A CLINICOPATHOLOGIC STUDY OF A PECULIAR FOVEOMACULAR DYSTROPHY*

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THIS REPORT CONCERNS A PECULIAR CENTRAL MACULAR DYSTROPHY IN PATIENTS with the following clinical features: 1) visually asymptomatic or visual blurring and metamorphopsia in one or both eyes, usually with the onset between ages of 30 and 50 years; 2) symmetrical, one-third-disc-diameter-size, round or oval, slightly elevated, yellow subretinal lesions with a central pigmented spot in the foveal area of each eye; 3) small drusen may or may not be present in the paracentral region; 4) slow progression of visual loss with most patients maintaining reading vision in at least one eye throughout life; 5) normal or slightly to moderately subnormal electro-oculographic findings; and, 6) normal electroretinographic findings and color vision. The disease is probably dominantly inherited. The histopathologic findings in one patient suggest that the disease affects primarily the retinal pigment epithelium and that it may be related to dominantly inherited drusen.

METHODS AND MATERIALS

The nine patients in this report were referred to the Bascom Palmer Eye Institute because of a disturbance of their central vision. Eight patients had a complete eye examination by the author. One patient was referred to the Eye Institute only for fundus photographs and fluorescein stereoangiography. All nine patients had fundus stereophotography and all but one had one or more fluorescein stereoangiographic studies. Seven patients had electroretinography and electro-oculography. The latter was done after the technique described by Arden.[1] In our laboratory a light-dark ratio of 1.65 is considered the lower limits of normal.

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REPORT OF CASES

CASE 1

A 30-year-old white woman was examined at the Bascom Palmer Eye Institute because of a positive scotoma and mild metamorphopsia which developed six weeks previously in the right eye. The symptoms improved by the time of examination. Her past medical history was unremarkable. Her mother and her maternal grandmother (Cases 2 and 3) had a history of macular degeneration. Ophthalmoscopic examination of her only sibling, a brother, and her seven-year-old son, was said to be normal.

The patient's visual acuity in the right eye was 20/25-1 and J-1, and in the left eye was 20/50 and J-1. Amsler grid testing in the right eye detected no abnormality, however, metamorphopsia was demonstrated in the left eye. Except for the ophthalmoscopic examination her eyes were otherwise normal. The optic disc and retinal vessels were normal. Symmetrical lesions were present in both macular areas (Figure 1, A and B). A slightly elevated, oval, discrete, one-third-disc-diameter-size, yellowish deposit was present at the level of the pigment epithelium. A small pigment clump was present at the center of the lesion. There was no subretinal exudate or blood. A few small, yellow spots interpreted as drusen were scattered in the left paramacular area. The early phases of fluorescein angiography showed a ring of hyperfluorescence in the area of the macular lesions, as well as a few discrete areas of hyperfluorescence corresponding with the drusen in the paramacular area (Figure 1, C and D). The diameter and the thickness of the ring zone of hyperfluorescence did not precisely correspond with the yellow portion of the lesion. The pattern of fluorescence did not change significantly during the course of angiography, but the presence of fluorescence one hour after the study suggested that there was some staining of the yellowish portion of the lesion. There was no apparent explanation for the patient's recent complaints in the right eye. An electroretinogram was normal. Electro-oculography was subnormal (O.U. - 1.4). Follow-up examination three years later revealed no change in the appearance of the fundi. Visual acuity in the right eye was 20/30 and in the left eye was 20/80.

CASE 2

The 54-year-old mother of the preceding patient (Case 1) first noted mild distortion of vision in her left eye ten years previously. This had not changed. The right eye was asymptomatic. Her past medical history was positive for mild diabetes, controlled with oral hypoglycemic medications. Two sisters and two brothers had no eye symptoms. The two sisters were normal on ophthalmic examinations done elsewhere. The patient's visual acuity in the right eye was 20/40 and J-2 and in the left eye was 20/30 and J-2. Slight metamorphopsia was evident on Amsler grid testing. In the center of the right macula there was an irregular, circular, light red zone with a central yellowish-grey spot. Several smaller circular zones of a similar color were clustered around and were continuous with the central zone. (Figure 2, A). A number of small, yellow-grey deposits of varying size were present in the

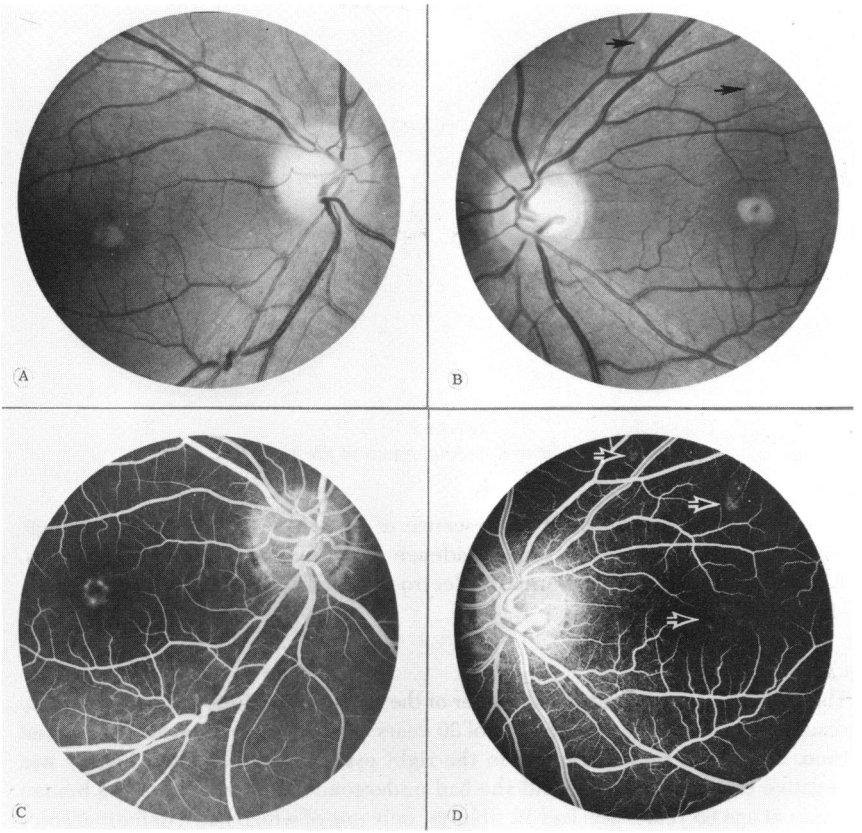

FIGURE 1
(Case 1) A: Right eye. B: Left eye. Note small paracentral lesions (arrows). C: Early angiogram of the right eye. D: Early angiogram of the left eye. Note faint fluorescent ring centrally (lower arrow) and fluorescence corresponding with the paracentral lesions (upper arrows). The thickness of the ring area of fluorescence is less than that of the nonpigmented peripheral portion of the macular lesions.

parafoveal area. A few small discrete yellowish lesions interpreted as drusen were scattered in the peripheral macular area and in the midperiphery of the fundus. Some of the larger drusen had central grey spots. Symmetrical changes were present in the left eye. The remainder of the eye examination was normal. Fluorescein angiography demonstrated that the central light red zones in the foveal areas were irregularly hypofluorescent (Figure 2, B). Some of the yellow-grey parafoveal lesions appeared irregularly hyperfluorescent. The small yellow lesions in the peripheral macular area and beyond were hyperfluorescent over an area that in general was slightly larger than the yellowish lesions seen ophthal-

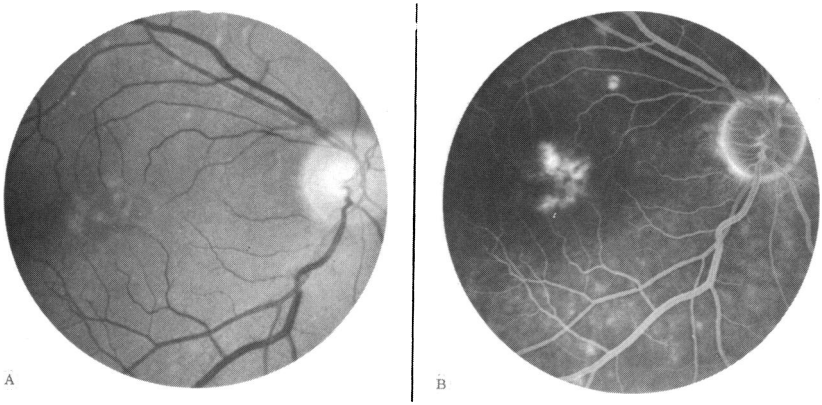

FIGURE 2
(Case 2) A: Right eye. B: Angiogram of the right eye.

moscopically. The pattern of fluorescence of all of the lesions did not change significantly and there was slight evidence of staining in the late angiograms. Electroretinography was normal. Electro-oculography was subnormal (O.D. -1.22, O.S. - 1.40).

CASE 3

The 70-year-old maternal grandmother of the first patient (Case 1) noted difficulty reading with her left eye at the age of 30 years. This remained constant since that time. She noted no abnormality in the right eye. Her past medical history was negative except for tinnitus and she had undergone a hysterectomy for a benign tumor at age 65 years. She had 12 siblings, only one of which had a definite history of poor vision of unknown cause in both eyes. The patient's visual acuity in the right eye was 20/40 and J-5 and in the left eye was 20/40 and J-2. Amsler grid testing was within normal limits. Ophthalmoscopic and biomicroscopic examinations of the fundi revealed a one-third-disc-diameter-size geographic zone of depigmentation and atrophy of the pigment epithelium in the central macular area of each eye (Figure 3, A). Surrounding the central lesions were several ill-defined, round or oval, slightly elevated, slightly yellowish lesions with dark grey centers surrounded by irregular hypopigmentation of the pigment epithelium. In the paramacular area of each eye there was an irregular pattern of faint depigmentation which was apparent only with the slit-lamp. Fluorescein angiography revealed the central macular lesions as well as the central portions of the paracentral grey-yellow lesions to be hypofluorescent (Figure 3, B arrows). In the paramacular areas angiography demonstrated evidence of greater pigment epithelial abnormality than would have been expected ophthalmoscopically. Electroretinography was normal. Electro-oculography in each eye was very abnormal (O.U. - 1.0).

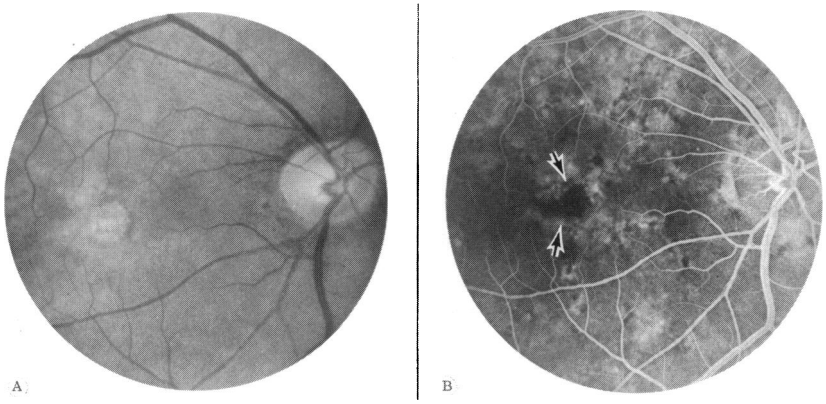

FIGURE 3
(Case 3) A: Right eye. B: Angiography of the right eye. Note the central non-fluorescent zone (arrows) which does not correspond precisely with the circular area of pigment epithelial atrophy in A above. Note also the widespread areas of hyperfluorescense due to pigment epithelial abnormalities which are not easily seen in A above.

COMMENT

Despite the ophthalmoscopic evidence of geographic atrophy of the pigment epithelium in the foveal areas, this patient's acuity was good and there was no demonstrable defect on Amsler grid testing. The unexpected angiographic findings of a zone of nonfluorescence or hypofluorescence corresponding with the central lesions indicates the presence of more pigment than is clinically evident in the foveal area. The pigment in this case, however, may be the normal intraretinal yellow pigment which is concentrated in the outer retinal layers of the fovea. The preservation of this pigment in this case would be in keeping with her good visual function and minimal damage to the outer retina in the foveal area.

CASE 4

A 42-year-old white woman had no previous eye symptoms until she noted metamorphopsia and a positive scotoma in her right eye. One week later she was examined by her local ophthalmologist who recorded her visual acuity in the right eye as 20/50 and in the left eye as 20/25. He found bilateral macular lesions and described a slight amount of subretinal fluid in the right macula. Angiography revealed symmetrical, ring-shaped, fluorescent lesions in both macular areas and no definite evidence of leakage of dye from the choroid. Her symptoms persisted and she received 30 mg of prednisone daily for one month. She noted no improvement and was referred to the Bascom Palmer Eye Institute three months after the onset of symptoms. Her past medical and family history were unremarkable. Her visual acuity in the right eye was 20/25 and in the left eye was 20/25.

There was slight doubling of the lines on Amsler grid when viewed with the right eye. The grid appeared normal with the left eye. Ophthalmoscopic examination revealed symmetrical, one-third-disc-diameter-size, slightly elevated, yellowish lesions with a small grey center (Figure 4, A and B) in the foveal area of each eye. There was no subretinal exudation. A review of the fundus photographs made two months earlier revealed no evidence of a change in the macular lesions. Fluorescein angiography revealed findings identical to that in Case 1. Electroretinography and electro-oculography were normal (O.D. - 1.8, O.S. - 2.0). Color vision with the A.O. HRR plates was normal. One year later her clinical findings were unchanged.

CASE 5

A 31-year-old white woman developed blurred vision and metamorphopsia in the right eye in October, 1972. She was examined four days later by her local ophthalmologist who found her visual acuity in the right eye was 20/25 and in the left eye was 20/20. Her Amsler grid findings were abnormal in the right eye. Her past ocular and medical history were unremarkable. There was no family history of eye trouble. Her symptoms were unchanged when she was examined at the Bascom Palmer Eye Institute in December, 1972. Her visual acuity in the right eye was 20/20 and in the left eye was 20/15. There was minimal metamorphopsia demonstrable on Amsler grid testing of the right eye. The test was normal in the left eye. Ophthalmoscopic examination revealed a one-third-disc-diameter-size, round, yellowish lesion with a central grey spot beneath the retina in the foveal area of both eyes. Except for the absence of any extrafoveal lesions, the fundus findings and fluorescein angiography were identical to those in Case 1. The fundi were otherwise unremarkable. Electroretinography and electro-oculography were normal (O.D - 3.1, O.S. - 3.2). Follow-up examination one year later revealed no change.

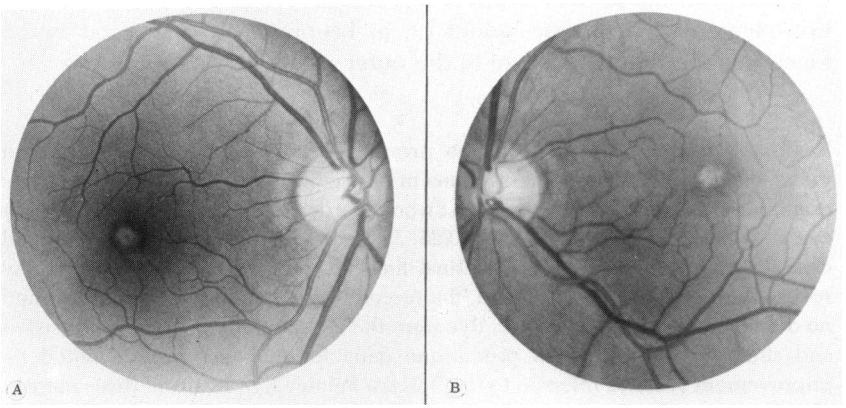

FIGURE 4
(Case 5) A: Right eye. B: Left eye.

CASE 6

A 50-year-old white male lawyer was struck in the left eye with a tree branch at age 46 years. One week later he noted metamorphopsia in this eye. Over a period of several years this incompletely resolved. Four weeks prior to his initial examination at the Bascom Palmer Eye Institute in April, 1967, he was struck with a tree branch in his right eye. Soon afterward he noted mild blurring of the right eye. His past history was unremarkable. His mother had poor vision secondary to cataracts in later life. There was no definite family history of macular degeneration, although he had no siblings. Visual acuity in the right eye was 20/20 and in the left eye was 20/25. He had mild metamorphopsia demonstrable in both eyes on Amsler grid testing. Ophthalmoscopic examination revealed a one-third-disc-diameter-size, oval, slightly elevated yellow lesion with a central pigment spot beneath the retina in the foveal area of both eyes (Figure 5, A and B). There was no serous retinal detachment and the fundi were otherwise normal. Over the subsequent year the metamorphopsia improved in the left eye. When last seen in August, 1973, he still had mild metamorphopsia in both eyes. Visual acuity in the right eye was 20/20 and in the left eye was 20/25. The fundi were unchanged. Electroretinography and electro-oculography were normal (O.D. - 3.0, O.S. - 3.2).

CASE 7

A 54-year-old white man first noted mild blurring of vision in 1960. His local ophthalmologist diagnosed retinal degeneration and the patient received oral corticosteroids for many months. His vision deteriorated further. He was first seen at the Bascom Palmer Eye Institute in May, 1972. His family history and past ocular and medical history were unremarkable. His visual acuity in the right eye

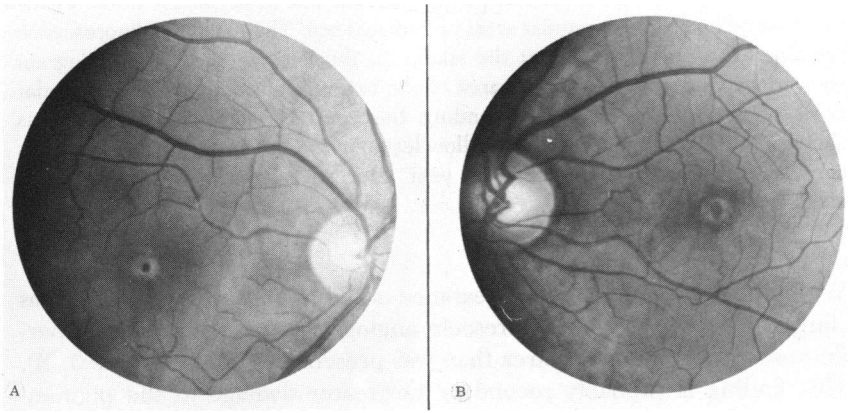

FIGURE 5
(Case 6) A: Right eye. B: Left eye.

was 20/25 and J-1, and in the left eye was 20/30 and J-1. Amsler grid testing in the right eye was normal. There was a small paracentral negative scotoma in the left eye. Ophthalmoscopic examination revealed a one-fourth-disc-diameter-size, round, yellowish lesion beneath the retina in the right foveal area. A small grey spot was present within its center. A similar but slightly larger lesion was present in the left foveal area. The fundus was otherwise unremarkable. Fluorescein angiography revealed findings in the macular area identical with those in Case 1. There was no evidence of pigment epithelial abnormality outside the foveal area. Electroretinography was normal. Electro-oculography in the right eye was normal (1.8) and in the left eye was subnormal (1.4). Follow-up examination one year later revealed no change.

CASE 8

A 60-year-old woman rapidly developed blurred vision which stabilized soon thereafter in her right eye. Seven months after the onset of symptoms an ophthalmologist told her that she had "scar tissue" in the back of both eyes. Her past medical history was negative. She had one brother with a "similar eye problem." Eighteen months after the onset of blurred vision she was examined by another ophthalmologist who recorded her visual acuity in the right eye as 20/200 and in the left eye as 20/40. He observed bilateral macular lesions and referred her to the Photographic Laboratory of the Bascom Palmer Eye Institute for fundus stereophotography and fluorescein angiography. In the right foveal area there was a one-third-disc-diameter-size, round area of loss of the pigment epithelium similar to that in Figure 3, A. A pigment spot was present within its center. Three smaller, less well-defined areas of depigmentation were present around this central lesion. The pigment epithelium and fundus were normal elsewhere. In the left foveal area there was a slightly oval, yellow, one-third-disc-diameter lesion with a grey center, identical with that depicted in Figure 1, A. Fluorescein angiography in the right eye revealed a ring-shaped area of intense fluorescence surrounded by smaller irregular areas of fluorescence. The pattern of fluorescence remained the same throughout the study. In the left eye the early angiogram showed hypofluorescence in the area of the central yellow lesion and irregular areas of hyperfluorescence surrounding the central lesion. Late angiograms showed evidence of staining of the yellow lesion in the left foveal area except in its center. Follow-up examination one year later revealed that no change had occurred.

COMMENT

While the ophthalmoscopic appearance of the lesion in the right eye was similar to that in Case 3, fluorescein angiography revealed more hyperfluorescence in the foveal area than was present in Case 3 (Figure 3, B). This finding is probably secondary to greater damage to the pigment epithelium and outer retinal layers in Case 8 than in Case 3.

CASE 9

A healthy 66-year-old white female was examined at the Bascom Palmer Eye Institute on March 15, 1968, with a four-month history of gradual decrease of vision in both eyes. Her family history revealed that her mother died at age 80 years with no visual trouble. Her father died at age 54 years of a heart attack. She had one sister, age 63, who had no visual difficulty. She had one son, age 45 years, who had a normal eye examination. To date, I have been unable to examine her sister. The patient's visual acuity in the right eye was 20/30-3 and J-1, and in the left eye was 20/40-2 and J-2. She had mild cataracts but most of her visual loss was attributed to peculiar macular lesions. In the central macular region of each eye she had slightly elevated, round, yellow, subretinal lesions with a central pigmented spot (Figure 6, A and B). In the right eye the pigment appeared to extend into the overlying retina. A few drusen were scattered in the posterior pole. The macular lesions were quite symmetrical. Fluorescein angiography demonstrated findings similar to that noted in Case 1 (Figure 6, C and D). Some, but not all of the drusen, were evident as hyperfluorescent areas angiographically.

The patient was last seen at the Bascom Palmer Eye Institute on April 16, 1969, with a history that her vision had deteriorated slightly. Visual acuity in the right eye was 20/50 and in the left eye was 20/70. A pinhole did not improve her vision. No attempt was made to improve her vision with lenses. There was no definite change in her cataracts. The macular lesions in both eyes were identical with those noted in her previous photographs. The patients's general health had always been excellent until June, 1969, when she noted the onset of weakness and weight loss. A diagnosis of carcinoma of the liver was made. The patient's vision deteriorated slightly but she was still able to read until the time of her death in November, 1969. Autopsy revealed that she died of metastatic carcinoma of the liver. Her eyes were obtained at autopsy.

On gross examination the eyes were normal except for the small foveal lesions which appeared identical to those noted previously. Histopathologic examination included serial sections of the macula and paramacular areas of both eyes. Except for mild lens changes the anterior segments were normal. There was artifactitious separation of the retina and pigment epithelium from the choroid posteriorly. A few scattered drusen were present in the periphery. The vitreous, retina, and choroid were otherwise normal except for changes in the macular and paramacular areas. Located eccentrically in the foveal area of the right eye there was a focal chorioretinal adhesion that was artifactitiously separated (Figure 7). There was focal loss of retinal receptor elements and atrophy and partial loss of the pigment epithelium. Large pigment-laden cells and a few small calcific bodies were clumped between the retina and Bruch's membrane in this area (Figures 7 and 8). Some of the pigment-laden cells were also present in the inner and outer plexiform layers of the overlying retina. In a ring-like zone surrounding the chorioretinal adhesion there was a thick layer of slightly granular eosinophilic, PAS positive material which appeared to lie primarily between thinned atrophic pigment epithelium and Bruch's membrane (Figures 7 and 8). A thinner layer of eosinophilic material was present beneath the more normal appearing pigment

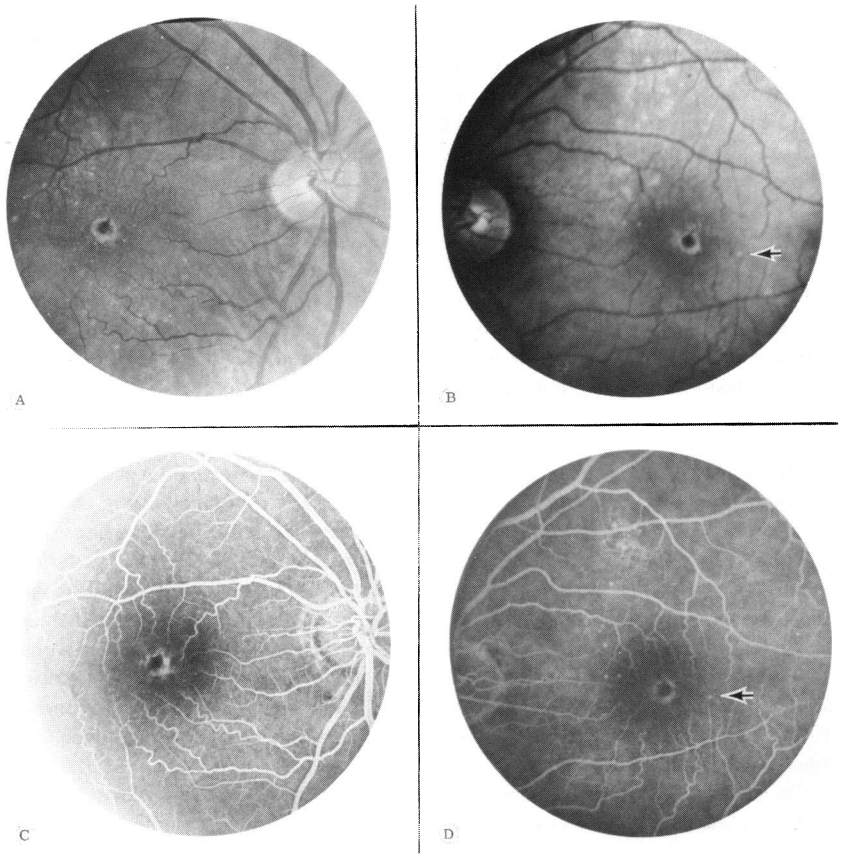

FIGURE 6
(Case 9) A: Right eye. B: Left eye. Note the multiple drusen of various sizes. See Figure 10D for the histopathology of the small drusen indicated by the arrow. C: Angiogram of the right eye. D: Angiogram of the left eye. Note that drusen (arrow) are fluorescent. (Compare with B).

epithelium throughout the extrafoveal portion of the macula. It was not possible to determine whether or not some or all of this material was within the basal portion of the pigment epithelial cells or was solely between the pigment epithelium and Bruch's membrane. In the center of the left macula there was no evidence of a chorioretinal adhesion. In the foveal area, however, the pigment epithelium was absent and was replaced by a large clump of extracellular pigment derived from pigment epithelial cells and a few pigment-laden cells (Figures 9 and 10). A zone of atrophy of the pigment epithelium and subpigment epithelial eosinophilic, PAS positive material identical to that seen in the right macula surrounded the clump of pigment. A few pigment laden cells were present within the outer plexiform

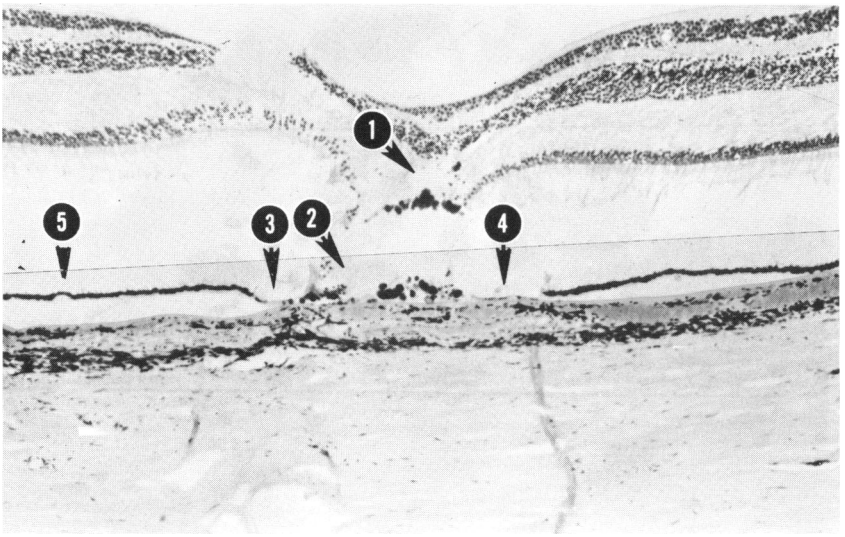

FIGURE 7
(Case 9) Histopathologic findings in the right macula. Note the focal loss of retinal receptor elements and pigment migration into the retina in the foveal area (arrow no. 1); clumping of pigment-laden cells and chorioretinal adhesion in the foveal area (arrow no. 2); the paracentral zone of thinning of the pigment epithelium (arrows no. 3 and no. 4); and the focal drusen (arrow no. 5). (hematoxylin and eosin × 54).

layer of the overlying retina. There was minimal loss of retinal receptor elements in the foveal area. In the paracentral region of both eyes, there were typical drusen (arrows in Figures 7 and 9) corresponding with the focal yellow spots noted ophthalmoscopically. The subpigment epithelial eosinophilic material comprising the drusen was tinctorially slightly different from that found in a thin layer beneath the pigment epithelium throughout the paracentral area (Figure 10, D). In the right macula the collagenous and elastic tissue portion of Bruch's membrane was slightly thickened but was intact (Figures 7 and 8). There was some thickening of the intercapillary septae in the choriocapillaris, but erythrocytes were present within the choriocapillaris throughout the macular area. The changes in Bruch's membrane and choriocapillaris were more prominent in the area of the chorioretinal adhesion than elsewhere in the macular area. In the left macula the collagenous and elastic portions of Bruch's membrane and the choriocapillaris were normal. Special stains revealed no evidence of calcium or iron in the collagenous portion of Bruch's membrane. A few calcium deposits were present within the eosinophilic material lying between the pigment epithelium and Bruch's membrane. The large choroidal vessels were normal.

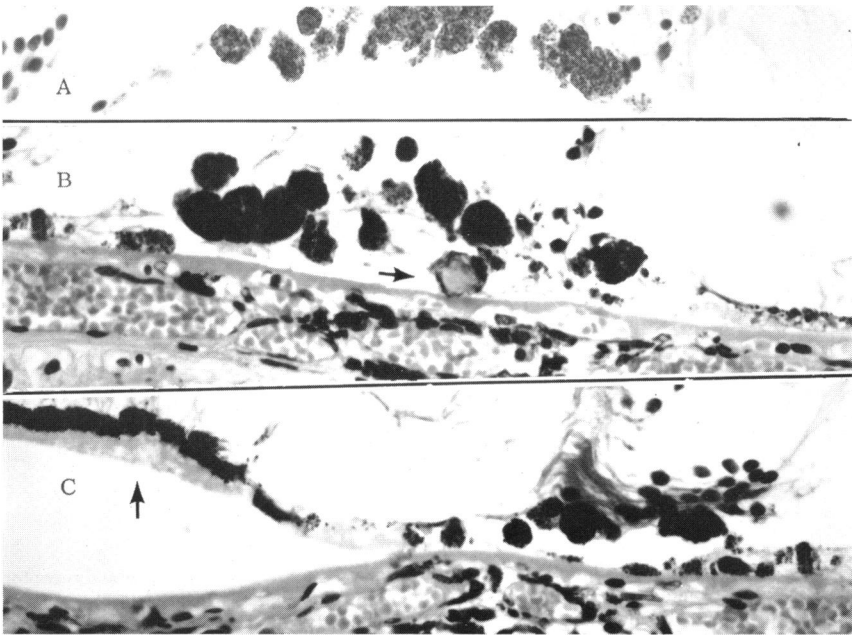

FIGURE 8

(Case 9) Higher power showing details of the right macular lesion. A: Pigment-laden cells within the retina (see arrow no. 1, Figure 7). (hematoxylin and eosin × 306) B: Clumps of pigment-laden cells and calcific body (arrow) surrounded by a zone of thinned degenerated pigment epithelium (arrows no.2 and no.4 in Figure 7). Note some thickening of the intercapillary pillars of the choriocapillaris. (hematoxylin and eosin × 306). C: Zone of thinning and degeneration of the pigment epithelium surrounding the chorioretinal adhesion in the foveal area (See arrow no.3 in Figure 7). Note the granular material which appears to lie between the pigment epithelium and Bruch's membrane (arrow). (hematoxylin and eosin × 306).

COMMENT

The histopathologic findings of the macular lesions in this patient correlate quite well with the ophthalmoscopic and angiographic appearance of the lesions. The yellow zone surrounding the central pigmented lesion corresponds to the ring zone where the pigment epithelium was thinned and degenerated and was separated from Bruch's membrane by eosinophilic material. The ring of hyperfluorescence corresponding with this zone during the early and late phases of angiography is secondary to the greater visibility of the choroidal fluorescence in this zone as well as to diffusion of dye across Bruch's membrane into the subpigment epithelial material. The histopathologic findings in the right eye were compatible with the visual acuity, but in the left eye they were less than expected.

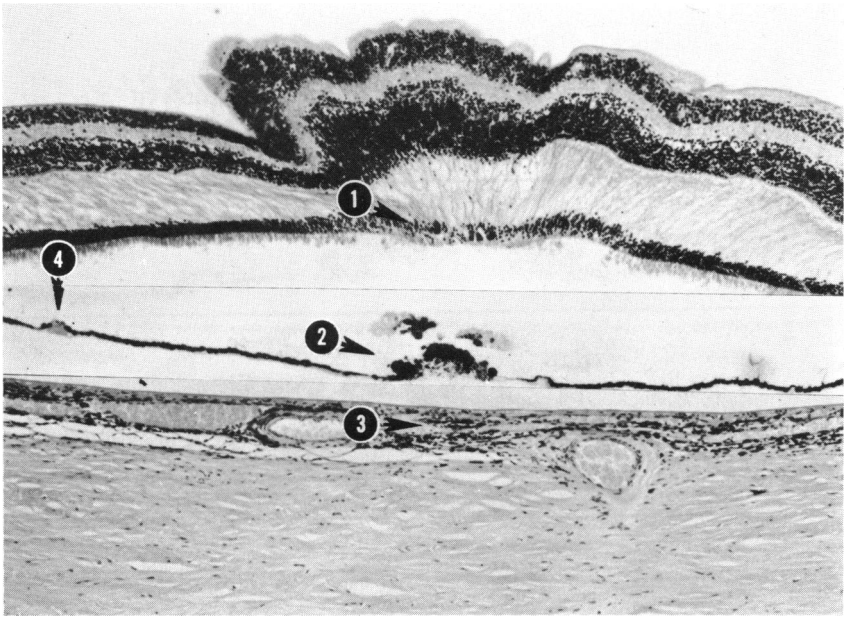

FIGURE 9
(Case 9) Histopathologic findings in the left macula. Note the mild loss of retinal receptor elements (arrow no.1); pigment clumping in the foveal area (arrow no.2); the normal choroid (arrow no.3); and a paracentral druse (arrow no.4). (hematoxylin and eosin × 49).

DISCUSSION

While the evidence presented is inconclusive these patients probably have a dominantly inherited foveomacular dystrophy affecting primarily the retinal pigment epithelium. It is apparent that many of these patients are relatively asymptomatic. They may notice a gradual mild decline in visual acuity or they may experience rapidly blurring of vision and metamorphopsia in one eye. Unlike patients who develop serous detachment of the macula, they usually do not complain of micropsia or a positive scotoma. Despite uniocular complaints the visual acuity and the appearance of the macular lesions are often similar in both eyes. In the younger patients the yellow color of the foveal lesions is striking and the size of the central pigment spot is often small. In the older patients, the lesions may become less yellow and the central spot larger. In some patients the lesion may be replaced by a zone of depigmentation of the pigment epithelium. Small paracentral discrete yellow lesions at the level of the pigment epithelium occur in some of these patients. They appear to

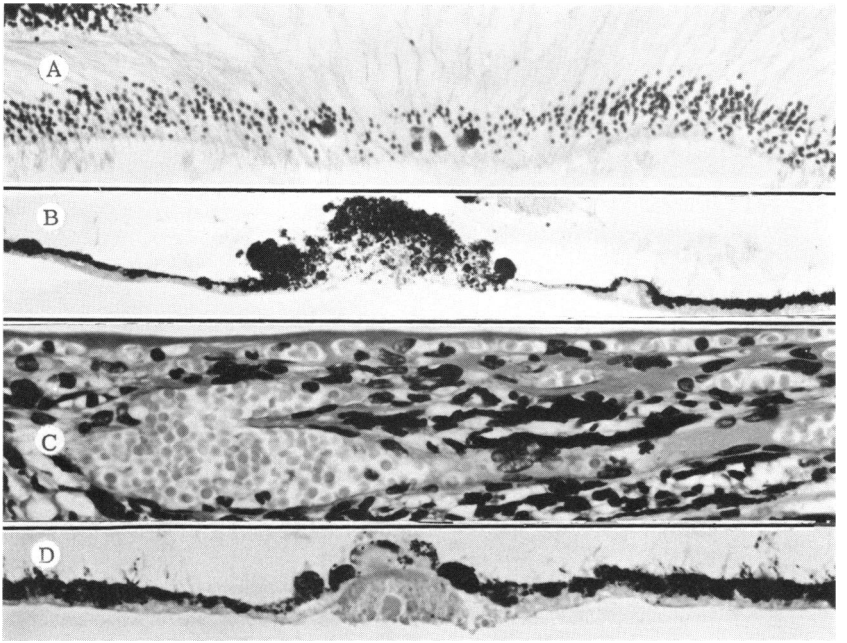

FIGURE 10

(Case 9) Higher power showing details of the left macular lesion. A: Pigment-laden cells within the outer retinal layer (see arrow no.1 in Figure 9). (hematoxylin and eosin × 122). B: Clump of extracellular and intracellular pigment centrally surrounded by a zone of thinned pigment epithelium and underlying eosinophilic material (see arrow no.2 in Figure 9). (hematoxylin and eosin × 122). C: Normal choroid in the foveal area (see arrow no.3 in Figure 9). (hematoxylin and eosin × 306). D: Paracentral drusen (see arrow no.4 in Figure 9). Note the thin layer of finely granular material which appears to lie beneath the pigment epithelium on either side of the druse which is composed of more deeply.

be more common in the older patients. The discreet appearance of these small yellow paracentral lesions during the early and late phases of angiography is evidence that these lesions are drusen and are not similar to the small yellow lesions seen in fundus flavimaculatus or Stargardt's disease.[2,3] To date, I have observed neither serous nor hemorrhagic disciform detachment in any of these patients.

The histopathologic findings in Case 9 demonstrated that the clinical and fluorescein angiographic appearance of the foveal lesions was primarily due to pathologic changes in the pigment epithelium. These consisted of depigmentation, degeneration, and disruption of the pigment epithelium centrally and subpigment epithelial deposition of eosinophilic

material paracentrally. The small paracentral lesions proved histopathologically to be drusen. No intracytoplasmic PAS positive material similar to that described in one case of fundus flavimaculatus[2] was found. There was minimal loss of the retinal receptor elements overlying the foveal lesions. There was slight thickening of Bruch's membrane and the intercapillary pillars of the choriocapillaris, but there were no unusual degenerative changes such as calcification, irregular thinning, or breaks in Bruch's membrane underlying the foveal lesions. These latter changes are found frequently in the macular area of patients with macular drusen and secondary disciform detachment.

While the circumscribed yellow foveal lesions in younger adult patients with this foveomacular dystrophy may simulate the egg-yolk appearance of the lesions seen in childhood in Best's vitelliform macular degeneration, they are typically smaller in diameter. They usually have evidence of a central pigment spot, and they do not show layering of yellow pigment in the dependent portion of the foveal lesion. Although electrooculography may occasionally be subnormal in patients with foveal dystrophy, none of these have shown the marked EOG abnormalities typical of Best's disease. Although the histopathology of the early stages of Best's disease is unknown, the egg-yolk lesion has been presumed to be secondary to deposition of an abnormal material within the pigment epithelial cells. There is little clinical, fluorescein angiographic, or histopathologic evidence to suggest that this foveomacular dystrophy is closely related to fundus flavimaculatus or Stargardt's disease.

The question arises as to whether or not this foveomacular dystrophy is anything more than an unusual manifestation of familial drusen.[4] Indeed, we have clinical, fluorescein angiographic, and histopathologic evidence that the small paracentral lesions are drusen. It is possible that initially the discrete yellow foveal lesions may be nothing more than a large solitary drusen or exudative detachment of the pigment epithelium. Their symmetrical appearance, their presence in relatively young patients in the absence of any other drusen in the eye, their failure to enlarge concentrically, and the rarity with which they progress to give rise to the various stages of serous and hemorrhagic disciform detachment of the macula are atypical findings in patients with macular drusen. The histopathologic findings in Case 9, on the other hand, are compatible although not completely typical of those seen in patients with macular drusen. The marked degenerative changes in the pigment epithelium found in foveal lesions in Case 9 might be the end result of a long-standing focal exudative detachment of the pigment epithelium. While the histopathologic changes in Bruch's membrane and the choriocapillaris were

minimal, they may be no different from that seen in elderly patients with multiple drusen in the macular region. They were not as marked, however, as those usually seen in the eyes of a patient who progressed to disciform detachment of the macula.

The small yellow foveal lesions seen during the early stages of solar retinopathy or eclipse burns may simulate to some degree the yellow focal lesions in foveomacular dystrophy. The early foveal lesions in solar retinopathy, however, are usually smaller, flatter, and are without a central pigment spot. Also, over a period of several weeks or months they undergo a series of rapid and characteristic changes unlike those seen in foveomacular dystrophy. None of the nine patients presented in this report gave a history of sun gazing.

Further clinical and histopathologic studies are needed to clarify the pathogenesis of this foveomacular lesion and its relationship to macular drusen, senile disciform macular degeneration, Best's disease, and fundus flavimaculatus or Stargardt's disease. For the time being because of its peculiar appearance and its association with a relatively good visual prognosis, it is worthwhile to consider these patients as a separate group in the ever expanding classification of macular dystrophies and degenerative diseases.

SUMMARY

Nine patients with a peculiar foveomacular lesion are reported. These patients may be asymptomatic or they may present because of visual blurring usually between the ages of 30 to 50 years. Typically they present with symmetrical, one-third-disc-diameter-size, slightly raised, round or oval, yellow, subretinal lesions in the foveal area of each eye. A central pigmented spot is usually present. Progression of visual loss is slow and most patients retain reading vision in at least one eye throughout life. The histopathologic findings in one patient suggest that the disease affects primarily the retinal pigment epithelium and that it may be related to dominantly inherited drusen.

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DISCUSSION

DR A. E. MAUMENEE. I wish to congratulate Dr Gass for making yet another very fine contribution to our knowledge of macular and retinal diseases. His excellent clinicopathologic correlations are amongst the best that have appeared in the ophthalmic literature.

It is extremely interesting how original observations are frequently made almost simultaneously by independent observers in various parts of the world. Drs Lawrence Singerman, Joseph Berkow, and Arnall Patz on April 19, 1974 at the Wilmer Residents Meeting described a dominantly inherited macular dystrophy which appears quite similar to that observed by Dr Gass. The vision in these patients remained good until late in life, although significant visual fluctation had been documented by their ophthalmologists over a period of many years. This fluctuation was associated with some ophthalmoscopic pigmentary changes, but serous or hemorrhagic detachments of the pigment epithelium were rarely observed. The macular changes included perifoveal pigment epithelial atrophy, hyperpigmentation in the foveal area, posterior pole flecks, or drusen-like lesions which became much more evident on fluorescein angiography. Other aspects of our fluorescein studies closely resembled those observed by Dr Gass in that in the early stages of the disease there was hyperfluorescence surrounding the foveal area, but immediately under the fovea the picture was dark, suggesting that there was a window defect in the pigment epithelium immediately surrounding the area of central vision. In the older patients the lesions developed an atrophic appearance similar to that seen in atrophic senile macular degeneration. In one patient there was a lesion that appeared to be a flat serous detachment of the pigment epithelium and in one other, the oldest patient, there was a hemorrhagic detachment of the pigment epithelium and the sensory retina. The differential diagnoses were thought to include fundus flavimaculatus, Stargardt's macular degeneration, dominant progressive foveal dystrophy, and senile macular degeneration associated with drusen.

Dr Gass suggested that this condition might have an autosomal dominant form of inheritance. I assume that this was based on the history that the condition had occurred in a member of the family for three generations. In the family observed by Dr Singerman, twelve members of the family out of seventeen of one generation were affected. This generation was composed of five different families. In the next generation, in which there were seven families, six members had early

manifestations of the disease out of twenty offspring, twelve of whom were examined.

The question of inheritance pattern is particularly important in differentiating this condition from Stargardt's disease, for in all except very rare instances which have not been well-documented, Stargardt's disease has been found to have a recessive mode of inheritance. On the basis of the family tree produced by Dr Singerman and his group, Dr Irene Maumenee has calculated that the chances of a recessive trait causing this pattern are 100-million times less than the chances of dominant inheritance.

Again, I wish to congratulate Dr Gass on his excellent presentation and emphasize that his careful clinical work-up of the patients and outstanding pathological correlations on these same patients is a model that we should all attempt to emulate.

DR HAROLD F FALLS. I too wish to congratulate Dr Gass for the excellence of his report of a well verified new entity.

This entity adds a new differential diagnostic consideration when one notes relatively good visual acuity despite rather extensive macular alteration. In the past I always considered such a picture to strongly suggest Best's Disease (vitelliform eruptive disease).

The European ophthalmologists, for the most part, are unitarians in respect to macular degenerative disease. They reason that there is a single underlying genetic causative factor which presents multiple variations differing from family to family. However, I believe that macular degeneration can be polygenic in etiology.

One must consider Sorsby's "exudative hemorrhagic macular degeneration" coming on in the early 30's to 40's in the differential diagnosis of Gass's entity.

While I agree on the uniqueness of Gass's family, I would suggest examination of the younger members of his family to rule out Best's Disease or a variant thereof.

DR J. DONALD M. GASS. I would like to thank Dr Maumenee and Dr Falls for their discussion.

I believe that the photographs of several of Dr Singerman's patients showed a macular lesion similar to that which I described. It also appeared that one of the family members did develop a disciform detachment. While none of my patients have developed a disciform detachment, the histopathologic findings in one of my patients confirmed that the small yellow paracentral spots were, indeed, drusen. Since patients with dominantly inherited macular drusen, and I believe that includes the majority of the patients described by Sorsby as fundus dystrophy, are the major cause of disciform macular detachment, we might expect that some of the patients with the foveomacular lesion which I described might develop a disciform detachment. Our evidence to date, however, would suggest that the visual prognosis for patients with foveomacular dystrophy is better than patients presenting with multiple drusen in the macula without the characteristic yellow foveal plaque.