

OPTICAL COHERENCE TOMOGRAPHY OF ADULT- ONSET VITELLIFORM DYSTROPHY

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ABSTRACT

Purpose: to report the cross-sectional structure of the retina and choroid in eyes with adult-onset vitelliform macular dystrophy as obtained by optical coherence tomography (OCT)

Methods: Seven patients with adult-onset vitelliform macular dystrophy and one patient with Best disease were examined by fundoscopy, fluorescein and indocyanine green angiography and OCT. Three patients underwent also electro-oculography.

Results: 1. Seven cases with adult-onset vitelliform macular dystrophy showed a well-circumscribed elevation of a highly reflective band, corresponding to the retinal pigment epithelium 2. In these 7 patients, the space below this band was inhomogeneous and moderately reflective. 3. Four cases out of 7 had a well defined posterior boundary. 4. The patient with Best disease disclosed a different aspect on OCT, although the contour of the lesion was similar to the others.

Conclusion: Optical coherence tomography disclosed the structure of the vitelliform lesion in vivo and could be helpful for its pathological interpretation.

SAMENVATTING

Doel: Analyse van de beelden van retinale profielen bekomen met behulp van optische coherentie tomografie (OCT) in ogen met adult-onset vitelliforme maculaire dystrofie.

Methode: Zeven patiënten met adult-onset vitelliforme maculaire dystrofie en één patiënt met ziekte van Best werden onderzocht met behulp van oftalmoscopie, fluoresceïne- en indocyanine groen angiografie en met OCT. Drie patiënten ondergingen eveneens een EOG.

Resultaten: 1. De zeven patiënten met adult-onset vitelliforme maculaire dystrofie vertoonden een wel omschreven sterk reflectieve band aan de bovenste kant van het letsel; deze band komt vermoedelijk overeen met het retinaal pigment epitheel. 2. Bij deze patiënten was de zone onder deze sterk reflectieve band, inhomogeen en weinig reflectief. 3. Bij 4 van de 7 patiënten was de achterste grens goed afgelijnd. 4. Het OCT patroon bij de patiënt met ziekte van Best was verschillend alhoewel het contour van het letsel vergelijkbaar was.

Besluit: OCT geeft in vivo de structuur weer van het vitelliform letsel en kan dus nuttig zijn bij de interpretatie van de pathologie.

RÉSUMÉ

Objectif: Décrire à l'aide de l'OCT les structures de la rétine et de la choroïde dans des yeux atteints de dystrophie maculaire vitelliforme de l'adulte.

Méthode: Sept patients avec dystrophie maculaire vitelliforme de l'adulte et un patient atteint de maladie de Best ont été examinés par ophtalmoscopie, angiographie fluorescéinique et au vert d'indocyanine et à l'OCT. Trois patients ont également bénéficié d'un EOG.

Résultats: 1. Sept cas de dystrophie maculaire vitelliforme de l'adulte présentaient au niveau de la limite antérieure de la lésion une bande réflexive,

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qui correspond probablement à l'épithélium pigmentaire de la rétine. 2. Chez ces patients l'espace en dessous de cette bande réfléchive était inhomogène et modérément réfléchif. 3. De ces 7 cas 4 présentaient une limite postérieure nettement définie. 4. Le patient avec la maladie de Best présentait un aspect différent bien que les contours de la lésion étaient semblables aux autres cas.

Conclusion: L'OCT démontre la structure in vivo de la lésion vitelliforme et pourrait être utile pour l'interprétation de la pathologie.

KEY-WORDS

Optical coherence tomography, adult-onset vitelliform macular dystrophy, Best disease.

MOTS-CLÉS

Tomographie à cohérence optique, dystrophie maculaire vitelliforme de l'adulte, maladie de Best.

INTRODUCTION

Adult-onset vitelliform dystrophy, first described by Gass (8-9), becomes manifest in adult life and is most commonly characterized by symmetric, solitary round to oval, one third to one disc diameter in size, yellowish subretinal macular lesions often with a central pigmented spot. It causes a mild to moderate, slowly progressing visual loss. Severe visual impairment is rare but has been reported (24). The electro-oculogram (EOG) is normal to slightly subnormal (8,9,17). Female patients are predominant in the reported series (4,12,14,22). According to some authors, adult-onset vitelliform dystrophy could be inherited in an autosomal dominant way (2,8). Since the first report by Gass, further studies showed that adult-onset vitelliform macular dystrophy is a heterogeneous group of disorders, which share many clinical features with pattern dystrophy, Best disease and age-related macular degeneration (3,4,10,20,25). In addition, the vitelliform lesion itself may present a variable evolution.

Up to now, few histopathological studies have been reported of adult-onset vitelliform macular dystrophy (5,8,15,19). However, the pathogenesis of this condition remains controversial.

Optical coherence tomography (OCT) can show in an uninvasive way the cross-sectional tomographic image of the eye, with a maximal longitudinal resolution of 10μ . (13,21). Hence we studied seven patients with presumed adult-onset vitelliform dystrophy with OCT and will discuss several findings that may be helpful for diagnosis and interpretation of the vitelliform lesion.

MATERIAL AND METHODS

We studied retrospectively the clinical files of seven patients who were diagnosed as adult-onset vitelliform macular dystrophy between June 1996 and March 2001 at the Ghent University Hospital. All patients underwent OCT between May 2000 and March 2001. Two were males and 5 females with ages varying from 40 to 76 years (mean age 60,5 years). The diagnosis was based on the presence of a sub-

foveal yellow lesion in at least one eye with the onset of visual symptoms (mild visual blurring and/or metamorphopsia) at adult age. The diagnosis was also verified by fluorescein and by indocyanine green angiography with evidence of autofluorescence and absence of choroidal neovascularization (17). Two patients underwent electro-oculography. For these seven patients the family history was negative and no other medical history was reported. As comparison an OCT was also performed in a 54 year old man with Best disease.

A commercially available optical coherence tomography unit (Zeiss-Humphrey Instruments Ltd) was used. Cross-hair scans of 5,65 mm length were performed through the macular region.

RESULTS

Seven patients with presumed adult-onset vitelliform macular dystrophy were examined with OCT. These 7 cases showed a well-circumscribed elevation with a highly reflective band corresponding to the retinal pigment epithelium. The space under the retinal pigment epithelium was inhomogeneous and moderately reflective. Four cases had well defined posterior boundaries; the other three cases revealed an optically empty space, consistent either with serous detachment or with liquid within the vitelliform lesion. The patient with Best disease (case 3) disclosed a different aspect on OCT, although the contour of the lesion was similar. The results of the OCT were correlated with the results of fundus photography, slit-lamp biomicroscopy, fluorescein angiography and indocyanine green angiography. We show two illustrative cases as well as the patient with Best disease.

CASE REPORTS

ADULT-ONSET VITELLIFORM DYSTROPHY (TABLE 1)

CASE 1

A 76 year old woman was referred in June 1999 for evaluation of decreased vision with metamorphopsia. Her medical history was noncontributory. Best corrected visual acuity in both

eyes was 4/10. On ophthalmoscopy a symmetrical, yellowish oval macular lesion of $\frac{1}{2}$ disc diameter was detected. On fluorescein angiography, the macular lesion showed a central blockage in the early phase and hyperfluorescence in the late phase. It also revealed autofluorescence under infrared videography and a starshaped hypofluorescent area on ICG angiography. No dye leakage suggestive of choroidal new vessels was observed. In January 2001, the patient complained of further decrease in vision in her left eye. The visual acuity was 5/10 in the right eye and 1/10 in the left eye. The vitelliform lesion of the right eye had not changed (Fig 1A), but an atrophic macular lesion in the left eye was observed (Fig 1B). Fluorescein angiography of the right macula revealed an oval hypofluorescent area in the early phase, and hyperfluorescence in the late phase (Fig 1C). The left macula showed a window defect, consistent with an atrophic lesion. No dye leakage suggesting choroidal neovascularization was observed. With OCT the macular lesion of the right eye disclosed a dome shaped thickening and disruption of the vitelliform lesion (Fig 1D). The overlying sensory retina was thin and slightly elevated. The normal foveal contour was not observed. The OCT of the left eye showed a thin (around 100μ) fovea corresponding to macular atrophy (Fig 1 E).

CASE 2

A 62 year old woman complained of slight blurring and metamorphopsia in her right eye for the past six months. Visual acuity was 8/10 in the right eye and 10/10 in the left eye. Ophthalmoscopic examination revealed some macular drusen and pigment epithelium mottling in both eyes as well as a yellow vitelliform macular lesion, one third disc diameter in size, in the right eye (Fig 2A). This macular lesion was autofluorescent under infrared light. On fluorescein angiography it showed irregular hyperfluorescence of the superior half in the early phase (Fig 2B) and hyperfluorescence of the whole lesion in the late phase (Fig 2C). No signs of choroidal neovascularization were observed on indocyanine green angiography. The OCT of the macular lesion disclosed a dome shaped elevation with a highly reflective anterior band and with inhomogeneous reflectivity

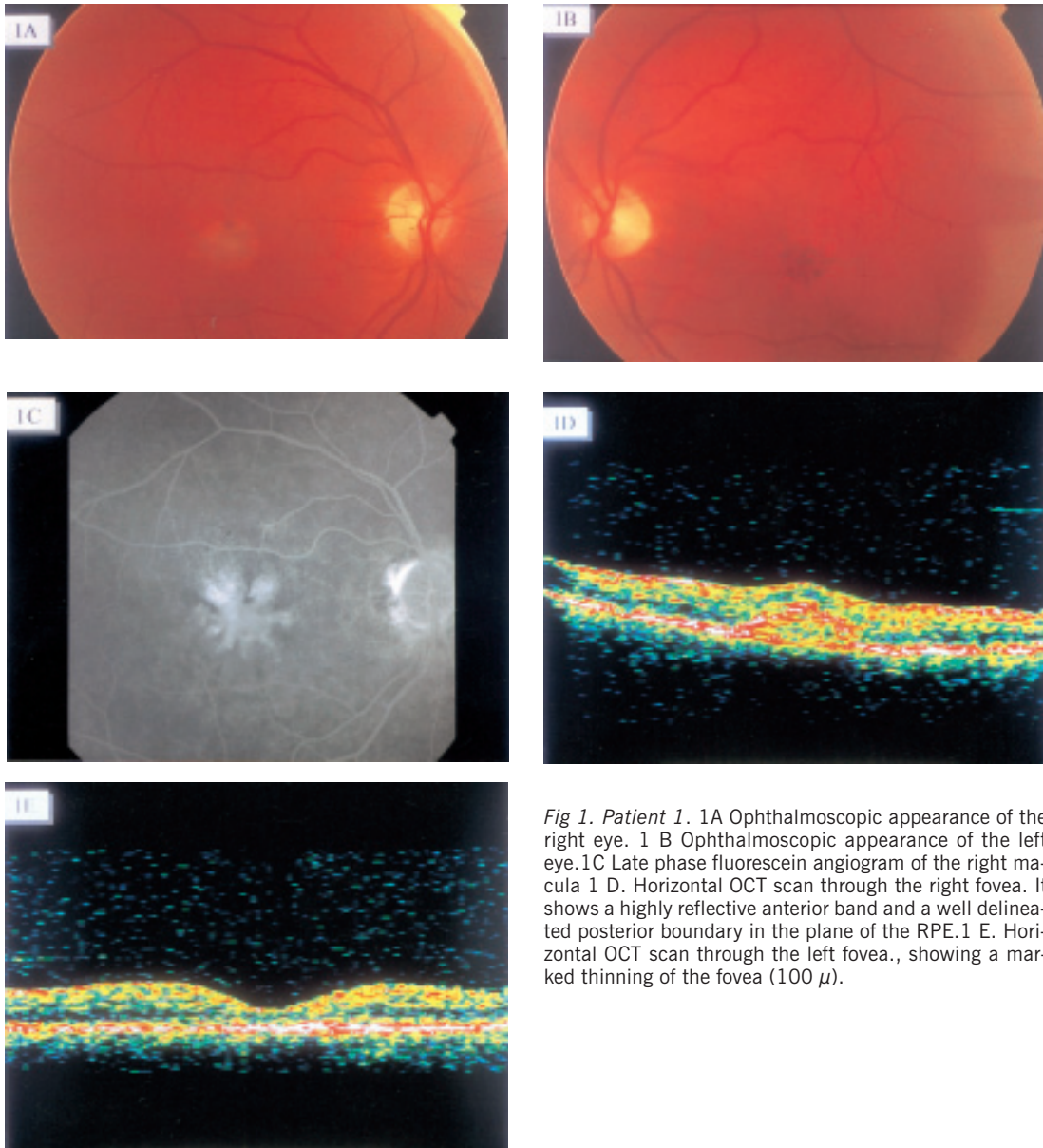


Fig 1. Patient 1. 1A Ophthalmoscopic appearance of the right eye. 1 B Ophthalmoscopic appearance of the left eye. 1C Late phase fluorescein angiogram of the right macula. 1 D. Horizontal OCT scan through the right fovea. It shows a highly reflective anterior band and a well delineated posterior boundary in the plane of the RPE. 1 E. Horizontal OCT scan through the left fovea., showing a marked thinning of the fovea (100 μ).

and an optically empty space beneath the red band (Fig 2D). At the edges of the lesion, the red band was thickened and irregular.

VITELLIFORM DYSTROPHY (BEST'S DISEASE)

A 54 year old man complained of decreasing visual acuity in both eyes since two years be-

fore referral. His medical and family history were unremarkable. Best corrected visual acuity was 6/10 in both eyes. Ophthalmoscopic examination showed symmetrical grey-yellowish macular lesions, which were slightly elevated and well demarcated and included some yellow material (Fig 3 A, B). Fluorescein angiography revealed a homogeneous hyperfluorescent area (Fig 3 C,D). The yellow material was

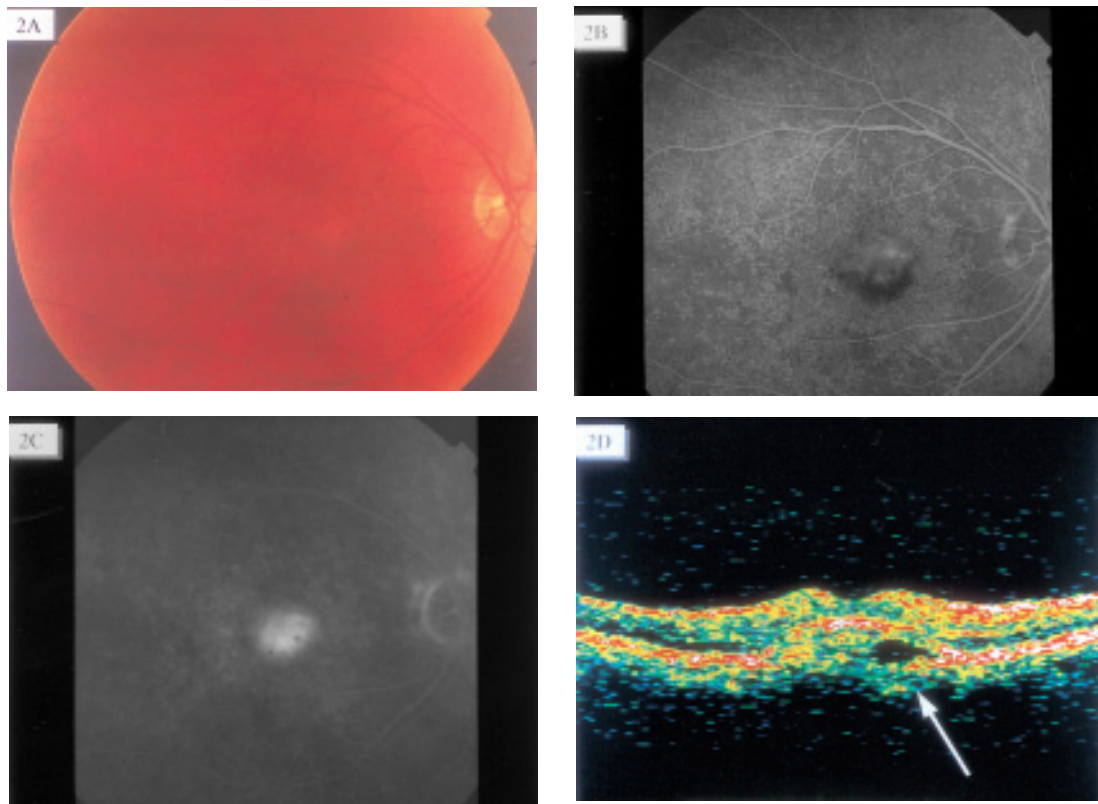


Fig. 2. Right eye of patient 2. 2A. Ophthalmoscopic finding 2B. Mid -venous phase and 2C Late venous phase fluorescein angiogram. 2D. Vertical OCT scan through the fovea. An optically clear space located in the superior part of the vitelliform lesion (arrow) is seen under the anterior reflective band. To either side, thickened and irregular edges of the posterior boundary corresponding to the RPE.

Table 1. Clinical and OCT characteristics of 7 patients with adult onset vitelliform dystrophy

Patient	Age/Sex	VA		Ophthalmoscopy.		OCT	
		RE	LE	RE	LE	RE	LE
1	78/F	0,6	0,1	Vitelliform lesion	Macular atrophy	DSE /IR/OES/ DPB	Foveal thinning
2	84/F	0,8	1,0	Vitelliform lesion	Macular drusen	DSE/ IR/OES/ DPB/ THRB	Foveal depression
3	47/M	1,0	0,8	normal	Vitelliform lesion	Foveal depression	DSE/DPB
4	71/F	1,0	1,0	Macular drusen	Vitelliform lesion	Foveal depression	DSE/IR/ DPB
5	40/F	1,0	0,4	Macular drusen	Vitelliform lesion Macular drusen	Foveal depression	DSE/IR
6	70/M	0,4	0,8	Vitelliform lesion Macular drusen	Vitelliform lesion	DSE/IR/OES	DSE/IR/DPB
7	62/F	0,8	0,8	Vitelliform lesion Macular drusen	Vitelliform lesion Macular drusen	DSE/IR/DPB	DSE/IR/DPB

List of abbreviations: DSE: dome-shaped elevation of the red band
 IR: inhomogeneous reflectivity
 DPB: well defined posterior boundary
 OES: optically empty space
 THRB: thickened highly reflective band

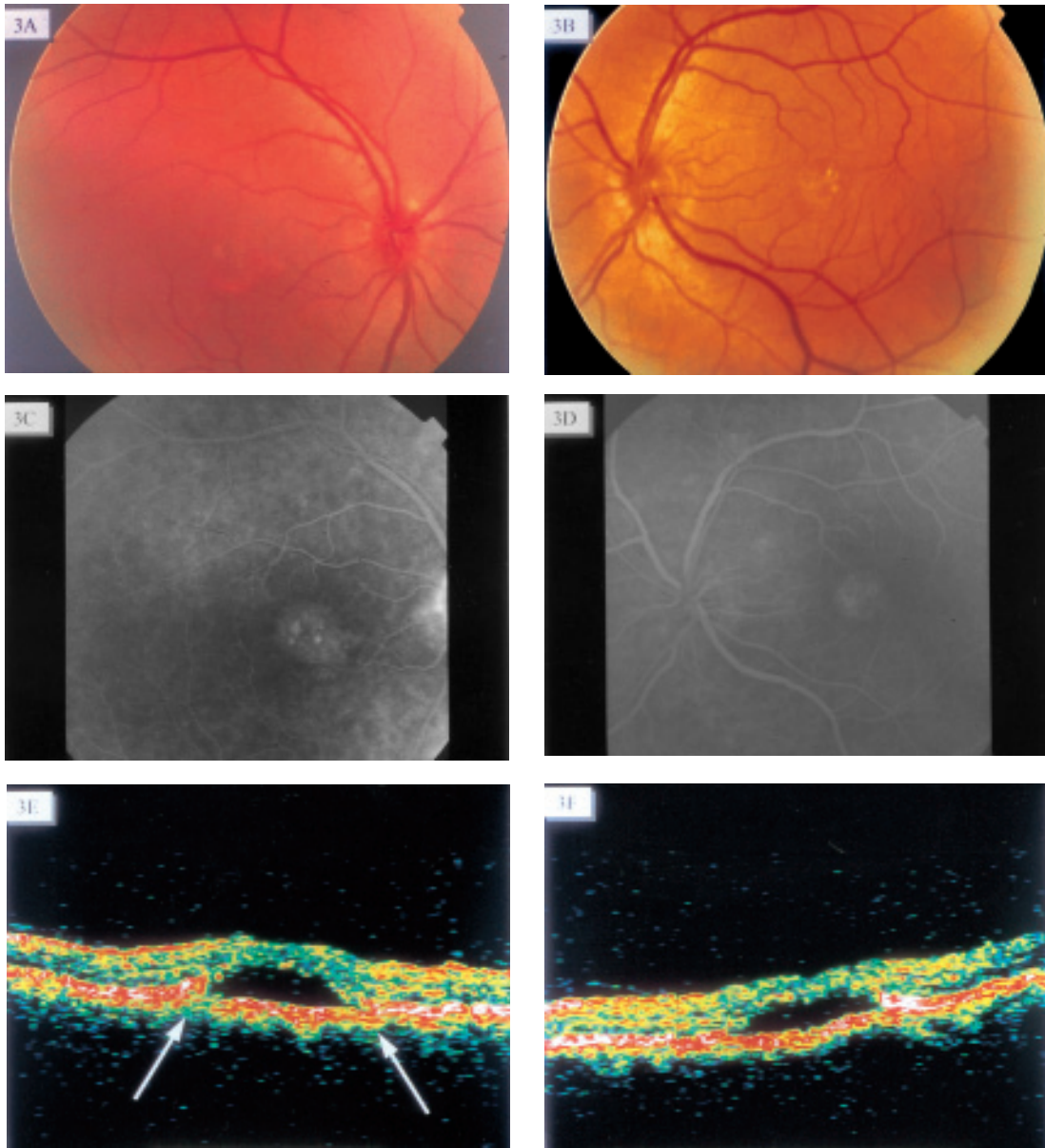


Fig. 3. Patient with Best's disease. 3A Right and 3 B left macular lesion. Symmetrical vitelliform lesions..3 C Right and 3D left fluorescein angiogram. 3 E. Horizontal OCT scan through the right fovea and 3 F through the left fovea. The posterior reflective band is thicker at both edges of the dome-shaped lesion. No reflective band is seen overlying the optically clear space.

autofluorescent under infrared light. OCT disclosed a dome shaped optically clear cavity (Fig 3 E,F). However a unique feature was a highly reflective (red) band, thicker at both edges of the dome-shaped lesion than elsewhere. Beneath the optically clear cavity the thickness of the red band was not modified. The overlying sensory retina at the dome-shaped lesion showed a low reflective layer. The electro-oculogram (EOG) was pathological (L/D ratio 114 % in the right eye and 117 % in the left eye).

DISCUSSION

Since the first report by Gass, several studies have described adult-onset vitelliform macular dystrophy as a heterogeneous group of disorders presenting variable features on fundoscopy, fluorescein angiography, histopathology and evolution. The inheritance of the disease has been considered as autosomal dominant (2,8), but many cases appear to be sporadic (4-6, 9, 14, 24). The variability of the fundus lesion, which resembles that of pattern dystrophy and Best disease has been also reported in different individuals within the same kindred (11,26). Mutations in the peripherin/RDS gene and also in the VMD2 gene have been found in adult-onset vitelliform macular dystrophy patients (7, 16). These studies support two hypotheses; one is that the variable phenotypes in adult-onset vitelliform macular dystrophy could be caused by genetic heterogeneity (7) and the other that there is an overlap between adult-onset vitelliform macular dystrophy and Best disease, but not with age-related macular degeneration (7). On fluorescein and on ICG angiography the yellowish material appears hypofluorescent which is suggestive for the presence of lipofuscin (9, 16).

We used OCT to study the variability of this disorder and to further analyze its morphology. Benhamou et al (1), using the same technique, described in 16 of the 21 eyes with adult-onset vitelliform macular dystrophy they studied, a hyperreflective structure located between the photoreceptors and the retinal pigment epithelium, whereas in the other 5 eyes the hyperfluorescent area was seen at the level of the retinal pigment epithelium with no material between this layer and the photoreceptors.

We believe that the OCT aspect of adult-onset vitelliform dystrophy varies according to the stage of the disease process. The major characteristics, which appear at the vitelliform stage, are as follows:

1. well-circumscribed dome-shaped elevation of the anterior reflective band
2. moderate backscattering below the anterior red reflective band
3. well-delineated posterior boundaries
4. increase in the reflectivity within the vitelliform lesion as the lesion becomes smaller.

The OCT of patient 2 disclosed an apparently optically clear space corresponding to the material inside the lesion (Fig 2D), which was observed at the vitelliruptive stage of the disease. The left eye of patient 1 presented an atrophic macular lesion (Fig 1 E).

Although histopathological studies were reported, we cannot be absolutely certain about the location of the yellow material during the vitelliform stage; mainly because these studies concerned eyes in an endstage of the disease. We also cannot be certain of how the vitelliform material eventually disappears.

According to a typical OCT image, (Fig 1D), there are two highly reflective bands. It appears that there is a larger quantity of material on OCT than observed on histopathology (15, 19). Gass (8) and Jaffe & Schatz (15) stated that the yellow zone corresponded to thinned RPE overlying periodic acid-Schiff positive sub-RPE material, whereas Patrinely et al (19) as well as Dubovy et al (5) suggested that the yellow zone corresponded to lipofuscin as a co-factor with RPE atrophy. Dubovy et al (9), also suggested that the vitelliform lesion initially increases as lipofuscin within the RPE and the macrophages and gradually clears as the RPE and overlying receptor layer become atrophic. According to Benhamou et al (1) the posterior reflective band corresponds to the RPE whereas the highly reflective anterior band represents the pseudovitelliform lesion. We believe however the anterior reflective band to be retinal pigment epithelium whereas the posterior line corresponds to the choriocapillaris/Bruch's membrane complex. On histopathology the PAS-positive material is typically situated between the retinal pigment epithelium and Bruch's membrane (5) The material is probably lipofuscin

as the vitelliform lesion is always autofluorescent under infrared videoscopia (23).

The OCT of patient 3 was different from those of the other patients with adult onset vitelliform macular dystrophy. As in serous retinal detachment, the OCT of patient 3 demonstrated an optically clear cavity and a well delineated posterior boundary. However it differed from the image seen in serous retinal detachment. The OCT in our patient had both the thickened edges of the optically clear cavity and a dome-shape (Fig 3 E, F). The thickened edge could be considered as hypertrophic RPE, as reported by Patrinely et al. (19). The OCT also revealed a reduced intraretinal optical reflectivity and decreased retinal thickness.

The OCT highlights the clinical variability in adult-onset vitelliform macular dystrophy and could be helpful in the pathological interpretation. Although patient 3 was initially considered as adult-onset vitelliform macular dystrophy, the OCT image was different from that expected. In adult-onset vitelliform macular dystrophy the EOG may be subnormal, but is not extinguished. On the basis of a pathological EOG this patient was diagnosed as Best disease.

Even though the OCT reveals the tomographic image in vivo, which may be of help in the diagnosis, the EOG remains essential in the differential diagnosis between Best disease and adult-onset vitelliform dystrophy.

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