whereas eyes with myopia of 6 diopters or more, a history of uveitis, trauma, ionizing radiation, or tapetoretinal dystrophy were excluded. The patients were evaluated for visual acuity, macular appearance, and the presence of glaucoma.
• RESULTS: There were 28 eligible eyes of 17 patients with a mean age 80.6 years (standard deviation, ±7.3 years). All eyes had a tessellated fundus appearance. The mean subfoveal choroidal thickness was 69.8 μm and became even more attenuated nasally. Of the 18 eyes that had no evidence of late age-related macular degeneration (AMD), the mean visual acuity was 20/40, there were rarefaction of the choroidal vessels under the macula, and the choroid potentially mimicking early AMD, and a rarefaction of the choroidal vessels under the macula. Concurrent late AMD was found in the 10 remaining eyes. Glaucoma was present in 6 patients (35.3%), all of whom had peripapillary atrophy. The choroid was seen to become nearly obliterated before the demarcation of the β-zone of peripapillary atrophy.
• CONCLUSIONS: Age-related choroidal atrophy affects older individuals in whom posterior pole abnormalities develop that may mimic and also be associated with findings typical for AMD. Patients with age-related choroidal atrophy may be at higher risk for glaucoma.

A GE-RELATED MACULAR DEGENERATION (AMD) IS A leading cause of vision loss in not only developed, but also in developing countries.1–4 The initial manifestations of the condition, drusen, focal hyperpigmentation, and focal hypopigmentation, are elements defining the category early AMD. These findings precede the development of more visually significant forms of the disease, either geographic atrophy or choroidal neovascularization (CNV), which are categorized as late AMD. Assessment of eyes for features of AMD is carried out either by clinical examination or evaluation of fundus photographs. Formal studies depend on protocol evaluation of fundus photographs, and the protocols used are structured reproducible methods based, in part, on what happens during careful clinical examination. The features and the methods used to grade them intend to classify and discriminate accurately levels of severity of AMD plus other concurrent factors or diseases. The chosen features expected for AMD and the confounding conditions are based on established concepts of the pathophysiologic features of disease. For example, disturbances of the retinal pigment epithelium (RPE) occur commonly in AMD, and these disturbances, according to the Wisconsin Age-Related Maculopathy Grading System,5,6 a widely used protocol method of evaluating fundus photographs, can “lead to deposition of granules or clumps of pigment in or beneath the retina.” The pigmentation grading system has the implied assumption that pigmentary changes are attributable to disturbances of the RPE.

The retina, particularly the photoreceptor layer, has a very high metabolic demand for oxygen, which is supplied by the underlying choroid, a structure with one of the highest blood flow per gram of tissue in the body.7 The choroid is located behind the RPE and also is pigmented. The pigmentation generally impedes visualization of the full-thickness of the choroid by ophthalmoscopy, fundus photography, fluorescein angiography (FA), or conventional optical coherence tomography (OCT). As such, the choroid is not frequently mentioned as participating in vision loss except for being the source of CNV. Recently, a method to obtain enhanced depth imaging (EDI) spectral-domain OCT has been developed that enables the cross-sectional structure and thickness of the choroid to be evaluated.8 EDI OCT was used to examine healthy eyes with no visual problems attributable to the macula, and the choroid thickness was found to decrease approximately 16 μm per decade of life.9 The thinnest subfoveal choroidal thickness measured among that series of 54 eyes was 159 μm. However, because EDI OCT became available, a...
subset of patients who were considered to have AMD and who had reported visual symptoms were found to have remarkably small choroidal thicknesses. Many of the eyes eventually were found to have no significant macular or RPE problems, although others were found to have concurrent geographic atrophy and CNV. Because the finding of the markedly thin choroid was found in elderly people with visual symptoms that occurred relatively recently over the course of their lives, this finding was thought to be acquired; as such the entity was termed age-related choroidal atrophy. The purpose of this study was to determine the features of age-related choroidal atrophy by cataloguing the findings of a series of eyes with this condition.

METHODS

THIS WAS A RETROSPECTIVE STUDY OF PATIENTS WHO underwent EDI OCT of the choroid in a private referral retinal practice during a 10-week period ending in August 2008. The method of obtaining EDI OCT images has been reported previously, as have the nomographic data. Conventional spectral-domain OCT has limitations in imaging deeper structures in the fundus because of depth-dependent sensitivity decay related to decreasing sensitivity and resolution with increasing displacement from zero-delay, diminished maximal dynamic range inherent in performing the Fourier transform after analog-to-digital conversion, and wavelength-dependent light scattering and signal loss in the image path. EDI OCT is performed by placing the instrument close enough to the eye to obtain an inverted image. This image is averaged for 100 scans, which in this study was obtained using the Heidelberg Spectralis (Heidelberg Engineering GmbH, Heidelberg, Germany) because of its automatic averaging and eye tracking features. Seven sections, each comprised of the 100 averaged scans, which in this study was obtained using the Heidelberg Spectralis (Heidelberg Engineering GmbH, Heidelberg, Germany) because of its automatic averaging and eye tracking features. Seven sections, each comprised of the 100 averaged scans, was obtained in a 5 × 30-degree rectangle encompassing the macula and optic nerve or a 5 × 15-degree rectangle centered on the macula.9 The resultant images were viewed and measured with the contained Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering). The subfoveal choroid was measured from the outer portion of the hyperreflective line corresponding to the RPE to the inner surface of the sclera. In eyes with CNV, the subfoveal choroidal thickness was measured between the Bruch membrane, which was visible in all such cases, and the inner portion of the sclera. The appearance of the choroid over the full-length of the scan was inspected as well.

In a previous study of the choroidal thickness, the mean subfoveal choroidal thickness was 287 μm ± a standard deviation of 75.7 μm.9 Two standard deviations less than the mean is 135.6 μm. However, the subfoveal choroidal thickness was found to decrease with age, so an arbitrary limit of 125 μm was chosen for the purposes of this study to be certain the eyes were quite different than what would be obtained from random sampling of a normal population. Patients were included in this study if at least 1 eye had a choroidal thickness of less than 125 μm. For the purposes of illustration, the images were reinverted in Photoshop (Photoshop CS3; Adobe Systems Inc, San Jose, California, USA). The patients were evaluated with a comprehensive ophthalmoscopic examination including best-corrected Snellen visual acuity (VA) measurement, fundus photography, and fluorescein and indocyanine green angiography, as indicated. Patients were excluded if they had any previous photodynamic therapy, intravitreal corticosteroid injection, history of myopia of more than 6 diopters spherical equivalent, amblyopia, proliferative retinopathies of any type, epiretinal membrane that caused distortion of the central macula, history of retinal detachment (RD), uveitis, tapetoretinal dystrophy, ocular trauma, ocular tumor, ionizing radiation, submacular surgery, transpupillary thermotherapy, focal laser, angioid streaks, use of any systemic or ocular corticosteroids, central serous chorioretinopathy, or any retinovascular abnormalities.

The eyes were classified as having late AMD if they had signs of CNV or central geographic atrophy. Eyes with late AMD were entered into the dataset only if they had new-onset disease or if the fellow eye had no late AMD and a choroidal thickness of less than 125 μm. Peripapillary atrophy was graded as per the method outlined by Jonas and associates.10 (Peripapillary atrophy had been referred to as parapapillary atrophy in earlier publications.10-15) Peripapillary atrophy was considered to be present only if there was a B-zone of atrophy, which was thought to represent full-thickness atrophy of the RPE and choroid.15 VAs were converted to logarithm of the minimum angle of resolution (logMAR) units before to any calculations.

RESULTS

THERE WERE 17 PATIENTS WITH A MEAN AGE 80.6 YEARS (± 7.3 years). Of the potential 34 eyes, 6 were excluded because of past photodynamic therapy to the macula, amblyopia, trauma, or history of RD repair. A diagnosis of glaucoma was present in 6 patients (35.3%). The mean VA in the total group of eyes was 20/53 (logMAR units, 0.42; right eye, 20/63; left eye, 20/46). The findings of eyes with age-related choroidal atrophy with no signs of late AMD at presentation will be reported separately from

FIGURE 1. Enhanced depth imaging (EDI) optical coherence tomographic (OCT) scan of a normal eye.
those eyes that did. Some patients had 1 eye in each group. Figure 1 shows a normal eye for sake of comparison.

**AGE-RELATED CHOROIDAL ATROPHY WITH NO SIGNS OF LATE AGE-RELATED MACULAR DEGENERATION:** There were 18 eyes among 13 patients with a mean age of 79.7 years; of these, 5 patients (38.5%) had at least 1 eye diagnosed with glaucoma. Peripapillary atrophy was seen in 13 eyes (72.2%), reticular pseudodrusen in 12 eyes (66.7%), and glaucoma in 6 eyes (33.3%). No eye had glaucoma without having peripapillary atrophy. The mean VA was 20/40 (logMAR units, 0.3; right eye, 20/36; left eye, 20/43). All patients had a tessellated appearance of the peripheral fundus. In the macular region, patients had 2 types of pigmentary change. The first type seemed to be an extension of the tessellated fundus appearance into the central macular region with varying amounts of pigment loss. The larger choroidal vessels were seen with polygonal patches of intervening pigment, which in some eyes was seen to be diminished. The second was a pigmentary clumping deep to the retina (Figure 2). Because the choroidal thickness was seen to be attenuated and areas of what looked like sclera were visible under the pigment. Given the EDI OCT findings of severe choroidal thickness diminution, it was not possible to be sure if the pigmentary changes were entirely at the level of the RPE or also originated from the choroid. The autofluorescence photographs in all these patients showed no focal defects suggestive of RPE atrophy or absence in the posterior pole. The EDI OCT findings in both pigmentary phenotypes were marked reduction in the thickness of the choroid under the central fovea and particularly nasal to the fovea. The juxtapapillary choroid approaching and particularly within the β-zone of the peripapillary atrophy was so thin it was not possible to measure it accurately. The choroidal thickness did not show a sharp change in thickness at the demarcation of the β-zone of peripapillary atrophy. Medium-sized choroidal vessels were seen sporadically, and these vessels occupied the full-thickness of the choroid. Each eye had areas in which the larger choroidal vessels either were sheathed or had no visible blood column.

**Case 1.** An 85-year-old man was referred because of a chronic RD in the left eye despite numerous reattachment procedures. He had numerous visual symptoms in the right eye and had a VA of 20/30. In the right eye, there was depigmentation of the fundus with large choroidal vessels being easily visible and intervening areas where no pigment was seen (Figure 3). The patient had peripapillary atrophy despite being emmetropic. There was nerve pallor and violation of the inferior-superior-nasal-temporal rule for normal rim thickness. The nerve fiber layer thickness...
as measured using the Stratus OCT (Humphrey Meditec, New Dublin, California, USA) was less than 1 percentile inferiorly. He was found to have a superior arcuate visual field defect. His mean intraocular pressure (IOP) measurement was 14 mm Hg and highest recorded IOP was 17 mm Hg. The patient had a choroidal thickness of 74 μm.

**Case 2.** An 85-year-old man reported blindness at presentation. He said he had difficulty functioning outside in bright daylight, he had a very hard time reading, and he could not see well in dim environments. He had a long-term history of hypertension and a 70 pack-year smoking history. He lost his right eye to trauma at an early age and had a diagnosis of glaucoma in the remaining eye (Figure 4). The VA in the remaining eye was 20/80. Threshold visual field testing showed a shallow depression in the central field, no arcuate defects, nor nasal step defects. The macula showed pigmentary disturbance with focal areas of pigmentation and depigmentation. There were a few small-diameter choroidal vessels visible through the pigmentation. The optic nerve was pallorous, had thinning of the neural rim, and was surrounded by peripapillary atrophy. The fundus autofluorescence was relatively intact. The patient was seen to have reticular pseudodrusen by infrared scanning laser ophthalmoscopy. The EDI OCT showed the subfoveal choroid to be 45 μm thick.

**Age-Related Choroidal Atrophy with Signs of Late Age-Related Macular Degeneration:** There were 10 eyes in 8 patients with a mean age of 83.3 years. The mean VA was 20/89 (logMAR units, 0.65; right eye, 20/152; left eye, 20/54). The eyes developing CNV in retrospect seemed to require infrequent injections of anti-vascular endothelial agents to maintain a stable macular appearance (Figure 5).

**Case 3.** A 90-year-old woman had new-onset CNV in the left eye with a VA of 20/30 and long-standing CNV in the fellow eye. She had 2 small dots of hemorrhage and areas of focal hyperpigmentation in the macula (Figure 6). FA showed subtle leakage from occult CNV. The patient had reticular pseudodrusen seen during infrared scanning laser ophthalmoscopy. EDI OCT showed no subretinal fluid, intraretinal edema, or evidence of cystoid changes within the macula. The choroidal thickness was 64 μm under the fovea, was attenuated nasally, and was extremely thin in the area of peripapillary atrophy.

**Case 4.** An 85-year-old woman had a history of what ophthalmoscopically looked like geographic atrophy (Figure 7). This began with small areas of noncentral geographic atrophy associated with pigmentary changes. Over a 2-year follow-up, she was seen to have increasing geographic atrophy that abutted the central fovea. She was
never seen to have any signs of exudation during follow-up. However, the FA pattern was not entirely consistent with simple geographic atrophy in that there was a subtle region of late staining outside of the areas of atrophy, and the atrophic regions themselves were not uniformly hyperfluorescent. She was seen to have reticular pseudodrusen outside of the macular region. Although EDI OCT showed a markedly thin choroid outside of the central macula, under the central macula the patient had an accumulation of hyperreflective material between the line attributed to the RPE and the one consistent with the Bruch membrane. The patient never had soft drusen. The possibility that the eye had an inactive form of occult CNV could not be ruled out.

**DISCUSSION**

In this study, elderly patients with decreased choroidal thicknesses had pigmentary changes and a paucity of visible choroidal vessels. The recent onset of their visual symptoms as compared with their age and the knowledge...
that choroidal thickness seems to decrease with increasing age suggests that the thinness of the choroid was an acquired disorder. The loss of choroidal thickness was associated with loss of visible vessels, implying that age-related choroidal atrophy is a manifestation of small-vessel disease affecting the choroid. The proportion of patients in the present study group having glaucoma seems to be higher than similarly aged historical controls. Some eyes showed associated late AMD as well. The supposition that choroidal vascular disease could cause vision problems is not new. The appearance of vascular sheathing or obliteration of the choroidal vascular channels has been called senile choroidal sclerosis. Histopathologic study of these patients found profound atrophy of the choroid with loss of small and medium vessels to the point that the Bruch membrane immediately was contiguous with the sclera in areas and the remaining larger vessels of the choroid occupied the full-thickness of the remaining choroid in others. There was a loss of the expected pigmented cells in the choroid with clumping of preserved pigmented cells in various regions in the choroid. Histopathologic study of reticular pseudodrusen showed loss of the inner and middle layers of the choroid. The finding of fundus tessellation (also known as a tigroid fundus) in this series of patients may have been the result of choroidal atrophy with baring of larger vessels, which ordinarily are deep in the choroid. The patients in the present study had pigmentary abnormalities in the macular region, thus suggesting the diagnosis of AMD. The retina and RPE are derived from the same progenitor cells, and specific deterioration in structure and function in this tissue is termed age-related macular degeneration. The choroid is derived from different embryologic precursors. In age-related choroidal atrophy, the macular function is undoubtedly decreased, but the primary abnormality appears to be in the choroid. The proportion of patients with glaucoma was higher than that seen in similarly aged groups of patients in

FIGURE 5. Images showing choroidal neovascularization (CNV) in eyes with age-related choroidal atrophy. (Top left) Fundus photograph from a 79-year-old female patient had CNV diagnosed 2 years previously when she had a subretinal hemorrhage and fluorescein angiographic (FA) findings of occult CNV. She received 1 injection of intravitreal bevacizumab and experienced a complete resolution of her exudative manifestations. She had a diagnosis of glaucoma. (Top right) EDI OCT image showing minimal thickening at the level of the RPE and a subfoveal choroidal thickness of 49 μm. The VA was 20/30. (Bottom left) Fundus photograph from an 82-year-old female patient with had a diagnosis of occult CNV made by FA years previously, but because of no signs of exudation, never underwent treatment. Eight months previously, subretinal bleeding finally developed in the patient, who was treated with intravitreal bevacizumab. Note the lack of visible scarring. (Bottom right) EDI OCT image showing the subfoveal choroidal thickness was 85 μm. The VA was 20/40.
large population studies. The high prevalence of glaucoma may represent sampling variation given the small number of eyes, but there are anatomic features that may offer a potential explanation for the association. The blood supply to the prelaminar portion of the optic nerve is derived in part from the choroid. The presence of peripapillary atrophy is highly associated with the diagnosis of glaucoma, particularly low-tension glaucoma. Glaucoma does not cause peripapillary atrophy; optic nerve damage does not lead to peripapillary atrophy, either. The size of peripapillary atrophy has been correlated spatially with the area of neuroretinal rim loss in glaucoma. Curiously, the presence of peripapillary atrophy was found to be associated with the tessellated fundus appearance. It is possible that optic nerve perfusion is influenced by a large number of factors, including IOP and the availability of blood supply. Eyes with choroidal atrophy to the point of peripapillary atrophy formation are likely to have profound decreases in the choroidal contribution of blood supply to the prelaminar optic nerve. It is also possible that patients with marked choroidal thinning also have concurrent small-vessel disease to the prelaminar optic nerve arising from other sources. To the extent that optic nerve perfusion influences the development of glaucomatous damage, it is likely that patients with age-related choroidal atrophy have lesser amounts of perfusion than do people with normal choroidal configurations. Glaucoma has been associated with choroidal sclerosis and (given the age of the publication) was termed senile sclerotic glaucoma. The present method of EDI OCT measurement of the choroidal thickness offers the possibility of objective quantification of the choroid and its relationship to glaucoma.

A large number of visual problems appear in older people, some of which seem difficult to explain. Certainly optical problems can cause decreased acuity, but none of the patients in this study had significant cataracts. Age is associated with a decrease in the number of rods present in the retina, but not the number of cones, which are responsible for central vision. The mean acuity in the age-related choroidal atrophy eyes without any signs of late AMD was 20/40. Although several had glaucoma, none of the patients had absolute scotomata, particularly none near fixation. One potential cause for the observed decrease in acuity, and reported visual function, was the observed atrophy of the choroid in these patients. Decreased VA secondary to CNV was seen in the affected patients in this study. The curious finding in Case 4 as illustrated in Figure 7 was the presence of areas of geographic atrophy associated with a plaque of hyperreflective material under the RPE that seemed to be consistent with a relatively inactive form of CNV. This material is not likely to have been accumulations from basal linear deposit or the like, because the patient was never seen to have
FIGURE 7. Images showing age-related choroidal atrophy with geographic atrophy and probable CNV in an 85-year-old female with a macular scar in the fellow eye from long-standing CNV. (Top left) Fundus photograph obtained 2 years before the EDI OCT scan showing that the patient had focal hyperpigmentation and small areas of noncentral geographic atrophy. There appeared to be a paucity of choroidal vessels in the macular region. (Top right) Fundus photograph obtained 2 years later showing more areas of geographic atrophy, but the patient retained 20/40 VA. She was never seen to have large soft drusen or any evidence of CNV. Note that the lack of large choroidal vessels evident through the apparent areas of geographic atrophy. (Second row left) Late-phase FA showing transmission defects associated with some of the areas appearing to be geographic atrophy. Note that there is a relative hypofluorescence of 1 region (arrow) as compared with the other areas and that the region inferonasal to the atrophic areas shows a subtle increase in fluorescence. (Second row right) Infrared scanning laser opthalmoscopic image showing the zones of what appear to be geographic atrophy and reticular pseudodrusen supertemporally. (Third row) EDI OCT image of the central macula through the fovea showing a layer of hyperreflective material between the boundary of the outer retina (top arrowhead) and the Bruch membrane (bottom arrowhead). Note the underlying choroid is thin with the choroidal thickness at the centerline of the arrowheads of 78 μm. (Bottom row) EDI OCT image taken well inferior to the geographic atrophy showing a thin choroid.
There are likely many causes of CNV in AMD, but Grossniklaus and Green postulated that for some patients, decreases in the ability of the choroid to deliver oxygen and other metabolites to the retina may lead to the growth of the neovascular tissue that “recapitulates the choriocapillaris [sic] and, theoretically, provides nutrients and oxygen to an ischemic RPE/outer retina that is expressing vascular endothelial growth factor.”

There are numerous weaknesses of the present study. It was a retrospective study examining a relatively small number of patients using a new imaging technique in a retinal referral practice. Therefore, no estimates of the prevalence of this condition can be made from this study. However, the findings using a noninvasive method mirrored those of reported histopathologic cases of autopsy eyes, similar information cannot be obtained by alternate means of imaging, and the cases were obtained in a short time frame. The cut-off used for choroidal thickness, namely 125 μm, was derived in part from examining the choroidal thicknesses of normal people, and does not represent an absolute demarcation. It is likely that decreasing choroidal thickness could represent an increasing risk for retinal and optic nerve pathologic features, and values of choroidal thickness larger than what have been examined in this study may portend some increase in risk. The cut-off in the present study was chosen to isolate a pure form of age-related choroidal atrophy and its associated findings. There are many subsequent studies that are indicated, including the choroidal thickness in patients with glaucoma, particularly low-tension glaucoma, geographic atrophy, and CNV, and the response to treatment of these diseases.

REFERENCES

20. Rudnicka AR, Mt-Isa S, Owen CG, et al. Variations in primary open-angle glaucoma prevalence by age, gender,