CLINICAL STUDY

Sorsby's fundus dystrophy: a case report of 24 years follow-up with electrodiagnostic tests and indocyanine green angiography

PECK-LIN LIP, PETER A. GOOD, JONATHAN M. GIBSON

Abstract

Purpose **Five families with dominantly inherited macular dystrophy were originally described by Sorsby *et al.* in 1949. Key features include early bilateral central visual loss secondary to either choroidal neovascularisation or central geographical atrophy and late progressive chorioretinal atrophy. We report a member of one of the original families who has been studied with a series of investigations over a long time, providing important information on differences in the phenotype and natural history of a rare genetically determined macular dystrophy.**

Methods **The patient has been followed up for the last 24 years, from asymptomatic to full manifestation of Sorsby's fundus dystrophy. Series of fundus photographs, colour vision, dark adaptation and electrodiagnostic tests were performed. The disease was also studied with fundus fluorescein angiography and indocyanine green angiography.**

Results **Unlike her other family members, who were reported in other studies as all having rapid loss of vision secondary to disciform macular disease, our patient has a unique clinical course in that she has a progressive bilateral central and generalised chorioretinal atrophy with a well-preserved minute central island of fovea. Nyctalopia was her early and only symptom. There was evidence of central scotoma, tritanopia and mild abnormality in dark adaptation. Rod function was affected earlier and to a larger degree than cone function.**

Conclusions **The overall features suggest phenotypic variability within a family in this autosomal dominant macular dystrophy. The findings from indocyanine green angiography and a consecutive series of electrodiagnostic tests in this condition support the theory of partial choroidal hypoperfusion and an interesting progressive rod–cone dystrophy as part of the pathophysiology.**

P.L. Lip
P.A. Good
J.M. Gibson
Birmingham & Midland Eye Centre
City Hospital NHS Trust
Birmingham, UK

Mrs Peck-Lin Lip ✉
Birmingham & Midland Eye Centre
City Hospital NHS Trust
Dudley Road
Birmingham B18 7QU, UK
Tel: +44 (0)121 554 3801
Fax: +44 (0)121 507 6791

Received: 30 June 1998
Accepted in revised form: 25 November 1998

Key words Electrodiagnostic tests, Indocyanine green angiography, Inherited, Macular dystrophy, Pseudoinflammatory, Sorsby's fundus dystrophy

Five families with dominantly inherited macular dystrophy were originally described by Sorsby *et al.*[1] in 1949. The disease manifests in the fourth decade of life. There were three key features described: autosomal dominant inheritance, bilateral central visual loss in the fifth decade of life secondary to choroidal neovascularisation, and progressive atrophy of the peripheral choroid and retina leading to loss of ambulatory vision by the seventh decade in most cases. Presence of haemorrhages and exudates over the maculae accounts for the sudden loss of central vision. Fundus fluorescein angiography[2] and histopathological[3] studies have confirmed the occurrence of choroidal neovascularisation. Loss of central vision can also be progressive as a consequence of atrophy of the outer retina.[4,5]

In recognition of its extensive macular and paramacular features, this disease has also been known as pseudoinflammatory macular dystrophy,[6] dominantly inherited disciform macular dystrophy[7] and hereditary haemorrhagic macular dystrophy.[8] In 1988, Capon *et al.*[4] stressed the important feature that consistent progressive peripheral changes occur later in life; hence the name was appropriately altered to Sorsby's fundus dystrophy to describe both central and peripheral changes.

Recently, the genetic defect in Sorsby's fundus dystrophy has been identified. Weber *et al.*[9,10] demonstrated point mutations in the TIMP3 gene in affected members of two Sorsby's fundus dystrophy pedigrees. These mutations predicted disruption of the tertiary structure and thus the functional properties of the mature protein. Considering all available data, it is assumed that Sorsby's fundus

dystrophy is a genetically homogeneous, clinically variable, autosomal dominant disorder.

Previous detailed studies on the expanded original pedigrees described by Sorsby revealed differences in the clinical manifestations of the disorder.[4,11] In particular, the family of which our patient is a member was restudied by Hoskin *et al.*[11] in 1981; they confirmed that visual loss in each affected member studied was due to a disciform lesion, and that rapid loss of vision in older relatives implied a similar process. They also stressed that no patient in this particular family has yet been recorded in whom central visual loss was due to geographical atrophy, which was manifested by other families studied.[11]

We would like to report a member of this family who was mentioned in Sorsby's original article but was not actually examined in either instance. She has shown a different and unique clinical course from the rest of the family members described and manifests a new clinical feature. Twenty-four years' follow-up of this patient have allowed us to study the natural history of this rare genetic disorder, its different clinical manifestation and progressivity, and perhaps the underlying pathology related to the disease.

Materials and methods

History

The patient was aged 29 years when she first attended Birmingham & Midland Eye Hospital for genetic counselling in 1973. She gave a history of her mother having been diagnosed with Sorsby's fundus dystrophy, and was one of the patients originally studied in 1949.[1] Our patient was aged only 4 years when she was quoted in the original paper[1] and aged 38 years in Hoskin's article[11] (Fig. 1).

She presented with a past medical history of successful unilateral mastectomy and was on no medication.

She was totally asymptomatic at first presentation with a best corrected visual acuity of 6/6 in both eyes. She is a low myope with a refraction of RE -3.25 DS LE -2.25 DS/-0.5 DC $\times 5^0$ in 1973. We have performed a series of investigations over 24 years of follow-up including fundus photography, dark adaptation test using the Goldmann–Weekers dark adaptometer, electro-oculogram (EOG), scotopic (rod) and 30 Hz (cone) electroretinogram (ERG) using Burien Allen contact lens electrodes and 18 and 2.8 foot-lambert stimulation respectively, Goldmann visual field, Farnsworth–Munsell 100-hue tests and fundus fluorescein angiography (FFA). In addition, indocyanine green (ICG) angiography, standard ERG and pattern ERG were also performed in recent years. Both FFA and ICG angiography were performed with a Topcon fundus camera (TRC-501A). A digitalised infrared fundus video camera system designed by Topcon IMAGEnet was also adapted to the camera part of the Topcon system.

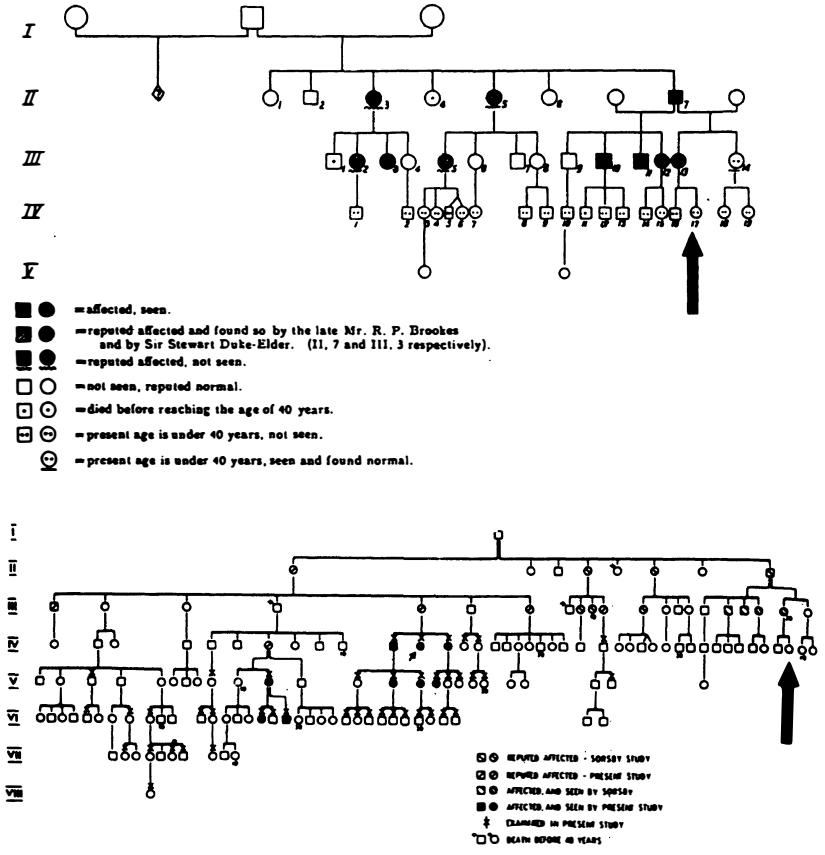


Fig. 1. *Pedigree charts showing our patient was originally mentioned but not studied by Sorsby[1] in 1949 (top) and later in the extended pedigree of the same family by Hoskin[9] in 1981 (bottom).*

Results

Clinical findings

Initial clinical examination revealed normal anterior segment, intraocular pressures and fundoscopy. The patient was then reviewed annually, with satisfactory clinical examination until 1979 when fundoscopy revealed fine drusen-like deposits scattered symmetrically over both maculae. The Farnsworth–Munsell 100-hue test was first performed at this stage giving evidence of a tritan colour defect. The patient remained asymptomatic with good visual acuity until the following year: she experienced nyctalopia which worsened over the following 14 years. However, a dark adaptation study showed a rod threshold only slightly elevated by 0.5 log units (Fig. 2).

The changes in both maculae were slow, and by 1989 there was small but clear evidence of parafoveal chorioretinal atrophy and a few areas of peripheral retinal pigmentation. The central geographical atrophy continued to enlarge but sparing the tiny island of fovea, which retained a healthy pinkish appearance (Fig. 3). When reviewed recently, there was also evidence of peripapillary and peripheral chorioretinal atrophy, not explained by her slightly progressive myopic refraction to RE −4.0 DS, LE −4.00 DS/+0.75 DC × 85°. With the progression of atrophy, the drusen-like deposits were noted to be diminishing. The patient's visual acuity remained at 6/6 in both eyes and she was able to read N5 print monocularly and binocularly. She never reported any history of sudden distortion and nyctalopia remained her only symptom through the years. The Farnsworth-Munsell 100-hue test was repeated in 1995 and 1997, showing constant and asymptomatic tritanopia. No change in dark adaptive rod threshold or duration was noted on review (Fig. 2).

Goldmann visual fields were recorded as normal up to 1980. Thereafter they started to show a paracentral scotoma in 1981, and at this stage the drusen-like deposit remained the more dominant feature on fundoscopy. The series of visual field charts showed enlarging central scotoma of 40°, preserving a minute island over fixation of less than 10° (Fig. 4), reflecting the clinical finding of a central island of healthy fovea.

The results of the series of electrophysiological tests on both eyes showed a slow deterioration of EOG responses to a subnormal level (Fig. 5), years before any symptoms or clinical evidence of the disease. The scotopic ERG to 18 foot-lambert stimulation (Fig. 6a) revealed slightly abnormal responses, again corresponding to the onset of symptoms, but were initially normal and had deteriorated to only 28% of the initial values after 24 years. Flicker ERG (30 Hz), however, has shown responses within overall normal limits so far, although there was a 65% deterioration in amplitude compared with initial recordings (Figs. 6b; 7, middle). Overall, the electrodiagnostic tests suggested that retinal pigment epithelial function had deteriorated corresponding to the peripheral changes and later became static. A recently performed standardised ERG (Fig. 7, top) suggested that rod function was primarily affected compared with cone function, since the red scotopic ERG showed preservation of the cone component of the b wave response but a reduction of the rod component. Furthermore, the photopic b wave was normal at 178 μV right and 175 μV left, but the scotopic b wave was reduced to 200 μV right and 207 μV left with the scotopic responses being only 15% higher in amplitude than the photopic, whereas the difference should be closer to 100% according to our laboratory normals. The pattern ERG reduction (Fig. 7, bottom) reflected the involvement of the central maculae.

Baseline FFA when first performed in 1973 was reported to be normal. The repeats in 1990 and 1997 (Fig. 8a–c) showed features of a prolonged choroidal filling phase and visibility of large choroidal blood vessels before the choriocapillaries. The late central hyperfluorescence corresponding to the geographical atrophy was noted as a result of extrachoroidal and scleral staining rather than a window defect. Peripheral irregular hyperfluorescence and fine mottling in the late phases were also recorded.

ICG angiography was performed as an adjunct to FFA (Fig. 9). The larger choroidal blood vessels in the early phase were visible through a large central area of relative hypofluorescence which was accentuated in the later phases. In contrast, the peripheral retina showed early mottling and late increased hyperfluorescence corresponding to the clinical pigmentary changes. Neither FFA nor ICG angiography revealed any evidence of choroidal neovascularisation.

Discussion

From the studies based on the original five families and a few others outside Britain, the presentations of the clinical features in Sorsby's fundus dystrophy may be categorised into three variations:[1,12] the most frequently reported variation is characterised by a disciform maculopathy, pale fundus spots distinct from drusen, and a frequent prodrome of nyctalopia. The second group has a disciform maculopathy but no pale spots or nyctalopia, and patients in the third group have an atrophic maculopathy and pale fundus spots but no nyctalopia. Other affected family members of our patient studied by Sorsby[1] and later by Hoskin[11] had placed this family into the first category, but our patient reported

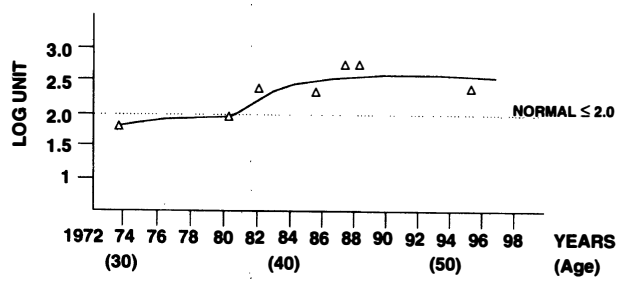


Fig. 2. *Dark adaptation tests showing an initial slight elevation of rod threshold that remains unchanged as the disease progressed.*

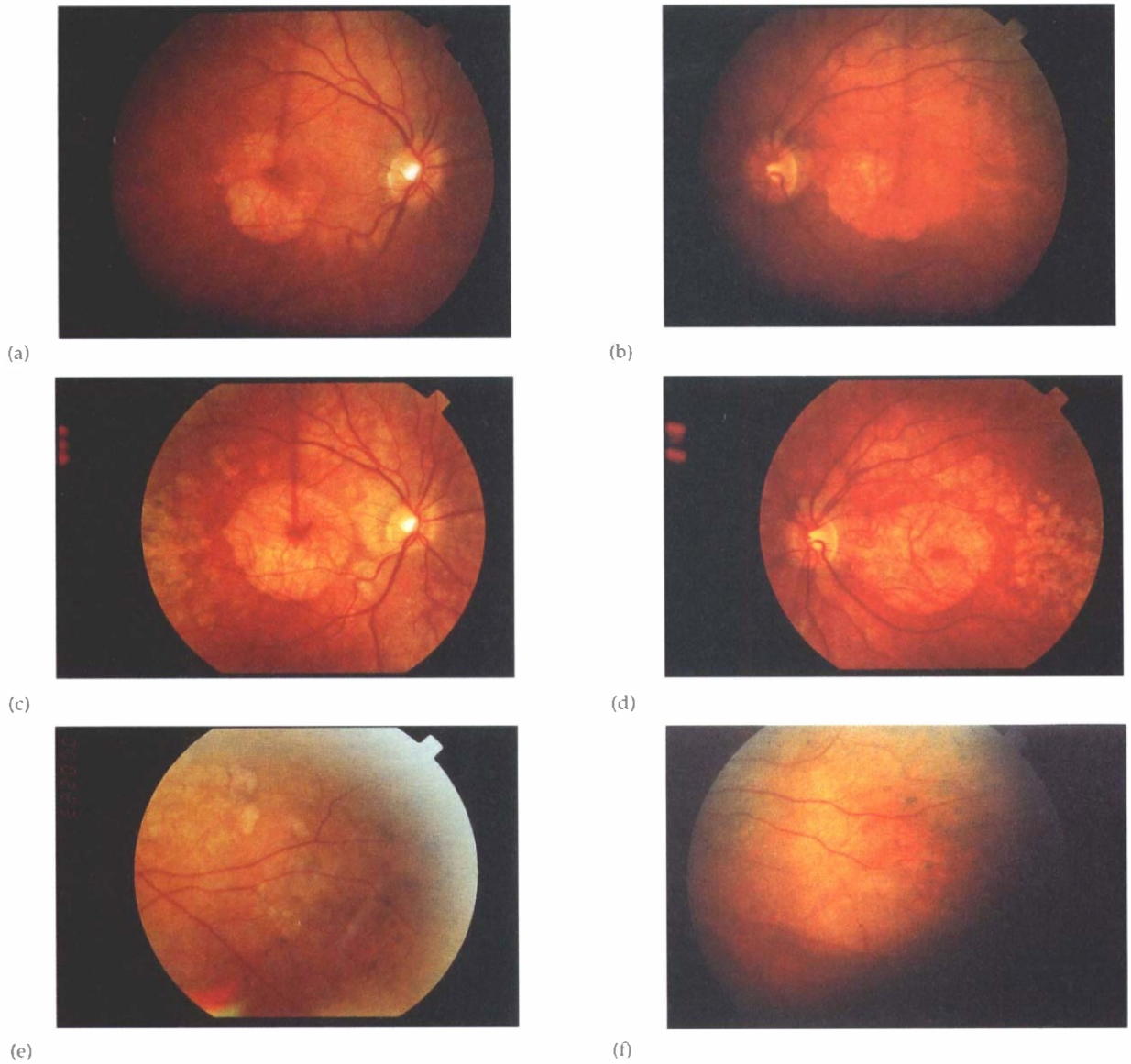


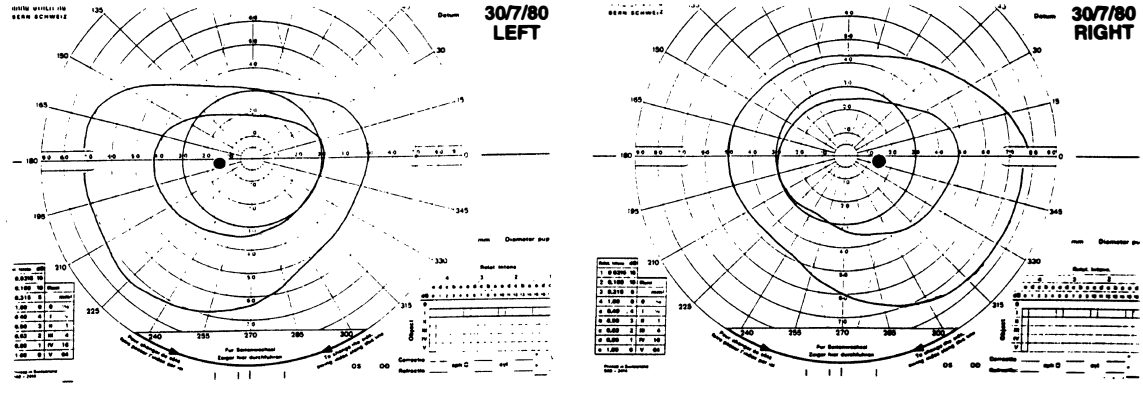
Fig. 3. *Fundus photographs showing established bilateral symmetrical central geographical atropy in 1990 (a, right eye; b, left eye) with evidence of enlargement of atrophy in 1997 (c, right eye; d, left eye). The disease also involved peripheral retina at an early stage in 1990 (e); it was more widespread by 1997 (f).*

here does not belong to the same group as the rest of her family and indeed presents a different category of manifestations.

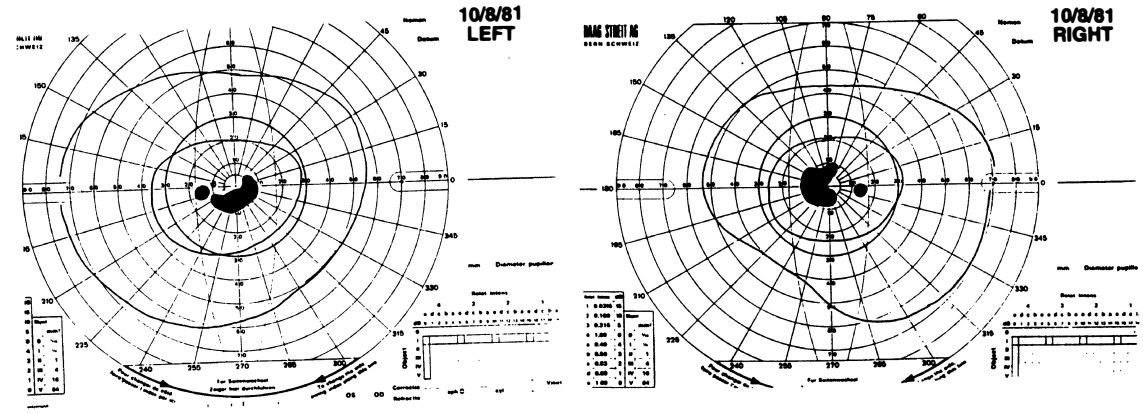
The recent exciting discovery of a defective gene in Sorsby's fundus dystrophy has opened an easier access to diagnosis and aids in identifying individuals at risk in a family. In a single large Sorsby's fundus dystrophy family, Weber *et al.*[9,10] demonstrated linkage to markers on 22q13-qter between D22S274 and D22S275. Later, they studied the gene encoding tissue inhibitor of metalloproteinase-3 (TIMP3) as a candidate gene on the basis of its chromosomal location at 22q12.1–q13.2 and its pivotal physiological role in extracellular matrix remodelling. They demonstrated point mutations in the TIMP3 gene in affected members of two Sorsby's fundus dystrophy pedigrees. These mutations predicted disruption of the tertiary structure and thus the functional properties of the mature protein. From the information available, it is thought that Sorsby's fundus dystrophy can present in various phenotypes but has a homogeneous genotype. The patient we are reporting manifested a less common phenotype. Should genetic analysis be available, it would be interesting to further confirm the genetic homogeneity in this disorder. Nevertheless, we do not have complete information regarding genetic confirmation in family members of the patient at this stage.

Central maculopathy

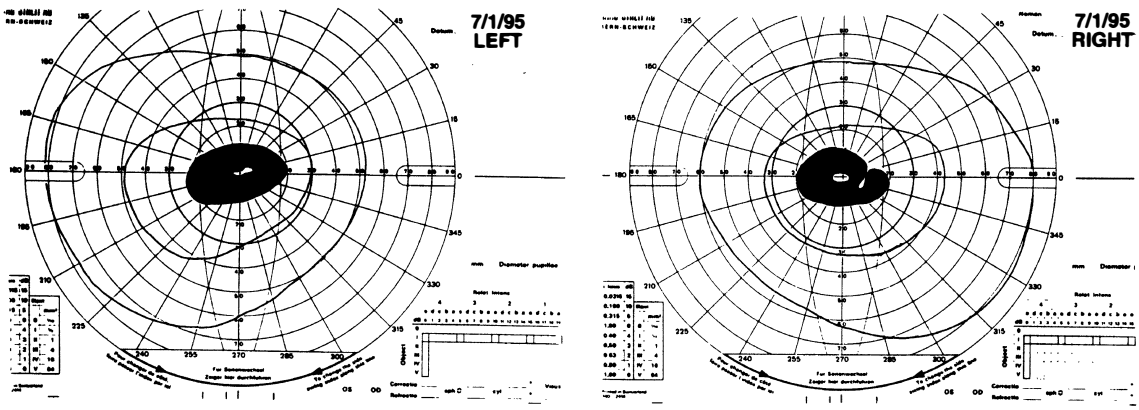
Yellow subretinal deposits resembling drusen are a common but not a uniform finding in patients with Sorsby's fundus dystrophy. Patients can remain asymptomatic for a long time when there is ophthalmological evidence of these deposits over both macula and peripheral retina.[4] These deposits were less apparent with age[4,13] and disappeared when atrophy supervened. Hoskin *et al.*[9] concluded that these anatomical changes were reliable markers of the abnormal genotype. Histological study[5] demonstrated



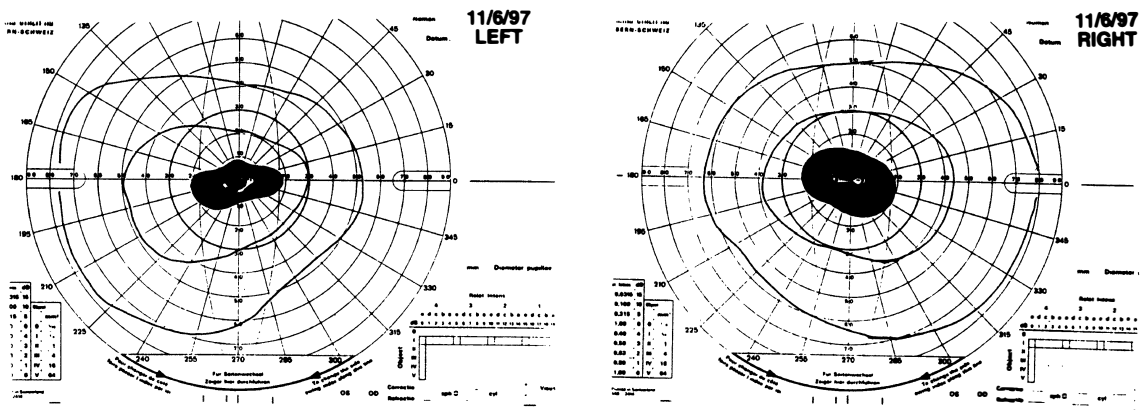
(a)



(b)



(c)



(d)

Fig. 4. *Series of Goldmann visual fields charted over the years. They were recorded as normal up to 1980. Thereafter they deteriorated rapidly to bilateral paracentral scotoma in 1981, showing enlarging central scotoma preserving a minute island over the fixation corresponding to her clinical manifestations (1995 and 1997). Peripheral visual fields, however, were grossly intact.*

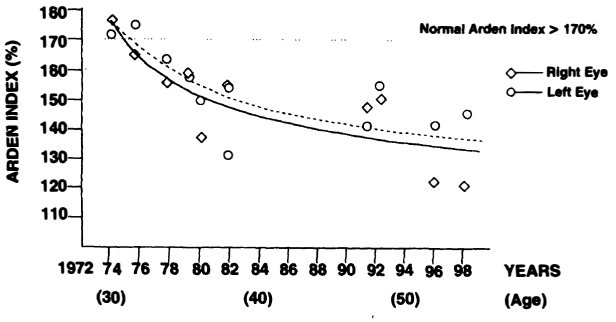


Fig. 5. *Series of EOG results showing responses had deteriorated to a subnormal level years before any symptoms or clinical evidence of the disease.*

this yellow material, 30 μm in thickness, within the inner collagenous layer of Bruch's membrane and the basement membrane of the retinal pigment epithelium; it stained positive for lipids. Capon *et al.*[5] reported the abnormal yellow deposit could have derived from the retinal pigment epithelium. The degeneration of the choriocapillaris is proposed as a consequence of the diseased retinal pigment epithelium,[14] which in turn leads to degeneration of photoreceptors at a later stage.

Disciform maculopathy is an established cause of sudden loss of vision in this disorder both histologically[3] and angiographically. Patients are at high risk of developing choroidal neovascularisation during their fourth and fifth decade of life,[15] but patients in their early twenties have been reported.[12,13] The results of laser photocoagulation on the choroidal neovascularisation of this group of patients demonstrated that laser treatment could not prevent severe visual loss, and untreatable recurrences were detected within 2 years of the initial treatment.[15]

Atrophic macular disease without evidence of choroidal neovascularisation was responsible for gradual loss of vision in some families studied. Patients often preserved good vision into their sixth decade of life with enlarging central geographical atrophy.[4] Our patient manifests this category of clinical features. The possibility of her having had asymptomatic choroidal neovascularisation at some stage in the past was unlikely, supported by the fact that there was no evidence of hyperpigmentation within the atrophic area, and no evidence on FFA and ICG angiography.

Night blindness

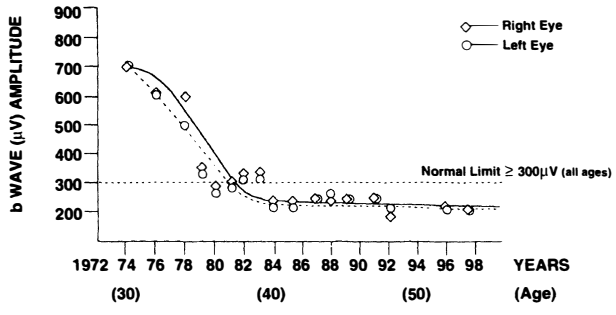
Nyctalopia has been regarded as the first symptom of Sorsby's fundus dystrophy, suggesting an abnormal genotype in this disorder.[4] It reflects the peripheral retinal dysfunction and can occur up to 25 years prior to the loss of central vision.[4] Nyctalopia was the earliest symptom in our patient, which worsened as her disease progressed. The slightly elevated dark adaptation rod threshold and prolonged time correspond to the onset of her symptom and may reflect the progressive spreading of the peripheral pigmentary and atrophic changes.

Colour defect

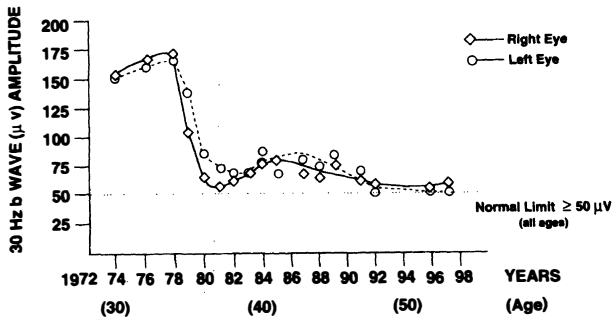
Our patient has shown a consistent tritan colour defect both when abnormality first appeared on fundoscopy and at a later stage when progressive geographical atrophy was well established. Both symptomatic and asymptomatic tritan as well as deutan colour defects have been documented[4,12,16] and attributed to the assumed blue cone damage in early macular disease which persisted until loss of central vision occurred. The colour defect in this case was tested only when there were visible drusen-like deposits at the maculae. It was proposed that colour anomalies could present simultaneously, or precede the onset of an ophthalmoscopic lesion.[17] If the functional defect was present before any ophthalmoscopic abnormality, this could be used to detect the abnormal genotype.[4,18]

Visual fields

The visual field pattern has not been well documented in previous literature on Sorsby's fundus dystrophy. Static perimetry was performed but was not described in the study by Capon *et al.*[4] Hamilton *et al.*[12] found relative central and paracentral scotoma depression in most of his studied patients before the maculopathy supervened; after that, slowly enlarging absolute central scotomas were the rule. Forsius *et al.*[13] reported the same field defects many years before any other clinical signs were noted, except that his study patients had pseudoinflammatory fundus dystrophy but of autosomal recessive inheritance.



(a)



(b)

Fig. 6. *Reduced ERG responses corresponding to the onset of symptoms. Scotopic ERG (a) revealed slightly abnormal responses and flicker ERG at 30 Hz (b) showed responses within the normal limits, although there was a deterioration in amplitude compared with initial recordings.*

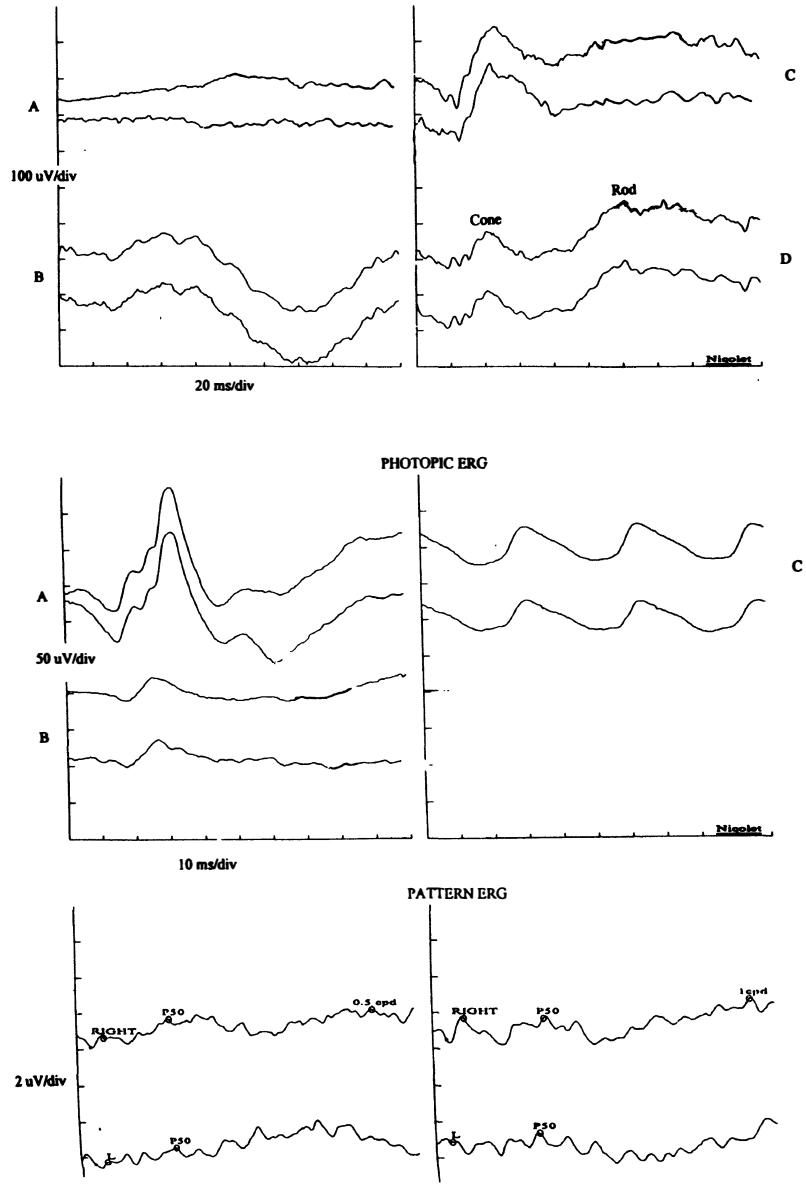
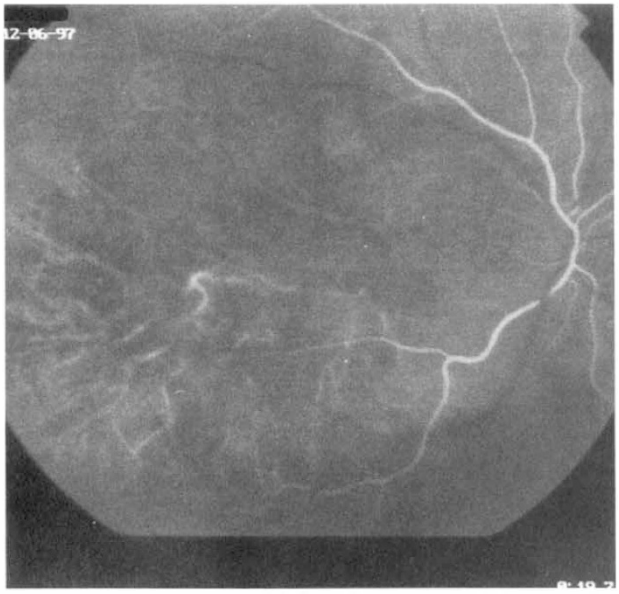


Fig. 7. *Standardised ERG (top) showing markedly reduced dim flash scotopic responses (−2 log units), slightly reduced standard flash responses, and an absent rod component to red scotopic stimulation. Photopic (middle) and 30 Hz (cone) responses are borderline normal. These responses imply a mainly rod dysfunction. Pattern ERG (bottom) responses show a gross reduction of p50 components in both eyes.*

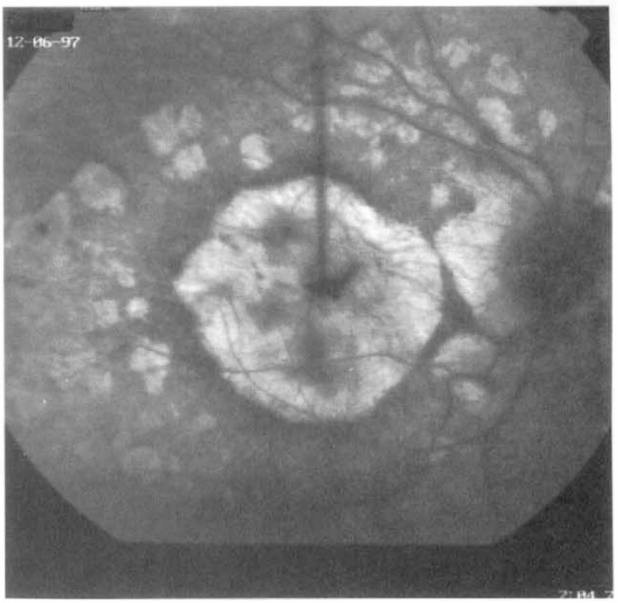
The series of Goldmann visual fields on our patient have shown a rapid development and later slow enlargement of bilateral central scotomata corresponding to the progressive geographical atrophy. Interestingly, the central island of 5° to 10° is spared, preserving her excellent vision in both distance and close work. The pattern and rapidity of abnormal visual field development in this disorder were under-reported in the literature and it is unclear whether other affected members of this family shared the same nature of the development of abnormal visual fields. In the study by Hamilton *et al.*[12] of a family from Eire, one of the nine members examined had a similar tiny central island in the scotoma; all of his studied patients, however, were reported to have disciform maculopathy and it was unclear how long that visual field was retained.

Fundus fluorescein angiography

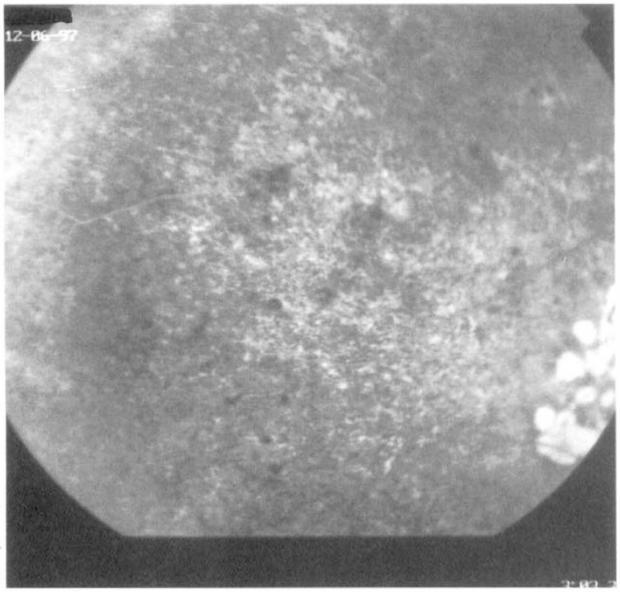
The first evidence of the abnormal phenotype was documented with FFA.[19] Unfortunately, FFA was not available on our patient when drusen-like deposits were first revealed at the maculae. At the later stage of the disease, however, FFA on our patient showed all the three key features[4,19,20] documented (Fig. 8): a delay in the choroidal filling phase; the appearance of large choroidal blood vessels before the choriocapillaries; and, lastly, diffuse fine mottling of irregular hyperfluorescence of peripheral retina and a well-demarcated hyperfluorescence window defect over the central macula at the late phases.



(a)



(b)



(c)

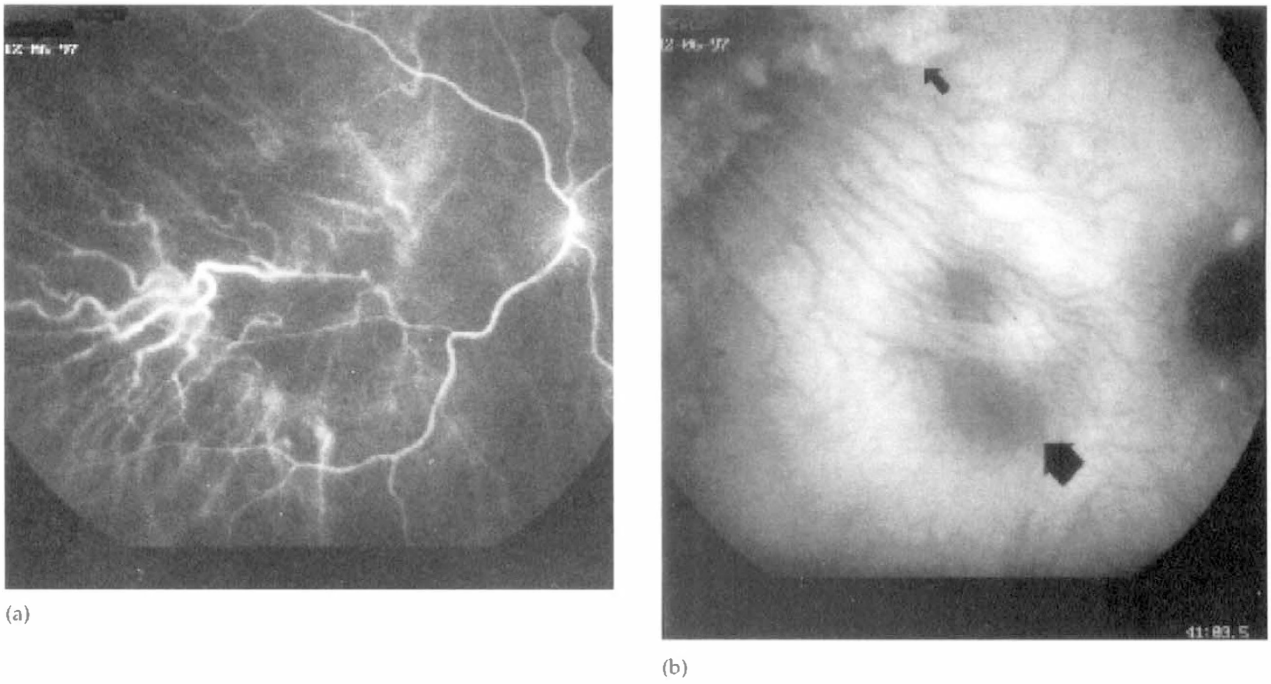
Fig. 8. *Fundus fluorescein angiography of the right eye revealed all three features: delay in the choroidal filling phase (a); appearance of the large choroidal blood vessels before the choriocapillaries (a); and diffuse fine mottling of irregular fluorescence at the late phases (c). (b) Late choroidal staining corresponding to the central geographical atrophy.*

Indocyanine green angiography

ICG angiography on this patient (Fig. 9) has shown enhanced imaging of the larger choroidal blood vessels in the early phase visible through a large central area of relative hypofluorescence corresponding to the clinical geographical atrophy. The appearance of this area of relative hypofluorescence, however, is accentuated in the later phases as a result of the drained fluorescence from large choroidal blood vessels and retained dye in the remaining encircling healthy retinal tissues. The pigmentary atrophic-looking peripheral retina is reflected by early mottling and late increased hyperfluorescence. Unlike the appearance on FFA, the changes at the central macula and peripheral retina show as contrasting hypo- and hyperfluorescence, respectively. The ICG findings therefore allow us to appreciate the different degree and thickness of disease involvement at the macula and peripheral retina.

As choriocapillaries are not directly imaged with ICG,[21] these contrasting findings could further suggest the loss of outer retina layers in the macula giving persisting hypofluorescence. The peripheral retinal pigment epithelial pathology with preservation of retinal cells is, on the other hand, reflected by persisting hyperfluorescence; these ICG findings correspond to the findings of central scotoma with full peripheral Goldmann fields.

It is believed that the delay in choroidal filling in FFA is more likely to result from hypoperfusion than obscuration of the choroid by yellow deposits visible clinically.[4,5,12,19] This is supported by the fact that the large choroidal blood vessels remain visible and appear normal on both FFA and ICG angiography. Pauleikhoff *et al.*[20] proposed that the prolonged choroidal filling phase may represent a clinical correlation of diffuse thickening of Bruch's membrane.[5] As there is a similarity to the



(a) (b)

Fig. 9. *Indocyanine green angiography of the right eye revealed enhanced imaging of the larger choroidal blood vessels in the early phase (a), visible through a large central area of relative hypofluorescence corresponding to the clinical geographical atrophy. The area of relative hypofluorescence (b, fat arrow) was accentuated in the late phases as a result of drained fluorescence from large choroidal blood vessels and retained dye in the remaining encircling healthy retinal tissues. In contrast, the peripheral retina showed early mottling and late increased hyperfluorescence (b, thin arrow) corresponding to the clinical pigmentary changes.*

angiographic features in acute multifocal placoid pigment epitheliopathy, it therefore may suggest that there is partial choroidal hypoperfusion selective only on the choriocapillaries. It is likely that the deposit in Bruch's membrane may be the primary pathological event,[19] with atrophy of the choriocapillaries occurring secondarily to impeded diffusion of the choroidal endothelial cell behaviour factor released by the retinal pigment epithelium.[14] The loss of retinal pigment epithelium and later choriocapillaries is likely to account for the loss of outer retina as a consequence.

Rod versus cone dystrophy

The prolonged and elevated dark adaptation with a reduced threshold rate of rhodopsin regeneration found in the study by Steinmetz *et al.*[20] had implied functional impairment of photoreceptors in Sorsby's fundus dystrophy. Capon *et al.*[4] demonstrated a functional defect of the retinal pigment epithelium in early disease from prolonged dark adaptation time and static perimetry. As a whole, dark adaptation deteriorates with disease duration, with relatively normal function of the retinal pigment epithelium until extensive peripheral degeneration has occurred, although in our patient the elevated rod threshold and duration remain static throughout the progression of the disease.

Studies of the ERG in patients with Sorsby's fundus dystrophy have revealed a range of results from normal[9] through minimally abnormal[4,23] to abnormal,[8,16,24] and in the EOG from minimally abnormal in some patients to severely abnormal in others.[4,23,24] These results correspond to the ophthalmoscopic findings at different stages and indicate progressive dysfunction of the retinal pigment epithelium. In the study by Hoskin *et al.*[11] only selected subjects with normal vision at 50% risk of having the abnormal gene proceeded to electrodiagnostic tests. None of them had any abnormal results in EOG, mass ERG, macular ERG or Panel D-15 colour vision tests. The clinical findings in these patients were limited to drusen-like yellow deposits. Of those patients who suffered from central geographical atrophy in different families, the ERG tests were not specific or standardised to clarify the dysfunction of different photoreceptors.

Our patient has been studied with a series of scotopic and flicker ERG, standard ERG and pattern ERG. Progressively abnormal responses to scotopic stimuli and relatively normal responses under photopic conditions were confirmed. The selective impairment of rod function was noted by the standard ERG, using scotopic red light stimuli and dim flash blue/white stimuli. Also, deterioration of the scotopic ERG was more marked than that of the 30 Hz response, which is primarily a cone response but contains some impaired central rods. This may explain the relative deterioration of the 30 Hz ERG over the years, although some degree of cone loss may also have occurred. It is hence proposed that amongst the photoreceptors, rods represent the main loss in outer retinal atrophy, although cones may also have been affected to a lesser degree.

One other factor supporting selective rod dystrophy comes from comparing the clinical findings with the anatomical distribution of rods and cones.[25,26] The central fovea, measuring about 1500 μm across and subtending about 5° at the nodal point of the eye, consists of the highest density of cone photoreceptors. The rod-

free territory is some 500–600 μm across, corresponding roughly to the foveal avascular zone. Beyond this limit rods appear and their proportion relative to cones increases progressively, the greatest rod density over the parafoveal area and the perifoveal area being associated with a further decrease in the proportion of cones relative to rods. Our patient has indeed shown an interesting geographical correspondence with the higher rod density distribution; this is further reflected by her visual field and visual acuity. Foveal sparing has been described in a variety of diseases associated with progressive, initially extrafoveal retinal pigment epithelial atrophy, such as age-related macular degeneration; it is therefore not a unique but a rare finding in Sorsby's fundus dystrophy.

The geographical nature of the retinal dystrophy, together with the preservation of the peripheral field, correlates with the relative preservation of the ERG even after 24 years of progression of the disease and the non-progression of the elevated rod threshold in dark adaptation tests. The high concentration of rod cells near the central retina would also correspond to the field loss and ERG changes.

Conclusion

Our patient with Sorsby's fundus dystrophy presented with progressive central atrophy and nyctalopia at an early stage; these have not been noted in previous reports on members of the same family but have been well documented in other series.[1,4,11,19] We have therefore demonstrated phenotypic heterogeneity within a family.[4,11] Of course, the possibility that the patient's father had another macular dystrophy could have modified her clinical manifestations, but the patient's father was reported to have no visual problems before dying from a cardiovascular cause at age 50 years. From previous histological studies, the diseased retinal pigment epithelium and Bruch's membrane were thought to give rise to choriocapillary degeneration; we support the theory of partial choroidal hypoperfusion as the cause, based on the findings of fluorescein and indocyanine green angiographies. We have further established that, in the case of progressive central macular atrophy in Sorsby's fundus dystrophy, it is predominantly a rod–cone rather than a cone–rod dystrophy, at least at the initial stage based on the electrophysiological results.

Obviously, these findings were based on one case report of long-term follow-up. Additional research with a larger number of patients with this disorder will be required to investigate these concepts further.

We thank the patient for her patience and contribution to this paper; and the medical illustration department and the staff in the macular clinic for their efforts in different aspects of contribution.

References

1. Sorsby A, Mason MEJ, Gardener N. A fundus dystrophy with unusual features. Br J Ophthalmol 1949;33:67–97.
2 Rosen ES, Leighton D. Fluorescein photography of generalised dominant fundus dystrophy. Br J Ophthalmol 1968;52:828–32.
3. Ashton N, Sorsby A. Fundus dystrophy with unusual features: a histological study. Br J Ophthalmol 1951;51:751–64.
4. Capon MRC, Polkinghorne PJ, Fitzke FW, Bird AC. Sorsby's pseudoinflammatory macular dystrophy: Sorsby's fundus dystrophies. Eye 1988;2:114–22.
5. Capon MRC, Marshall J, Krafft JI, Alexander RA, Hiscott PS, Bird AC. Sorsby's fundus dystrophy: a light and electron microscopic study. Ophthalmology 1989;96:1769–77.
6. Duke-Elder S, editor. System of ophthalmology. Vol IX. Diseases of the uveal tract. London: Kimpton, 1966:715–9.
7. Deutman AF. The hereditary dystrophies of the posterior pole of the eye. Assen: Van Gorcum, 1971:400–8.
8. Carr RE, Noble KG, Nasaduke I. Hereditary haemorrhagic macular dystrophy. Am J Ophthalmol 1978;85:318–28.
9. Weber BHF, Vogt G, Pruett RC, Stohr H, Felbor U. Mutations in the tissue inhibitor metalloproteinases-3 (TIMP 3) in patients with Sorsby's fundus dystrophy. Nature Genet 1994;8:352–6.
10. Weber BHF, Vogt G, Woltz W, Ives EJ, Ewing CC. Sorsby's fundus dystrophy is genetically linked to chromosome 22q13-q. Nature Genet 1994;7:158–61.
11. Hoskin A, Sehmi K, Bird AC. Sorsby's pseudoinflammatory macular dystrophy. Br J Ophthalmol 1981;65:859–65.
12. Hamilton WK, Ewing CC, Elizabeth JI, Carruthers JD. Sorsby's fundus dystrophy. Ophthalmology 1989;96:1755–62.
13. Forsius HR, Eriksson AE, Suvanto EA, Alanko HI. Pseudoinflammatory fundus dystrophy with autosomal recessive inheritance. Am J Ophthalmol 1982;94:634–49.
14. Korte GE, Reppucci V, Henkind P. RPE destruction causes choriocapillary atrophy. Invest Ophthalmol Vis Sci 1984;25:1135–45.
15. Holtz FG, Haimovici R, Wagner DG, Bird AC. Recurrent choroidal neovascularisation after laser photocoagulation in Sorsby's fundus dystrophy. Retina 1994;14:329–34.
16. Balyeat RM, Kingsley RM. Dominant macular subretinal neovascularisation with peripheral retinal degeneration. Ophthalmology 1987;94:1140–7.
17. Sorsby A, Davey JB. Dominant macular dystrophy. Br J Ophthalmol 1955;39;385–97.
18. Fraser HB, Wallace DC. Sorsby's familial pseudo-inflammatory macular dystrophy. Am J Ophthalmol 1971;71:1216.
19. Polkinghorne PJ, Capon MRC, Beninger T, Lyness A, Sehmi K, Bird AC. Sorsby's fundus dystrophy: a clinical study. Ophthalmology 1989;96:1763–8.
20. Pauleikhoff D, Chen JC, Chisholm IH, Bird AC. Choroidal perfusion abnormality with age-related Bruch's membrane change. Am J Ophthalmol 1990;109:211–7.
21. Yanuzzi LA, Flower RW, Slakter JS. Indocyanine green angiography. St Louis: Mosby, 1997:128–50.
22. Steinmetz RL, Polkinghorne PC, Fitzke FW, Kemp CM, Bird AC. Abnormal dark adaptation and rhodopsin kinetics in Sorsby's fundus dystrophy. Invest Ophthalmol Vis Sci 1992;33:1633–6.
23. Dreyer RF, Hidayat AA. Pseudoinflammatory macular dystrophy. Am J Ophthalmol 1988;106:154–61.
24. Wu G, Pruett RC, Baldinger J, Hirose T. Hereditary haemorrhagic macular dystrophy. Am J Ophthalmol 1991;111:294–301.
25. Davson H. Physiology of the eye. 5th ed. Macmillan, 1990:208–10.
26. Tasman W, Jaeger EA. Duane's foundations of clinical ophthalmology. Vol 1. Philadelphia: JB Lippincott, 1991:6–9.