Extensive Macular Atrophy with Pseudodrusen-like Appearance: A New Clinical Entity

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• PURPOSE: **To describe a previously unreported clinical entity of progressive extensive macular atrophy and pseudodrusen-like appearance in middle-aged patients.**

• DESIGN: **Clinical, electrophysiologic, and molecular retrospective study.**

• METHODS: **The database of an outpatient clinic unit for genetic sensory diseases was screened for patients older than 40 years with uncharacterized macular dystrophy. Patients with extensive macular atrophy and pseudodrusen-like appearance were included.**

• RESULTS: **Eighteen patients of 45 records (40%) matched the inclusion criteria. Bilateral polycyclic well-delineated chorioretinal atrophy extending to the temporal vascular arcades, with a larger vertical axis and without sparing of the fovea featured the macular lesion. The pseudodrusen-like appearance was widespread throughout the posterior pole and the peripheral retina. In the extreme periphery, paving stone lesions were located mostly in the inferior quadrants. In contrast to age-related macular degeneration, a rapid progression of the atrophy was observed with an early involvement of the foveal zone, thus leading to a severe visual loss. All the patients except 2 were legally blind at the end of the follow-up. Unlike age-related macular degeneration, in none of these patients did choroidal neovascularization develop. In all patients, the scotopic and photopic electroretinography responses were reduced.**

• CONCLUSIONS: **Extensive macular atrophy with pseudodrusen should be considered as a possible pattern of severe macular dystrophy occurring in the middle-aged adult.** (Am J Ophthalmol 2009;xx:xxx. © 2009 by Elsevier Inc. All rights reserved.)

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MACULAR GEOGRAPHIC ATROPHY INDUCES SIGHT-threatening complications that result in permanent central vision loss in patients with various macular disorders including inflammatory and infectious diseases, intoxication, hereditary conditions such as Stargardt disease, and most frequently, age-related macular degeneration (AMD).

The clinical course of the geographic atrophy in AMD has been well characterized.[1–12] After drusen deposits form,[1–3] multiple small round patches of atrophy occur in the perifoveolar region. The patches extend slowly toward confluence of the atrophy over the years.[4–8] The areas of atrophy tend to follow the disappearance or the flattening of soft drusen. In addition, the limits of the geographic atrophy generally do not extend beyond the foveal and perifoveal area, although this can occur in some patients at a late stage. Therefore, the atrophy eventually covers the entire foveal area and the patients become legally blind over the ensuing decade (age, 70 years).

In this study, 18 patients with an atrophic macular disorder resembling dry AMD but with a distinct clinical appearance are described. The main striking feature is the early onset of bilateral, symmetric macular atrophy, in average before the age of 50 years, with a rapid involvement of the fovea and of the entire posterior pole up to the temporal vascular arcades. This macular atrophy is surrounded by numerous drusen-like deposits spread throughout the posterior pole and the midperiphery in all cases. In addition, all patients have paving stone degeneration in the far periphery. A retrospective analysis of clinical, functional, and photographic records for these 18 patients is presented.

METHODS

• PATIENTS: The database of the outpatient clinic for genetic sensory diseases was screened for patients older than 40 years with uncharacterized macular dystrophy. These patients were referred to our clinic from 1990 through 2008 with the diagnosis of early dry AMD, central areolar choroidal dystrophy, or retinal dystrophy.

• METHODS: For each patient, the age at onset and at presentation, refraction, and initial and final visual acuity (VA) were noted. All patients were questioned about decreased central vision, poor night vision, loss of peripheral

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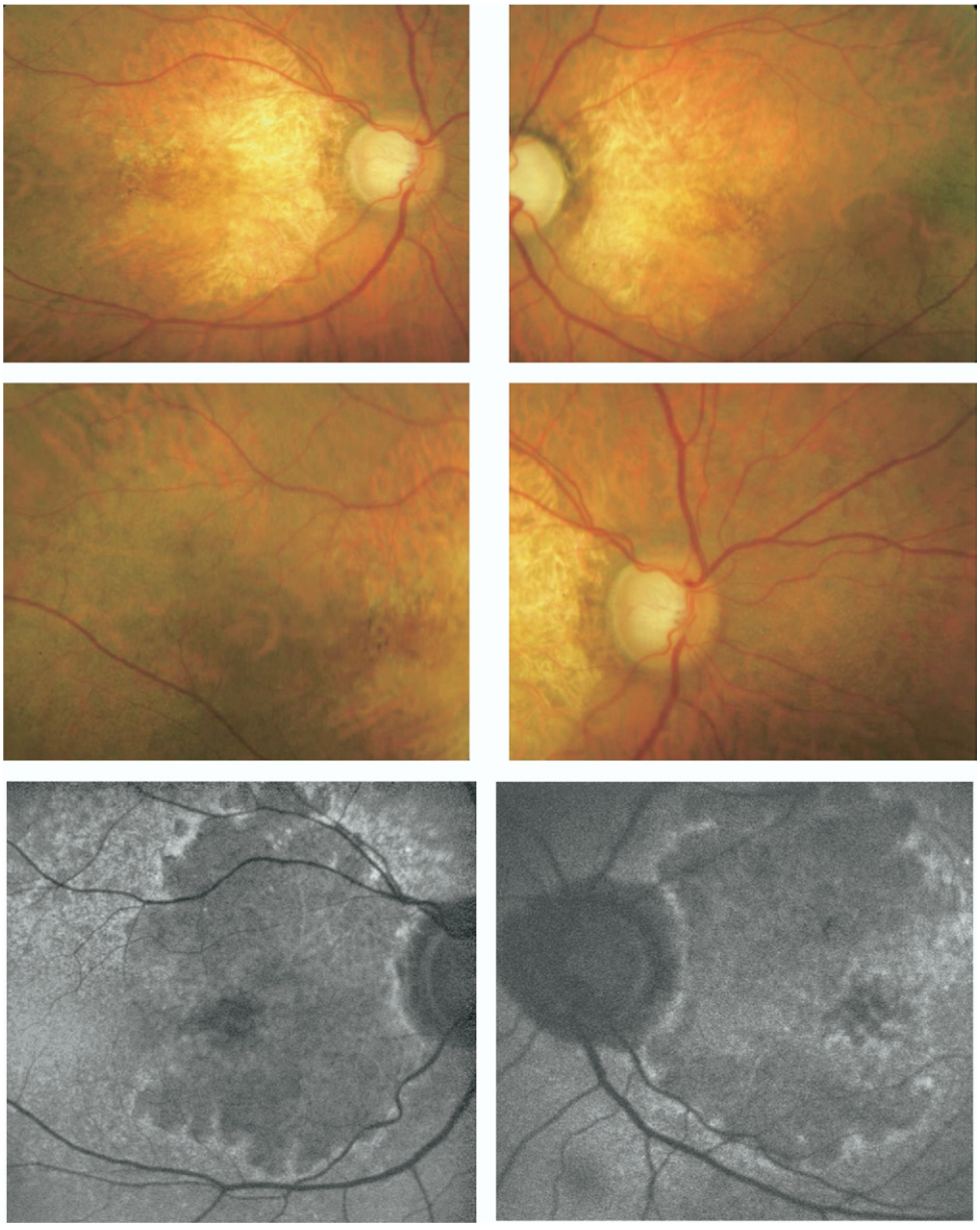

FIGURE 1. Images obtained from Case 1 (age, 56-year-old) showing extensive geographic macular atrophy. (Top) Fundus photographs of the (left) right and (right) left eyes demonstrating bilateral and extensive geographic atrophy with the largest vertical diameter and polycyclic limits. (Middle) Fundus photographs of the (left) temporal and (right) nasal midperipheral areas of the fundus from the right eye: drusen-like patterns mimicking clusters of small drusen are visible. (Bottom) Autofluorescence images showing well-delineated atrophy sparing the foveola and surrounded by a hypofluorescent pseudodrusen-like appearance in both eyes.

vision, and glare sensitivity. The best-corrected visual acuity (BCVA) was obtained with Snellen charts. Reading VA was assessed with the near vision Parinaud card. The patients underwent examination of the anterior segments with intraocular pressure (IOP) measurement.

Goldmann perimetry was performed using several isopters (stimuli V4e, III4e, I4e, I3e, I2e, I1e) and completed in some cases with static perimetry on a WIN8000F (Moniteur Ophtalmologique, Pérenchies, France). The Lanthony Farnsworth 15-Hue test was performed if VA was better than 20/200. Dark adaptation curves were obtained with the Goldmann Weekers adaptometer. Full-field electroretinography (ERG) was performed according to the guidelines of the International Society for Clinical Electrophysiology of Vision using a Ganzfeld apparatus (Ophthalmologic Monitor, Métrovision, Pérenchies, France). Color fundus imaging (Topcon Imagenet; Ophthalmic Imaging Systems, Tokyo, Japan) and autofluorescence imaging (Heidelberg Retina

TABLE 1. Summary of Clinical Data of Patients with Extensive Macular Atrophy with Pseudodrusen-like Appearance

Case No.	Gender	Age at Onset (yrs)	Age at Examination (yrs)	Symptoms	Refraction		Visual Acuity	
					Right Eye	Left Eye	Right Eye	Left Eye
1	M	45	56	Night blindness Photophobia	−5.5 (−1.25, 170 degrees)	−6 (−1, 0 degrees)	20/25	20/50
2	F	50	60	Night blindness Photophobia Vision decrease	−0.5 (−0.75, 40 degrees)	−0.5 (−0.25, 150 degrees)	CF	20/30
3	F	41	49	Night blindness Photophobia Vision decrease	−1.5 (−0.75, 0 degrees)	−2	20/50	20/100
4	F	45	55	Night blindness Photophobia	−3.75 (−1.25, 0 degrees)	−4 (−1.25, 0 degrees)	20/40	LP
5	M	50	56	Photophobia Dyschromatopsia Vision decrease	−2.75 (−0.5, 15 degrees)	−3 (−0.75, 45 degrees)	CF	20/30
6	F	50	55	Night blindness Photophobia	−10 (−1.5, 100 degrees)	−7 (−1, 60 degrees)	20/400	20/60
7	F	52	56	Vision decrease Scotoma	1 (−5, 154 degrees)	1.5 (−4.75, 30 degrees)	20/200	20/200
8	F	54	57	Photophobia Vision decrease Scotoma	−0.75 (−0.5, 175 degrees)	−0.5 (−0.75, 100 degrees)	20/400	20/100
9	F	48	52	Photophobia Scotoma	−6.25 (−1.25, 15 degrees)	−5.5 (−1.5, 150 degrees)	20/25	20/40
10	M	46	56	Night blindness Photophobia	−0.75 (−0.5, 150 degrees)	−1.75 (−0.5, 20 degrees)	20/30	20/25
11	F	48	53	Scotoma	(−0.75, 80 degrees)	0.25	20/200	20/400
12	M	40	50	Night blindness Photophobia	−2 (−2, 15 degrees)	−2.75 (−1.25, 165 degrees)	20/30	20/25
13	F	48	58	Night blindness Photophobia	−1.75 (−1.5, 180 degrees)	−1.75 (−1, 170 degrees)	20/200	20/200
14	F	—	48	Night blindness Photophobia	NP	NP	20/100	20/80
15	M	—	52	Photophobia	NP	NP	20/400	CF
16	M	—	51	Scotoma	−2.75 (−0.5, 25 degrees)	−3	20/20 (amblyopia)	20/30
17	F	—	45	Night blindness Photophobia	NP	NP	CF	CF
18	M	—	53	Photophobia Scotoma	−0.5	−0.5	20/100	20/60

CF = counting fingers; F = female; LP = light perception; M = male; NP = not performed; yrs = years.
[a]Normal values: dark-adapted maximum at 0 dB (rod cone) = >300 μV; light-adapted 30-Hz flickers (cone) = >105 μV.

Continued on next page

Angiograph 2; Heidelberg Engineering, Dossenheim, Germany) documented retinal findings. The macula was analyzed using optical coherent tomography [OCT] (Stratus OCT3; Carl Zeiss Meditec Inc, Dublin, California, USA; retinal thickness map, 512 pixels).

RESULTS

• **CASE 1:** A 56-year-old man reported night blindness, reduced visual field, and marked photophobia. There was no family history of ocular disease. Onset of the disease was

TABLE 1. Summary of Clinical Data of Patients with Extensive Macular Atrophy with Pseudodrusen-like Appearance *(Continued)*

Fundus Atrophy	Goldmann Visual Field			Electroretinography Results (μV)[a]	
Right Eye/Left Eye	Right Eye	Left Eye	Dark Adaptation	Dark-Adapted Maximum at 0 dB	Light-Adapted 30-Hz Flicker
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	Delayed, 2 log	238	57
Foveal sparing	I4, 10 degrees	I4, 10 degrees			
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 2 log	222	62
Foveal sparing	I4, 20 degrees	I4, 15 degrees			
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	Monophasic curve,	288	43
Subfoveal	I4, 15 degrees	I4, 20 degrees	3 log		
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	Monophasic curve,	246	82
Subfoveal	I4, 10 degrees	I4, 10 degrees	4 log		
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 2 log	302	94
Foveal sparing	I4, 20 degrees	I4, 20 degrees			
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 4 log	218	66
Foveal sparing	I4, 20 degrees	I4, 20 degrees			
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 3 log	65	80
Subfoveal	I4, 15 degrees	I4, 15 degrees			
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Monophasic curve,	268	87
Subfoveal	I4, 20 degrees	I4, 20 degrees	3 log		
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	Delayed, 1 log	79	44
Foveal sparing	I4, 20 degrees	I4, 20 degrees			
Foveal sparing	Not done	Not done	Delayed, 1 log	185	108
Foveal sparing					
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 2 log	172	57
Subfoveal	I4, 10 degrees	I4, 20 degrees			
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	Monophasic curve,	50	62
Foveal sparing	I4, 20 degrees	I4, 20 degrees	4 log		
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	Delayed, 2 log	219	70
Subfoveal	I4, 15 degrees	I4, 20 degrees			
Subfoveal	Central scotoma	Central scotoma	—	—	—
Foveal sparing					
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	—	184	40
Subfoveal	I4, no fixation	I4, no fixation			
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	—	216	68
Foveal sparing	I4, 10 degrees	I4, 15 degrees			
Subfoveal	Central scotoma, absolute	Central scotoma, absolute	—	183	34
Subfoveal	I4, 20 degrees	I4, 20 degrees			
Foveal sparing	Central scotoma, absolute	Central scotoma, absolute	—	80	45
Foveal sparing	I4, 10 degrees	I4, 10 degrees			

noted at the age of 45 years with moderate night blindness. VA deteriorated within 5 years to 20/25 (−5.5 (−1.25; 170 degrees)) in the right eye and 20/50 (6 (−1; 0 degrees)) in the left eye at presentation. Goldmann perimetry disclosed an absolute central scotoma (10 central degrees) sparing the fovea in both eyes. The V4e isopter was respected. The dark adaptation examination showed an impaired rod adaptation (2 log elevation of the threshold at 30 minutes).

No anterior chamber or vitreous abnormalities were detected. IOP was 18 mm Hg in both eyes. A symmetrical oval-shaped macular patch of atrophy with a larger vertical diameter and polycyclic limit was noted (Figure 1). Autofluorescence imaging disclosed a well-delineated dark atrophy sparing the foveola and surrounded by widespread hypofluorescent pseudodrusen in both eyes (Figure 1). Paving stones were noted in the far periphery. On OCT, the macular thickness was reduced

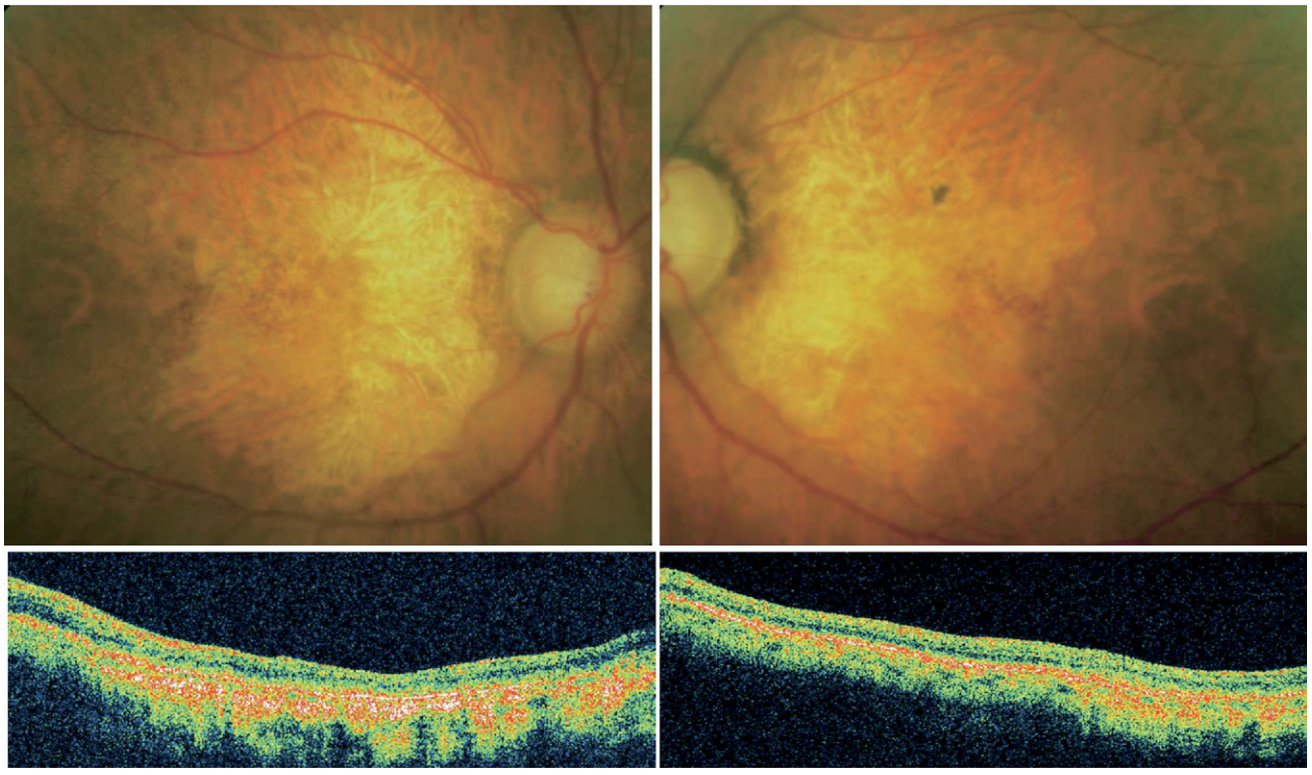

FIGURE 2. Images obtained from Case 1 (age, 59-year-old) showing progression of macular atrophy. (Top) Fundus photographs of the (left) right and (right) left eyes demonstrating complete atrophy without foveal sparing either both eyes. (Bottom) Optical coherence tomography images of the (left) macular and (right) temporal sections: the macular thickness is reduced to 120 μm and the choroidal signal is enhanced inside the atrophic area. No nodular thickening of the pigment epithelium–Bruch membrane complex is disclosed in the pseudodrusen area, temporal to the macular atrophy.

to 150 μm in the right eye and 140 μm in the left eye; the choroidal signal was enhanced inside the atrophic area. Full-field ERG showed moderately reduced mixed cone and rod responses; 30-Hz flicker responses also were decreased (Table 1).

This patient was reevaluated 28 months later. VA dramatically decreased to 20/400 in both eyes. The initial central scotoma (10 central degrees) had enlarged to 15 to 20 degrees in both eyes. On fundus examination, the atrophy was complete with no sparing of the foveola (Figure 2). The peripheral limits of the atrophy had progressed slightly. The pseudodrusen were still visible all around the atrophy. On OCT, the macular thickness was reduced to 120 μm in the right eye and 110 μm in the left eye (Figure 2).

• **CASE 2:** A 60-year-old female reported night blindness, photophobia, and severe decrease of VA in the right eye for the previous 10 years. Her past medical history included autoimmune thyroiditis. There was no family history of eye disease. At presentation, the BCVA was counting fingers at 3 feet in the right eye and 20/30 in the left eye (−0.5 (−0.25; 150 degrees)). In the left eye, the color vision test showed a blue-yellow axis. Goldmann perimetry disclosed an absolute central scotoma, 20 degrees and 15 degrees in right and left eyes, respectively (Figure 3). This scotoma did not include the foveal zone in the left eye, as shown on octopus perimetry (Figure 3).

The anterior segment was unremarkable. IOP was 14 mm Hg in both eyes. Fundus examination showed a geographic atrophy in the right eye with a larger vertical diameter near the temporal vascular arcades, including the fovea (Figure 4). In the left eye, there were 2 patches of sharply defined geographic choroidal atrophy above and below the fovea (Figure 4). On autofluorescence imaging, the atrophy was dark and well delineated, partly sparing the fovea in the left eye (Figure 4). Many pseudodrusen surrounded the atrophy and were spread in the mid-periphery in both eyes. As in case 1, paving stones were noted in the far periphery (Figure 4). On OCT, the foveal thickness was reduced in the right eye (160 μm) and was subnormal in the left eye (206 μm). ERG showed reduced mixed cone and rod responses. The 30-Hz flicker responses also were decreased (Figure 3).

• **CASE 3:** A 49-year-old woman reported night blindness and photophobia followed by decreased VA. There was no family history of eye disease. At presentation, the BCVA was 20/50 with −2 (0.75; 90 degrees) in the right eye and 20/100 in the left eye with −2. The color vision test

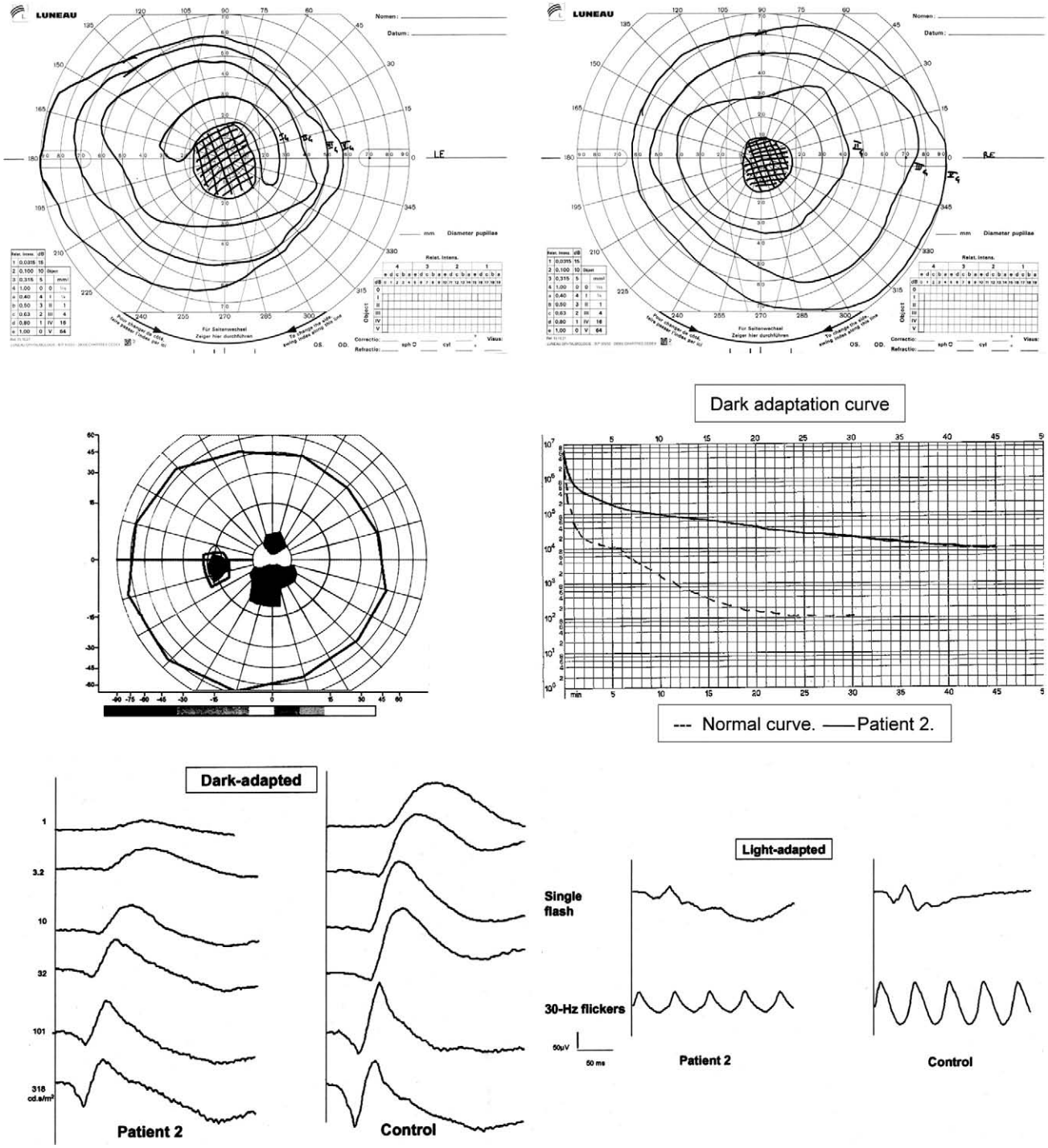

FIGURE 3. Images obtained from Case 2 (age, 60-year-old) showing functional impairment in extensive macular atrophy. (Top) Goldmann perimetry showing an absolute central scotoma in both (left) left and (right) right eyes at 20 degrees and 15 degrees, respectively. (Middle) Static perimetry showing (right) the absolute scotoma with the foveal sparing; dark adaptometry showing (left) an impaired rod adaptation (2 log elevation of the threshold at 30 minutes). (Bottom) International Standard for Clinical Electrophysiology of Vision electroretinography recording from the patient and a normal individual in dark-adapted and light-adapted conditions, showing decreased responses.

revealed a blue-yellow axis and Goldmann perimetry showed an absolute central scotoma sparing the fovea in both eyes (15 degrees in the right eye, 20 degrees in the left eye). The dark adaptation examination showed an impaired rod adaptation (more than 3 log elevation of the threshold at 30 minutes).

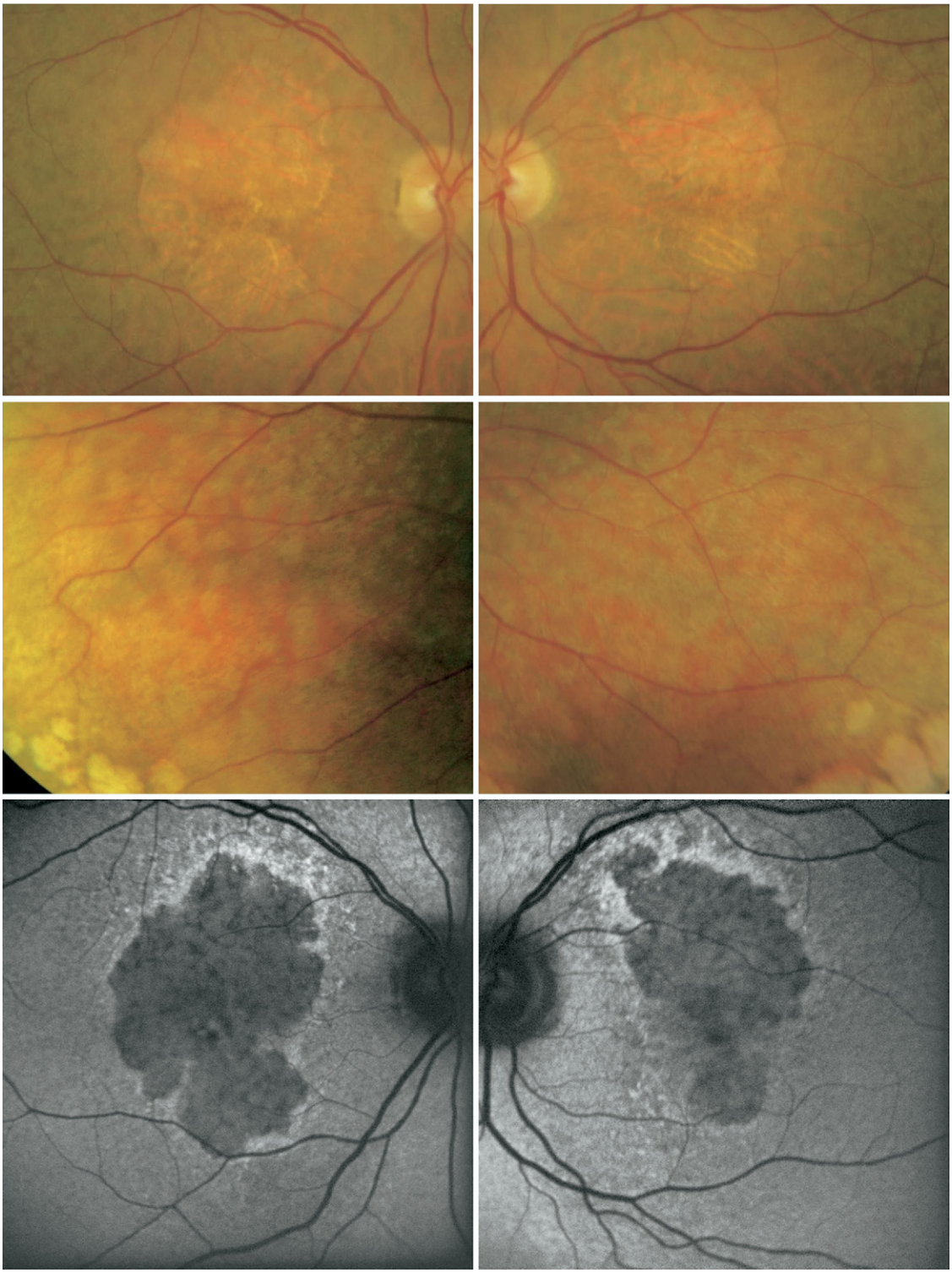

FIGURE 4. Images obtained from Case 2 (age, 60-year-old) showing extensive geographic macular atrophy and pseudodrusen. (Top) Fundus photographs of the (left) right and (right) left eyes showing a geographic atrophy in the right eye with the largest vertical diameter. In the left eye, there are two patches of sharply defined geographic choroidal atrophy superior and inferior to the fovea. (Middle) Fundus photographs showing inferior and temporal peripheral areas in the (left) right and (right) left eyes demonstrating dense pseudodrusen-like appearance and paving stones in the far periphery. (Bottom) Autofluorescent frame from the (left) right and (right) left eyes. The atrophy is dark and well delineated, partly sparing the fovea in the left eye.

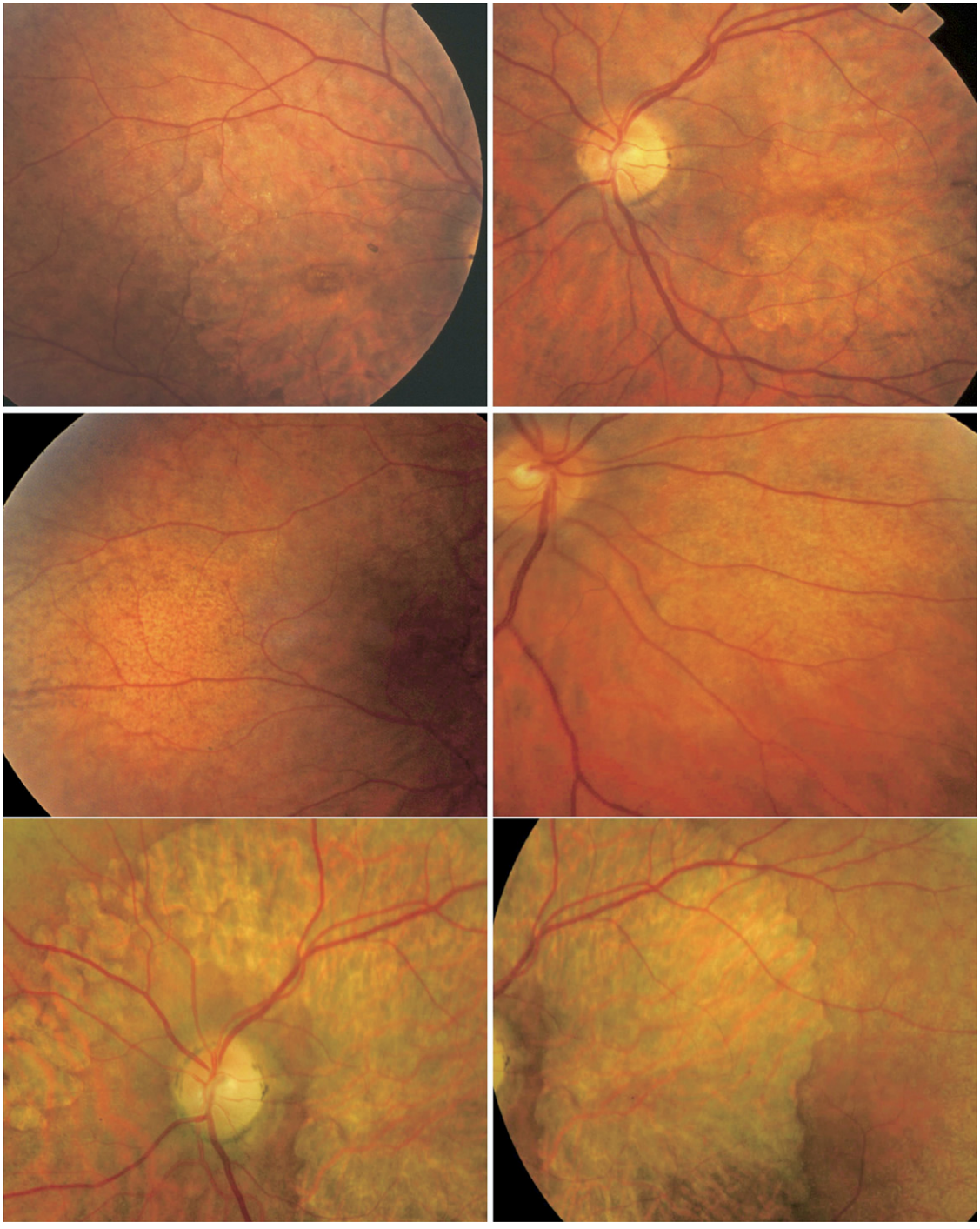

FIGURE 5. Fundus photographs obtained from Case 3 (age, 49-year-old) showing atrophy of the posterior pole. (Top) Fundus photographs of the (left) right and (right) left eyes demonstrating extensive geographic atrophy involving the entire posterior pole, excluding the fovea, in both eyes. (Middle) Fundus photographs showing a pseudodrusen-like appearance extending toward the (right) nasal and (left) temporal mid peripheral areas. (Bottom) Fundus photographs from Case 3 obtained at reexamination 8 years later (age, 57 years old). The atrophy (right) involves the fovea and (left) has progressed up to the optic nerve head and to the nasal retina.

The anterior segment was unremarkable and ocular pressure was 15 mm Hg in both eyes. On fundus examination, a geographic atrophic lesion was seen in both eyes with a larger vertical diameter involving the entire posterior pole and excluding the fovea (Figure 5). Dense pseudodrusen surrounded the macular lesion and extended toward the nasal and temporal midperiphery. We reexamined the patient 8 years later. She has been legally blind for

5 years. On fundus examination and the red-free frames, the atrophy involved the fovea and had progressed to include the optic nerve head and a part of the nasal retina (Figure 5). The ERG showed subnormal mixed cone and rod responses, whereas 30-Hz flicker responses were severely reduced (Table 1).

• **GENERAL DESCRIPTION:** From 1990 to 2008, among 45 patients older than 40 years with uncharacterized macular dystrophy, 18 patients (11 women and 7 men) fulfilled the inclusion criteria: a macular atrophy, drusen-like deposits in the mid periphery, and paving stones in the far periphery. The mean age was 47.5 years (range, 41 to 54 years) at onset and 53.5 years (range, 49 to 60 years) at inclusion. There was a mean follow-up of 41 months (range, 23 to 92 years) for 7 patients. No family history of a similar visual impairment was reported.

Visual loss was the most commonly presented clinical symptom. Patients reported central scotoma and decreased near vision first, then decreased far vision. A recent night blindness was noted in 10 patients and photophobia was noted in 15 of 18 patients. Six patients reported central scotoma and near vision decrease.

Initial VA varied from light perception to 20/20, with a mean VA of 20/100. A VA of 20/40 or better in 1 eye was found in 8 patients. A VA of 20/200 or worse was noted in both eyes in 5 patients. Myopia was a common finding (14 patients, −0.5 to −11 diopters [D]; mean, −3 D). Anterior segment examination results were unremarkable. None of the patients had evidence of vitreitis at presentation or during follow-up.

Morphologic Appearance. Geographic atrophy of the retinal pigment epithelium and choriocapillaris was bilateral in all cases and usually was symmetrical, except in 1 case. The atrophic lesion with polycyclic limits had an oval shape with a larger vertical diameter. The geographic atrophy involved the entire posterior pole sparing the fovea in 1 eye in 12 patients (2/3) at presentation. In all cases, the size of the atrophy was larger than 6 papillary areas. Mild pigmentation within the atrophic area was noted in only 1 eye. The pattern of fundus autofluorescence was similar in all patients with a single patch of dark and sharply demarcated atrophy at the end of the disease process. OCT data were in line with a retinal atrophy, a thinning of the macular thickness, and an enhanced choroidal signal. The photoreceptor line was undetectable in all eyes. During follow-up, the atrophy generally spread rapidly into the fovea. One patient (Case 3), however, initially with a central atrophy, eventually developed a large extension beyond the temporal retinal vessels up to the nasal side of the optic disc (Figure 5).

Besides macular atrophy, all patients displayed drusen-like patterns mimicking clusters of small, flat drusen. These lesions were localized all around the central atrophy up to the vascular temporal arcades and in the entire midperiphery, even in the nasal retina adjacent to the optic nerve head. On the scanning laser ophthalmoscope, this drusen-like appearance was not visible on Helium-Neon laser images, and a diffuse inhomogeneous autofluorescence was observed. On peripheral OCT scans performed in the location of these drusen-like lesions (Figure 2), no nodular thickening of the pigment epithelium–Bruch membrane complex was disclosed. The paving stones predominantly were observed in the inferior part of the peripheral retina.

TABLE 2. Follow-up of Seven Patients with Extensive Macular Atrophy with Pseudodrusen-like Appearance

	Initial Visual Acuity		Final Visual Acuity		
Case No.	Right Eye	Left Eye	Right Eye	Left Eye	Follow-up (mos)
1	20/25	20/50	20/400	20/400	28
3	20/50	20/100	HM	HM	92
4	20/40	LP	20/400	LP	23
6	20/400	20/60	20/400	20/400	36
7	20/200	20/200	20/400	20/400	24
9	20/25	20/40	20/200	20/200	69
12	20/30	20/25	20/200	20/60	12

HM = hand movements; LP = light perception; mos = months.

Functional Data. A Lanthony Farnsworth 15-Hue test was performed in 8 patients. In all 8 patients, a blue-yellow axis dyschromatopsia was documented. In all eyes, an absolute central scotoma, well correlated with the extension of atrophy, and a normal peripheral isopter (V4e) were noted, even in cases of fair VA and night blindness. The dark adaptation curve, evaluated in all patients, mostly was monophasic, indicating a delayed rod dark adaptation (Table 1). Full-field ERG impairment was present in all cases, and in some cases severely affected the rod responses (Table 1).

Global Visual Outcome. Final VA was reduced to 20/400 in all but 2 patients (Table 2). One patient retained a final VA of 20/200 in both eyes; the other patient had a final VA of 20/200 in the right eye and 20/60 (excentric fixation) in the left eye. In all cases, atrophy eventually spread into the fovea of the unaffected fellow eye within 3 years. In none of the patients did choroidal neovascularization, macular edema, or epiretinal membrane develop.

DISCUSSION

AMONG PATIENTS REFERRED FOR MACULAR DYSTROPHY TO a medical center specialized in genetic sensory disorders, a noteworthy number of them presented with a distinct entity of severe geographic atrophy combined with pseudodrusen and paving stone degeneration in the far periphery.

TABLE 3. Extensive Macular Atrophy with Pseudodrusen-like Appearance as Compared with Dry Age-Related Macular Degeneration

Features	EMAP	AMD
Age at onset of visual impairment (yrs)	41 to 54 (average, 47.5)	Frequently ≥ 65
Features of macular atrophy		
Size	Extended more than 6 papillary diameters	Small foci after drusen regression
Shape	Oval polycyclic	Round regular
No. of foci	One single patch	One or multiple
Foveal involvement	In many cases at early age	Not frequent at early age
Features of drusen		
Number	Numerous	Few to many
Type	Lattice of small, yellowish spots	Soft drusen
Location	Posterior pole and midperiphery	Posterior pole
Fluorescein angiography	No fluorescence	Hyperfluorescence
Complications	No CNV	CNV in 8% to 10%
Clinical course	Rapid foveal involvement with severe visual loss in both eyes	Visual acuity slowly worsening except in cases of primary foveal involvement (25 % of the cases)
Peripheral lesions	Frequently encountered	Not determined

AMD = age-related macular degeneration; CNV = choroidal neovascularization; EMAP = extensive macular atrophy with pseudodrusen-like appearance; yrs = years.

The age of disease expression was a defining feature. The earliest symptoms of this extensive macular atrophy with pseudodrusen (EMAP) were difficulties with dark adaptation by age 50 years, followed by central scotoma and decreased vision. By this time, all the patients demonstrated single and bilateral extensive chorioretinal atrophy centered on the fovea with a mean VA of 20/100. The ERG responses were variably decreased. The disease rapidly progressed to central vision loss in both eyes without occurrence of choroidal neovascularization, subretinal fibrosis, or macular edema. Most of these patients had no family history of a similar visual impairment. A few of them reported a deceased parent who had a loss of central vision, although the age of onset was suggestive of AMD.

Subfoveal extension of the atrophy was the main complication of this entity. In the present study, a bilateral subfoveal involvement was observed in 5 (27%) of 18 cases at presentation and in all cases at 41 months of follow-up. These patients had a poor visual outcome and were not eligible for low vision rehabilitation attributable to the large size and to the vertical pattern.

Extensive macular atrophy with pseudodrusen could easily be distinguished from several retinal dystrophies inherited as mendelian conditions, such as cone dystrophies, cone rod dystrophies, and inverse retinitis pigmentosa,[13–16] because no pigment deposits could be found in the macula or in the periphery, the retinal vasculature remained normal, and the ERG responses were moderately decreased. Differential diagnosis of EMAP patients also includes 3 forms of autosomal dominant macular dystrophies, that is, Sorsby fundus dystrophy,[17,18] North Carolina macular dystrophy,[19,20] and central areolar choroidal dystrophy.[21–26] There was no evidence of pseudoinflammation as in Sorsby fundus dystrophy, and the limits of the lesion were not sharply defined as in North Carolina macular dystrophy. EMAP also was different from central areolar choroidal dystrophy, which demonstrates, in the early stages, a subtle, mottled depigmentation of the macula.[24] The macular depigmentation gradually enlarges, being progressively replaced by a circular area of geographic atrophy. In most cases, no drusen or flecks are described.[27]

This entity has to be distinguished from late-onset macular retinal dystrophy (L-ORD or L-ORMD). Both conditions are characterized by the appearance of difficulties with dark adaptation by the age of 50 years, a rapid progression to central vision loss, and extensive geographic atrophy.[28–31] In contrast with L-ORD, which is inherited as an autosomal dominant condition, no evidence of a familial heritability could be found in EMAP. In addition, no peripheral visual loss was noted in our patients. The fundus pattern of EMAP also could be distinguished easily from L-ORD that is characterized by multiple atrophic spots first involving the midperiphery. As in L-ORD, ERG changes could be observed. However, there was no deterioration detectable during the 3.5-year follow-up.

Extensive macular atrophy with pseudodrusen should also be distinguished from dry AMD and basal laminar drusen combined with vitelliform macular detachment. In dry AMD, geographic atrophic lesions appear after the age of 50 years. The atrophy results from the confluence of multiple small foci after drusen regression.[1–12] There is a perifoveal progression of atrophy with a slow growth rate toward the fovea itself.[4–8] Thus, the atrophy is circular, centered on the fovea, with a larger horizontal axis (Table 3). This pattern is in contrast with that seen in EMAP patients, who already have an extended macular atrophy at

the age of 50 years. In basal laminar drusen combined with vitelliform macular detachment, the macular atrophy can follow the resolution of the material.[32–35] This atrophy, more frequently encountered after the age of 50 years, is less extensive (not larger than 2 to 4 disc areas) and less complete. Moreover, in our patients, the pseudodrusen-like appearance did not reproduce the striking Milky Way pattern of cuticular drusen on fluorescein angiography.

The cause of EMAP remains unknown. An inflammatory origin is unlikely because no anterior or posterior inflammation was noted. The patients had no history of specific medication intake, particular lifestyle, or exposure to chemicals. Although there is no evidence for familial cases, an autosomal recessive disorder or a genetic predisposition cannot be ruled out, especially because EMAP, like other inherited macular dystrophies, exhibits bilateral and roughly symmetrical lesions. In conclusion, EMAP should be considered as a possible pattern of severe macular dystrophy occurring in middle-aged adult patients.

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