ARTICLE

Congenital-onset central chorioretinal dystrophy associated with high myopia

M. IQBAL, I.K. JALILI

Abstract

We describe six siblings of a 12-member sibship affected with a macular dystrophy that is congenital in onset and is associated with progressive myopia. The age of these siblings ranged from 7 months to 19 years. The presenting feature was visual impairment and the best corrected visual acuity ranged between 1/60 and 6/36. Myopia ranged from −3.00 dioptres in the youngest to −10.50 dioptres in the second-eldest member. The macular lesions in our patients are characterised by a well-defined area of atrophy of choriocapillaris and retinal pigment epithelium. These lesions progressed with age in both size and depth. The extent of choroidal involvement in the lesions varied from only loss of superficial vasculature to sparing of large choroidal vessels as confirmed by fundus fluorescein angiography. One patient also exhibited bilateral Duane's syndrome (type III) and right unilateral ptosis. To the best of our knowledge such a fully established macular lesion presenting at the age of 6 months and associated with progressive myopia has never been described in literature.

Key words Central areolar choroidal dystrophy, Congenital macular dystrophy, High myopia

The macular lesions in our patients resemble stage IV of central areolar choroidal dystrophy (CACD), a hereditary form of macular dystrophy first described in 1884[1] that commonly presents with a low visual acuity.[2] In stage IV disease of CACD, which develops by the fourth decade of life, there is a well-demarcated area of atrophy of the choriocapillaris (CC) and retinal pigment epithelium (RPE).[3] Fundus fluorescein angiography demonstrates the loss of RPE and atrophy of CC. Classically the results of electrophysiological testing and peripheral visual fields are normal,[2] though recently Hoyng and Deutman[3] have described an abnormal electroretinogram (Ganzfeld) in stage IV of CACD.[3]

M. Iqbal
Moorfields Eye Hospital
City Road
London EC1V 2PD, UK

I.K. Jalili ✉
Ophthalmology Department
Peterborough Hospitals
(NHS) Trust
Thorpe Road
Peterborough
Cambs PE3 6DA, UK

Patients and methods

We studied a 12-member sibship who were the product of a first-cousin marriage and of whom six members were affected with the disease. These patients were encountered during a study of children with early-onset visual impairment in the West Bank and Gaza between 1985 and 1987. The patients were further assessed and investigated at St John's Hospital, Jerusalem. Detailed genetic, prenatal, obstetric and postnatal histories were recorded. Affected members also underwent complete paediatric examination and no associated general pathology was found. Blood and urine biochemical analysis and haematological tests were performed to screen for intercurrent systemic disease. A detailed pedigree chart was drawn from the compiled data (Fig. 1). All the members of the sibship underwent a complete ophthalmological examination including refraction. Psychophysical tests including colour vision and perimetry were performed (when possible) on these patients using Ishihara pseudo-isochromatic plates and Goldman's field analyser respectively. Fundus fluorescein angiography (FFA) and electrophysiological tests including the electrooculogram (EOG) and electroretinogram (ERG) were carried out to ascertain the diagnosis.

Electroretinography was carried out as described by Arden *et al.*[4] (pseudo-Ganzfeld) with a Medelec Neuropter (Medelec, Manorway, Old Woking, Surrey, UK). The patients were dark-adapted and their pupils were dilated; the amplitude of bandwidth used was 0.16–300 Hz and a non-standard programme was keyed in. *Ground and reference electrodes used were standard Ag/AgCl disc electrodes and the corneal electrodes used were gold foil electrodes.[4] Electro-oculography was carried out with a light box stimulator (Medelec) and the technique used was as described by Arden *et al.*[5]

Both parents were screened to exclude any ophthalmological problem. The parents and the rest of the sibship showed no ophthalmic or medical problems.

*The ISCEV protocol was established after these tests were carried out.

Eye (1998) 12, 260–265

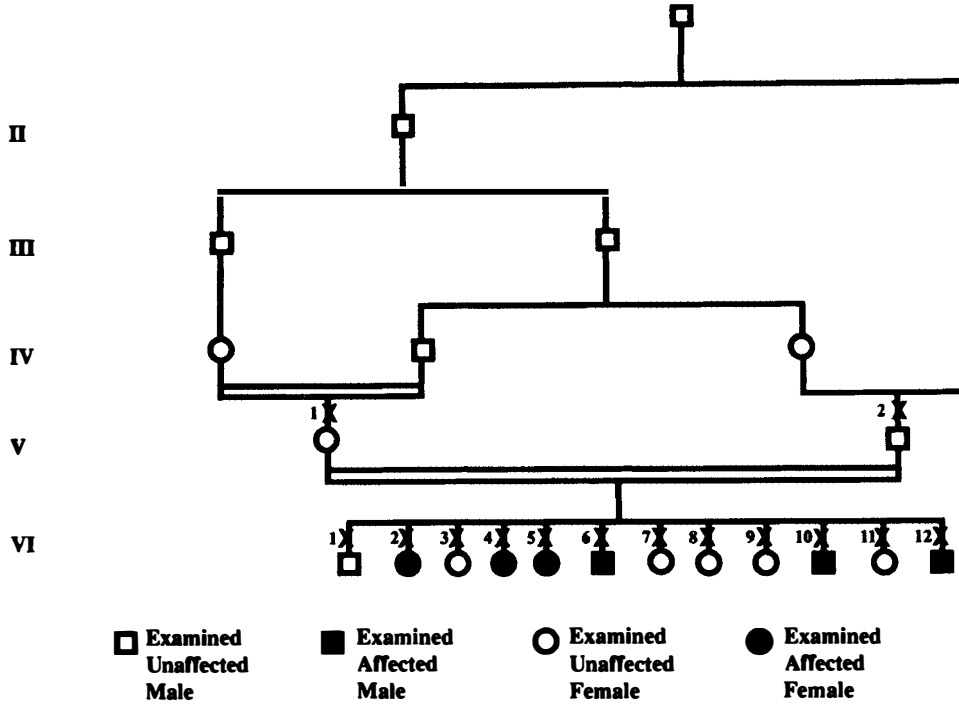


Fig. 1. *Pedigree chart shows an autosomal recessive inheritance and consanguinity through the generations.*

Results

All the patients we studied had reduced visual acuity ranging between 6/36 (V1-6) and 1/60 (VI-5). When tested, they had slightly reduced colour vision, full peripheral visual fields and normal electrophysiology (Fig. 2). The ages of these patients ranged from 7 months (VI-12) to 19 years (VI-2). All findings and the results of various tests are summarised in Table 1.

The proband (VI-2) was a 19-year-old girl at the time of examination. Unfortunately her notes were lost and she never returned for a review.

VI-4 was a 14-year-old girl who had a visual acuity of 2/60 in the right eye and a myopia of −10.50 dioptres (D). The left eye was blind following a traffic accident,

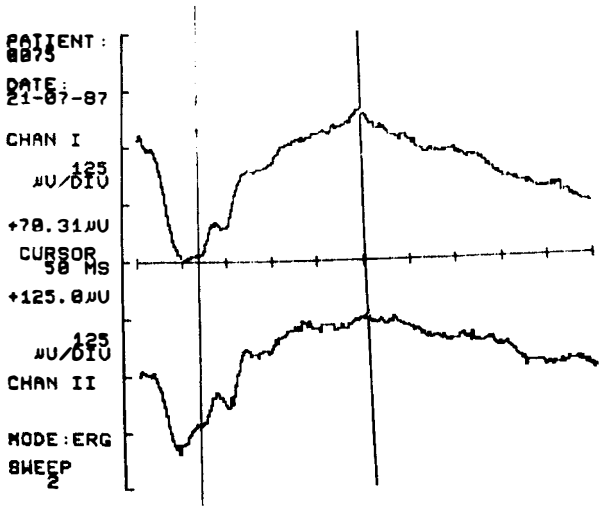


Fig. 2. *Electroretinogram (ERG) of patient VI-5, saturating blue light* (V/V_{max} *100%) within normal limits. ERG equivalent to ISCEV standard flash.*

with a dense cataract and no view of the fundus. In the right eye there was an area of chorioretinal atrophy affecting the macula approximately 6 disc diameters in size simulating a macular coloboma (Fig. 3). She was found to have vitreous degeneration (vitreous syneresis and lacunae formation). FFA demonstrated an almost total loss of RPE and CC, with only the largest choroidal vessels being spared. There was a separate area of chorioretinal atrophy superior to the disc (Fig. 4). Results of electrophysiological tests and peripheral visual fields were normal.

VI-5 was a 12-year-old girl. Her visual acuities were 1/60 and 4/60 in the right and left eyes respectively, with myopia of −8.00 D in both eyes. The macular lesion was approximately 4 disc diameters in size (Fig. 5a). FFA revealed chorioretinal atrophy simulating macular colobomas with only the larger choroidal vessels being spared (Figs. 5b, 6). The results of electrophysiological tests were normal (Fig. 2).

VI-6 was an 11-year-old boy. Recorded visual acuities were 6/60 and 6/36 in right and left eyes respectively with myopia of −6.00 D in each eye. The macular lesion resembling a coloboma (with two smaller lesions close to the main lesion) was approximately 3.5 disc diameters in the right eye (Fig. 7) and 4 disc diameters in the left eye (Fig. 8). FFA was not carried out in this patient. Results of electrophysiological tests were normal in this patient.

VI-10 was a 6-year-old boy with visual acuities of 6/60 and 3/60 in right and left eyes respectively with a myopia of −10.50 D in each eye. The size of the macular lesion was 4 disc diameters in each eye (Fig. 9). In addition this patient exhibited bilateral Duane's syndrome type III and right-sided ptosis with esotropia.

Table 1. *Patient data*

Patient no.	Sex	Age	Eye	VA	Ref. SE	Area	Choroid	EP tests	Other findings
VI-2	F	19 years	R	—	—	—	—	—	—
			L	—	—	—	—	—	—
VI-4	F	14 years	R	2/60	−10.50 D	6.0 dd	LgV, CCa	N	VD, Col.
			L	NPL		No view			
VI-5	F	12 years	R	1/60	− 8.00 D	4.0 dd	LgV, CCa	N	Col.
			L	4/60	− 8.00 D	4.0 dd	LgV, CCa	N	Col.
VI-6	M	11 years	R	6/60	− 6.00 D	3.5 dd	LgV, CCa	N	Col.
			L	6/36	− 6.00 D	4.0 dd	LgV, CCa	N	Col.
VI-10	M	6 years	R	6/60	−10.50 D	4.00 dd	—	—	VD; Rt ptosis and ET
			L	3/60	−10.50 D	4.00 dd	—	—	VD, Bilateral DS
VI-12	M	7 months	R	Fix.	− 3.00 D	2.00 dd	—	N	
			L	Fix.	− 3.00 D	2.00 dd	—	N	

CCa, choriocapillaris atrophy; Col., coloboma-like appearance; D, dioptres; dd, disc diameters; DS; Duane's syndrome type III; EP tests, electrophysiological tests; ET, esotropia, Fix. steady fixation; N, normal; NPL, no perception of light; LgV, large choroidal vessels present; Ref. SE, spherical equivalent; VA, visual acuity; VD, vitreous degeneration.

Cranial nerve examination was normal. There was evidence of bilateral vitreous degeneration. This patient did not undergo psychophysical tests and FFA.

VI-12 was a boy who was 7 months old when first examined. The child could maintain steady fixation but no accurate estimate of the vision could be made with 'hundreds and thousands'. On examination under anaesthesia he was found to have a macular lesion approximately 2 disc diameters in size which on fluorescein angiograph revealed early atrophy of the choroid and RPE (Fig. 10). Results of electrophysiological tests in this patient were normal.

In our patients we observed the following features which in addition to the above findings are very interesting and unique. These findings are not known features of CACD and therefore we refrained from diagnosing our patients as having CACD.

Congenital onset

Stage IV of CACD usually manifests itself by the age of 40 years.[3] Our patients, in contrast, exhibited a fully established lesion in the first two decades of their lives. The disease in V-12 was fully established by the age of 7 months, which suggests it existed before birth; we can therefore safely infer a congenital onset of the disease.

Association with progressive myopia

An association of CACD with myopia has not previously been described in the literature. As is evident from Table 1, in our patients myopia tends to increase with age, being −3.00 D in the youngest (VI-12) increasing to −10.50 D in the second eldest (VI-4). The exception is (VI-10), who showed myopia of −10.50 D in both eyes at the age of 6 years.

The myopia in our cases follows the natural history of high myopia in that it increases in severity with increasing age. An interesting observation in our patients was that their electrophysiological tests were normal, though those tests are usually abnormal in pathological high myopia.[2]

Two of our patients (VI-4 and VI-10) had vitreous degeneration (syneresis and lacunae formation). Both these patients had myopia of −10.50 D and we think the vitreous degeneration was secondary to high myopia.

Evolution of macular lesion

The youngest patient (VI-12) showed a well-circumscribed area of atrophy involving the macula with a crenate margin. There was early hyperfluorescence on FFA, the superficial choroidal vessels were absent but the medium and large-sized choroidal vessels were present (Fig. 10), and there was no generalised thinning of the RPE. Such thinning became evident with increasing age and myopia, as in VI-10 (Fig. 9), who showed widespread tessellation from thinning of the RPE. These lesions progressed in size and depth reaching 6 disc diameters as in VI-4 (age 14 years), giving rise to a coloboma-like appearance (Fig. 3). FFA demonstrated loss of small and medium-sized vessels in CC but the preservation of the large choroidal vessels even in the most advanced lesions (Fig. 4). This is important to note as it differentiates the condition from true coloboma where there is absence of choroid and retina from within the confines of the lesion. It is important to note from the point of view of diagnosis that none of our patients exhibited the earlier stages of CACD as described in the literature.[3,6,15]

Inheritance

Our patients showed an autosomal recessive inheritance of the disease with high penetrance. There is concurrent atrophy of both RPE and CC in patients as young as 7 months (VI-12), which could have been the result of the same genetic mutation.

All our patients had myopia (which was absent in the unaffected siblings) that could also have been the result of the same genetic mutation that caused the chorioretinal dystrophy. Hoyng *et al.*[7] have described an Arg-142-Trp mutation in the peripherin/RDS gene that is responsible for autosomal dominant CACD. Lotery *et al.*[8] have localised the CACD gene to chromosome 17. Our

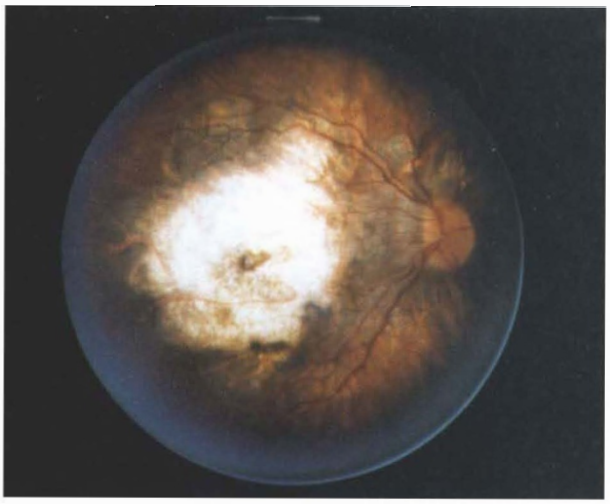


Fig. 3. *Colour photograph of the right eye of patient VI-4 shows chorioretinal atrophy 6 disc diameters in size resembling a macular coloboma. The optic nerve is normal.*

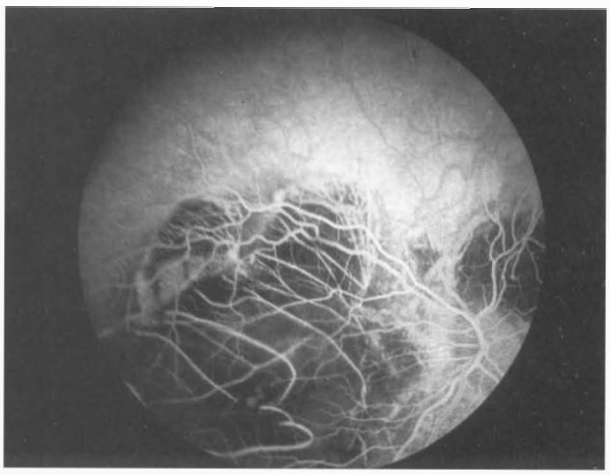
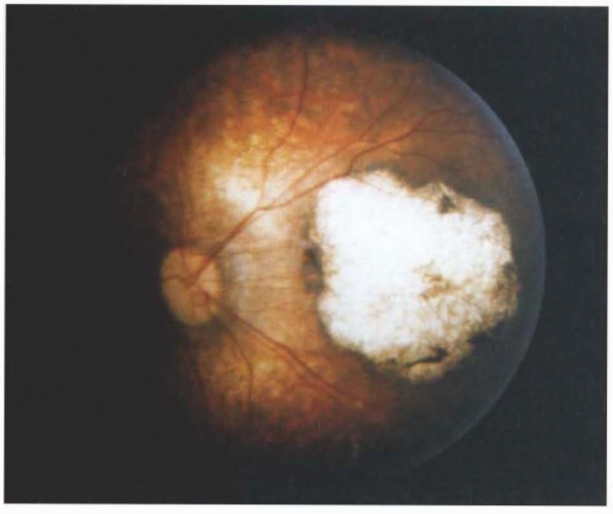
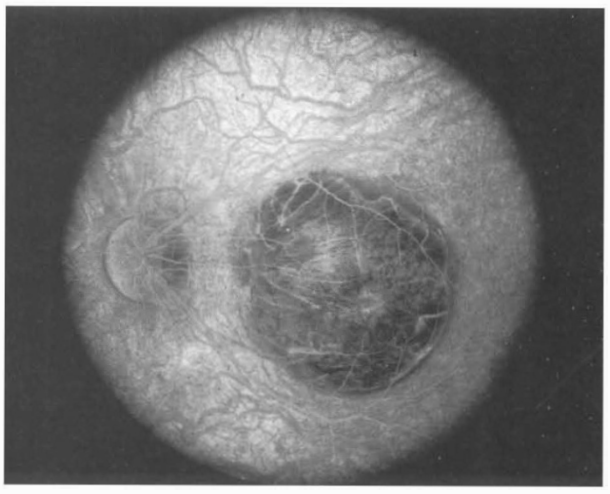


Fig. 4. *Fundus fluorescein angiography (FFA) of the right eye of patient VI-4 confirms chorioretinal atrophy traversed by normal retinal vessels; a similar but smaller area supranasal to the optic disc is seen. The large choroidal vessels are visible in the base of main lesion, differentiating it from a true coloboma.*



(a)



(b)

Fig. 5. *Colour photograph (a) and FFA (b) of the left eye of patient VI-5 reveal a 4 disc diameter area of chorioretinal atrophy. Only the medium to large choroidal vessels are visible within the confines of the lesion.*

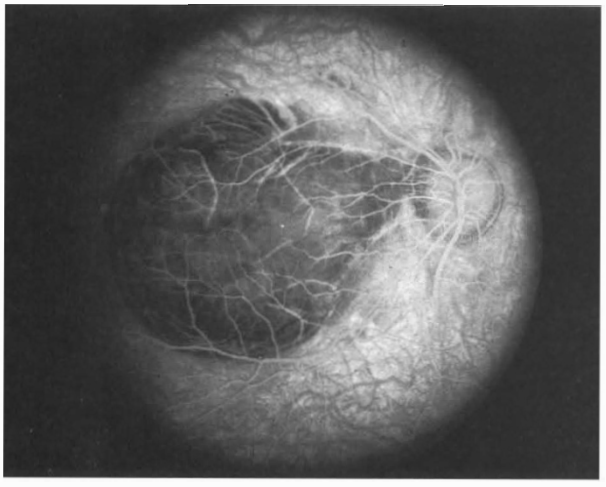


Fig. 6. *FFA of the right eye of patient VI-5 shows an area of atrophy larger than that in the left eye that extends up to the optic disc.*

patients exhibited an autosomal recessive pattern and genetic screening of our patients in future would perhaps be helpful in establishing the diagnosis.

Discussion

The condition should be differentiated from:

(1) A form of rod-cone dystrophy with macular coloboma, high myopia and hypercalciuria as described by Meier *et al.*[9] In our patients there was no systemic illness and the results of electrophysiological tests were normal, contrary to the findings in the rod–cone dystrophy.

(2) Moore *et al.*[10] have also described a form of retinal dystrophy with macular coloboma, which differs from the disease we describe in that their patients had substantially abnormal or absent ERGs, fundal abnormalities such as scleral ectasia and optic disc pallor.

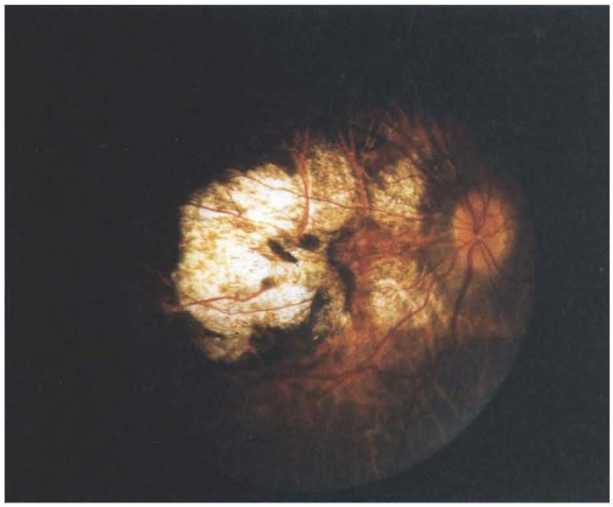


Fig. 7. *Colour photograph of the right eye of patient VI-6 shows an area of chorioretinal atrophy approximately 3.5 disc diameters in size resembling a macular coloboma. There are two smaller areas temporal to the disc with the superior of the two being a direct continuation of the main lesion.*

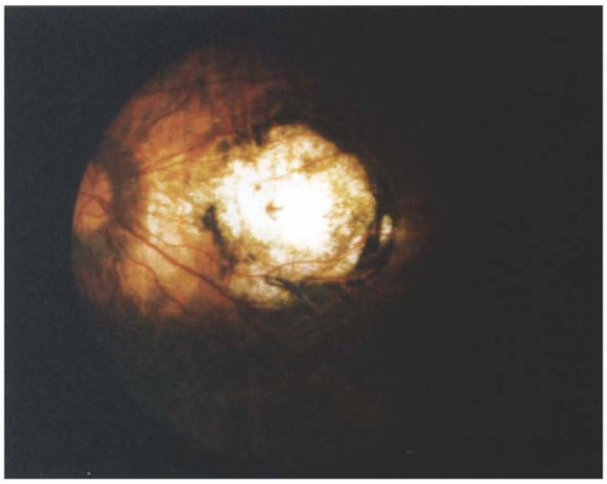
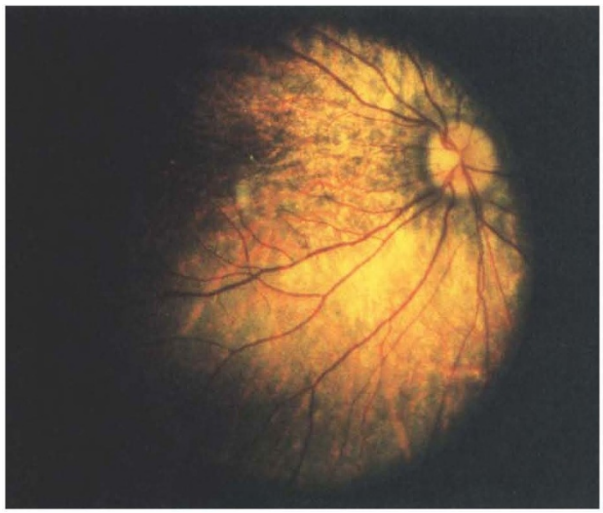
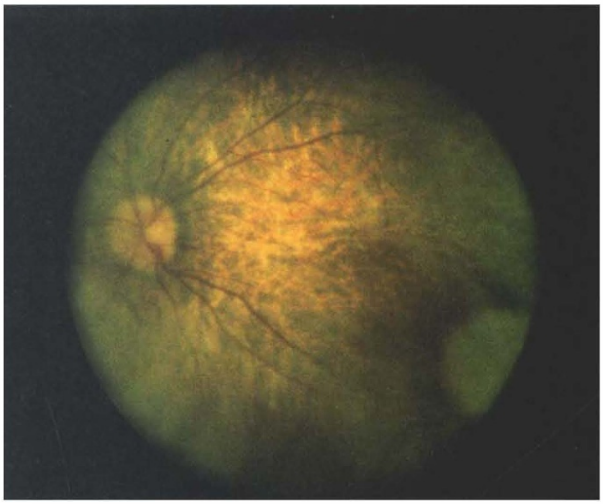


Fig. 8. *Colour photograph of the left eye of patient VI-6 reveals a solitary lesion of chorioretinal dystrophy approximately 4 disc diameters in size.*

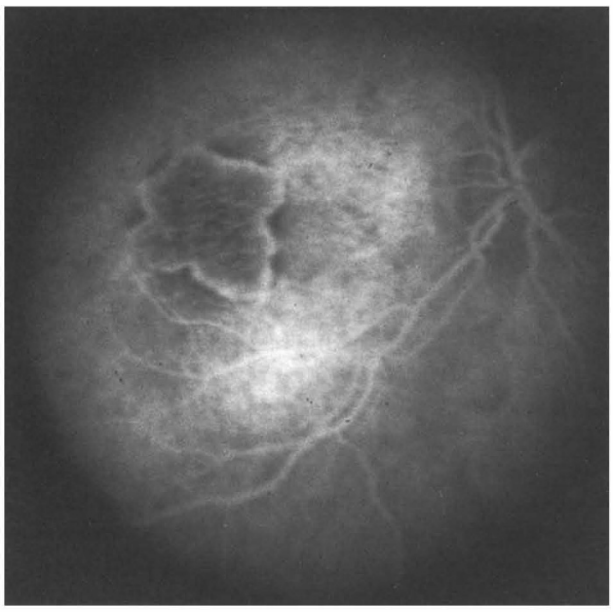


(a)

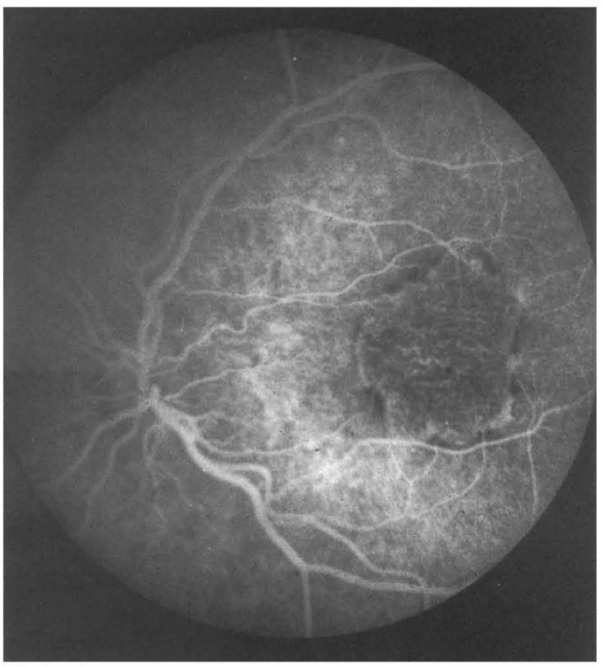


(b)

Fig. 9. *Colour photographs of the right (a) and left (b) eyes of patient VI-10 show widespread tessellation and atrophy of pigment epithelium.*



(a)



(b)

Fig. 10. *FFA of the right (a) and left (b) eyes of patient VI-12 show lesions approximately 2 disc diameters in size, atrophy of the RPE, and only the superficial choroidal blood vessels affected by the disease.*

The patients in their series also had other physical abnormalities including skeletal, central nervous system, kidney and lung abnormalities, representing a heterogeneous group of patients. In addition these findings were not present in all of Moore *et al.*'s patients. Our patients in contrast were, apart from their ocular lesions, physically normal.

(3) An association of macular coloboma with Leber's congenital amaurosis has also been described by Margolis *et al.*[11] These patients also had high myopia, but in addition there was bone spicule pigmentation of the peripheral fundus, a markedly reduced ERG and other signs of Leber's congenital amaurosis. With the exception of myopia these findings were absent in our patients.

(4) Progressive bifocal chorioretinal dystrophy[12] is an autosomal condition that, as the name suggests, is bifocal in nature. The fundal lesions in this condition are both nasal and temporal to the disc. Whereas on cursory examination our patients (Figs. 4, 7) appear to have bifocal lesions, on closer examination these were not strictly both nasal and temporal to the optic disc. Chopdar[13] in his description of a family with CACD has clearly shown that some of the members (in the fourth and fifth decades of life) have similar lesions to ours around the optic disc, completely surrounding the optic disc. The patients with bifocal chorioretinal dystrophy had a reduced ERG whereas our patients had a normal ERG. Though this disease did present as early as 3 weeks and some (but not all) patients had myopia, it would be difficult to label our patients as having bifocal chorioretinal dystrophy in the light of above findings.

(5) Congenital areolar pigment epithelial dystrophy[14] is a dominantly inherited condition with normal visual acuity. These findings were absent in our patients. Our patients had poor vision even when very young, as noted in patient VI-12.

(6) In North Carolina macular dystrophy (NCMD)[16] the macular lesions have a similar appearance to the macular lesions seen in our patients. An important differentiating point is the poor vision in our patients as compared with the relatively good vision in patients with NCMD. Our patients did not reveal any areas of leakage on angiograms, which are a recognised feature of NCMD.[17] Gass[17] in his report on NCMD has described macular colobomas in two families. These were not associated with myopia, the patients had better vision and there was a markedly abnormal ERG in one of the family members. In contrast our patients have poor vision and normal ERGs.

We would once again like to stress the special features of these patients: congenital onset in at least one of the patients, an association with high myopia and the progression of these lesions in both size and depth with age. To profess that we have excluded all possible diagnoses would be presumptuous, but to our knowledge this condition as an entity has not been described before. There is a resemblance to CACD but the differentiating points mentioned in Results make it difficult for us to call it a variant of CACD – though it is very tempting. Perhaps it would be best to report it without a formal name, and then if similar cases were reported in future it could be defined as a separate entity.

We wish to thank Professor Alan Bird and for his guidance in the preparation of this paper and the staff of St John's Ophthalmic Hospital, Jerusalem for their assistance and support. We also wish to thank Mr Chris Hogg from Moorfields Eye Hospital for carrying out the electrophysiological tests and his subsequent help in the preparation of the paper.

References

1. Nettleship E. Central senile areolar choroidal atrophy. Br J Ophthalmol 1884;165–6.
2. Deutman AF. Macular dystrophies. In: Ryan SJ, editor. Retina, vol 2, St Louis: CV Mosby, 1989:243–98.
3. Hoyng CB, Deutman AF. The development of central areolar choroidal dystrophy. Graefes Arch Clin Exp Ophthalmol 1996;234:87–93.
4. Arden GB, Carter RM, Hogg CR, *et al.* A modified ERG technique and the results obtained in X-linked retinitis pigmentosa. Br J Ophthalmol 1983;67:419–30.
5. Arden GB, Barrada A, Kelsey JH. New clinical test of retinal function based upon the standing potential of the eye. Br J Ophthalmol 1962;46:449–67.
6. Sorsby A, Crick RP. Central areolar choroidal sclerosis. Br J Ophthalmol 1953;37:129.
7. Hoyng C, Heutink P, Testers L, *et al.* Autosomal dominant central areolar choroidal dystrophy caused by a mutation in codon 142 in the peripherin/RDS gene. Am J Ophthalmol 1996;121:623–9.
8. Lotery AJ, Eunis KT, Silvestri G, *et al.* Localisation of a gene for CACD to chromosome 17p. Hum Mol Genet 1996;5:705–8.
9. Meier W, Blumberg A, Imahorn W, *et al.* Idiopathic hypercalciuria with bilateral macular colobomata: a new variant of oculorenal syndrome. Helv Paediatr Acta 1979;34:257–69.
10. Moore AT, Harden A, Taylor DSI. Bilateral macular dysplasia and congenital retinal dystrophy. Br J Ophthalmol 1985;69:691–9.
11. Margolis S, Sher BM, Carr RE. Macular coloboma in Leber's congenital amaurosis. Am J Ophthalmol 1977;83:27–31.
12. Waheed AA, Wyse CT. Progressive bifocal chorioretinal atrophy. Br J Ophthalmol 1968;52:742–50.
13. Chopdar A. A variant of central areolar choroidal dystrophy. Ophthalmic Paediatr Genet 1993;14:151–64.
14. Fetkenhour CL, Gurney N, Dobbie JG, Choromokos E. Central areolar pigment epithelial dystrophy. Am J Ophthalmol 1976;81:745–53.
15. Hoyng C, Pinkers A, Deutmann A. Juvenile atrophy of pigment epithelium. Graefes Arch Clin Exp Ophthalmol 1992;230(3):230–2.
16. Small KW, Killian J, Mclean WC. North Carolina's dominant progressive foveal dystrophy: how progressive is it? Br J Ophthalmol 1991;75:401–6.
17. Gass JDM. Diseases causing choroidal exudative and haemorrhagic localised (disciform) detachments of the retina and pigment epithelium. In: Gass JDM, editor. Stereoscopic atlas of macular diseases, vol 1, 3rd ed. St Louis: CV Mosby, 1987:98–102.