patient are characteristic of demyelination, there are similarities with the MRI findings reported in association with sub-acute necrotising encephalomyelopathy.[11]

Two further separate reports of Revesz syndrome are very similar to these three cases except that both patients had severe aplastic anaemia and one patient did not have intracranial calcification.[8,9] These patients also had more typical skin signs of dyskeratosis congenita including skin pigmentation and leukoplakia, although dyskeratosis congenita has not been associated with ophthalmic abnormalities and the age of onset is usually in the second decade.[12] A fifth patient has been reported who demonstrated mild dyskeratosis including sparse hair and abnormal dentition with retinal telangiectasis, but this child had characteristics distinct to oculo-mandibulofacial dyscephaly (Hallerman–Streiff syndrome).[10]

No chromosomal abnormalities have been found in our case or any of the previously reported cases of retinal telangiectasis and dyskeratosis, but the small number of cases to date in the absence of a family pedigree may preclude assumptions regarding a mode of inheritance. Dyskeratosis congenita has been linked to locus Xq28 and pedigree analysis has suggested an X-linked inheritance in non-sporadic cases.[12]

As in all cases of bilateral idiopathic retinal telangiectasis repeated examinations and aggressive treatment with laser photocoagulation increase the likelihood of preserving useful vision in at least one eye.[5–7,10,13] While the girl presented in this report has remained normal intellectually the documented progressive intracranial white matter lesions may result in deterioration of neurological function in the long term.

In conclusion, we present a third case of a familial syndrome characterised by idiopathic retinal telangiectasis, progressive intracranial calcification and ectodermal dysplasia. While not identical, similarities between these three cases, Revesz syndrome and Hallermann–Streiff syndrome suggest that these may all be variable expressions of an as yet unidentified underlying genetic abnormality.

References

1. Reese AB. Telangiectasis of the retina and Coats' disease. Am J Ophthalmol 1956;42:1–8.
2. Coats G. Ueber retinitis exudativa (retinitis haemorrhagica externa). Graefes Arch Ophthalmol 1912;81:275–327.
3. Casswell AG, Clifford-Jones R, Grewal K, Gregor ZJ. Isolated retinal telangiectatic masses. Trans Ophthalmol Soc UK 1986;105:94–9.
4. Gass JD, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis: update of classification and follow-up study. Ophthalmology 1993;100:1536–46.
5. Khan JA, Ide CH, Strickland MP. Coats'-type retinitis pigmentosa. Surv Ophthalmol 1988;32:317–32.
6. Pauleikhoff D, Bornfeld N, Bird AC, Wessing A. Severe visual loss associated with retinal telangiectasis and facioscapulohumeral muscular dystrophy. Graefes Arch Clin Exp Ophthalmol 1992;230:362–5.
7. Tolmie JL, Browne BH, McGettrick PM, Stephenson BP. A familial syndrome with Coats' reaction retinal angiomas, hair and nail defects and intracranial calcification. Eye 1988;2:297–303.
8. Revesz T, Fletcher S, Al-Gazali LI, DeBuse P. Bilateral retinopathy, aplastic anaemia and central nervous system abnormalities: a new syndrome? J Med Genet 1992;29:673–5.
9. Kajtar P, Mehes K. Bilateral Coats' retinopathy with aplastic anaemia and mild dyskeratotic signs. Am J Genet 1994;49:374–7.
10. Newell SW, Hall BD, Anderson CW, Lim ES. Hallerman–Streiff syndrome with Coats disease. J Pediatr Ophthalmol Strabismus 1994;31:123–5.
11. Heckmann J, Eastmann R, Handler L, *et al.* Leigh disease (sub-acute necrotizing encephalomyelopathy): MR documentation of an acute attack. Am J Neuroradiol 1993;14:1157–9.
12. Davidson IR, Connor JM. Dyskeratosis congenita. J Med Genet 1988;25:843–6.
13. Pauleikhoff D, Wessing A. Long-term results of the treatment of Coats disease. Fortschr Ophthalmol 1989;86:451–5.

M. Cahill[1,2]
A. Mulvihill[1]
R.W. Acheson[2]
M. O'Keefe[1]
[1]Department of Paediatric Ophthalmology
The Children's Hospital
Dublin 1, Ireland
[2]The Institute of Ophthalmology
Mater Miscericordiae Hospital
Dublin, Ireland

Mr Mark Cahill ✉
Department of Paediatric Ophthalmology
The Children's Hospital
Temple Street
Dublin 1, Ireland
Tel: +353 1 874 8763
Fax: +353 1 874 8355
e-mail: mcahill@indigo.ie

Sir

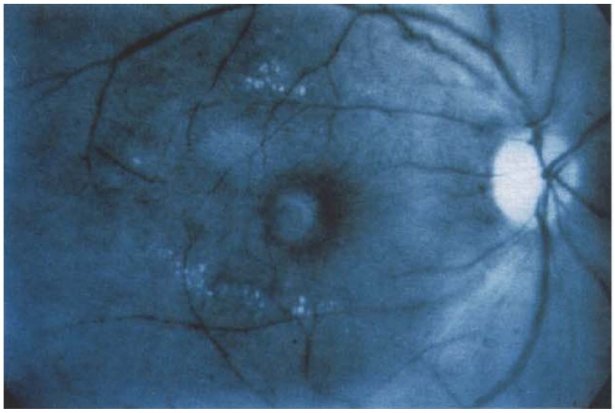
Indocyanine green angiography in a case of idiopathic retinal vasculitis, aneurysms and neuroretinitis

The term idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) was first applied by Chang and associates[1] in 1995, although sporadic reports of this condition had previously been described.[2–5] This rare, bilateral disease – only 15 patients have been reported in the literature – typically affects young healthy individuals.

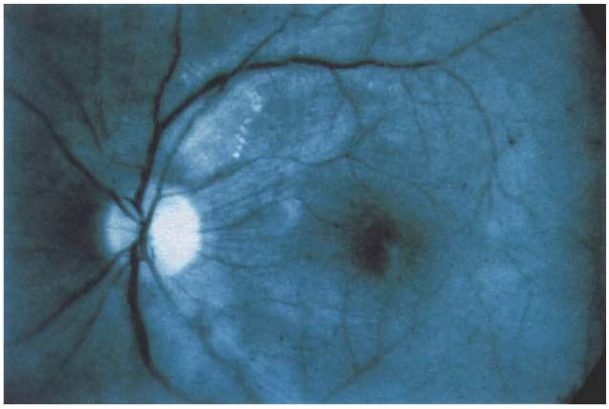
We report a patient who appeared to present with features typical of IRVAN and who showed abnormalities of the choroidal vasculature as demonstrated by indocyanine green (ICG) angiography. To our knowledge this is the first report of ICG findings in this condition.

Case report

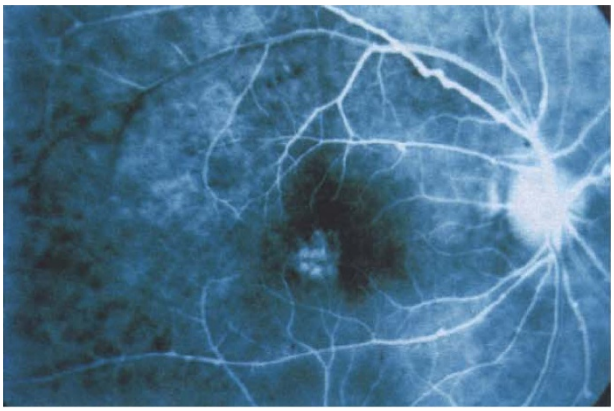
A 42-year-old Italian woman presented in October 1997 with a 3 week history of reduced central vision in her right eye. She was taking no medications and she had had no preceding systemic illness. The patient was the product of an uneventful full-term pregnancy. Her



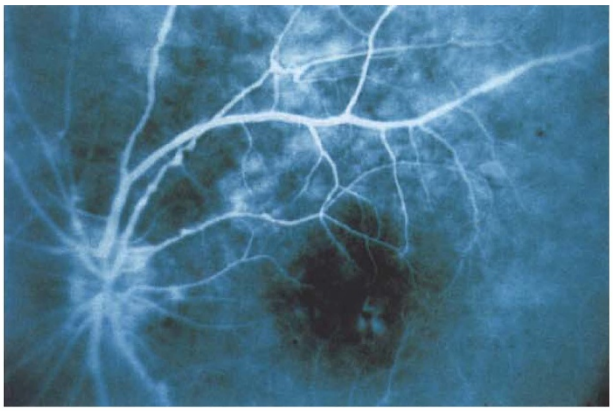
(a)



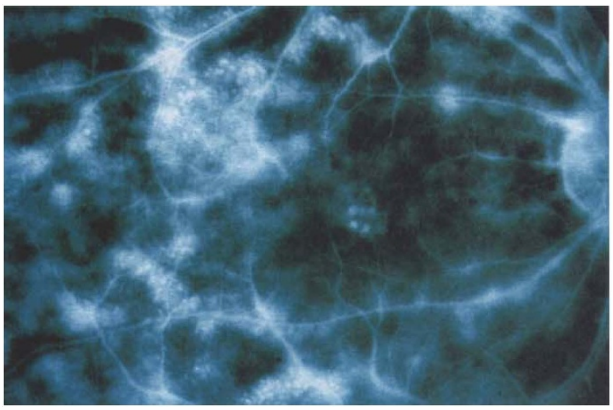
(b)



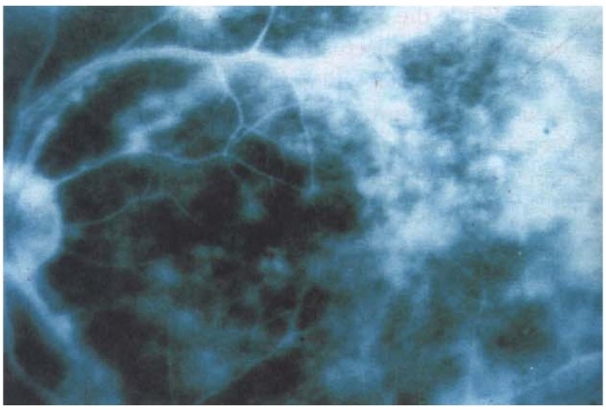
(c)



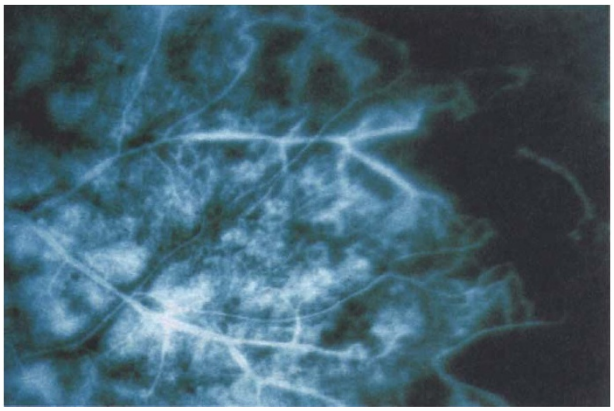
(d)



(e)

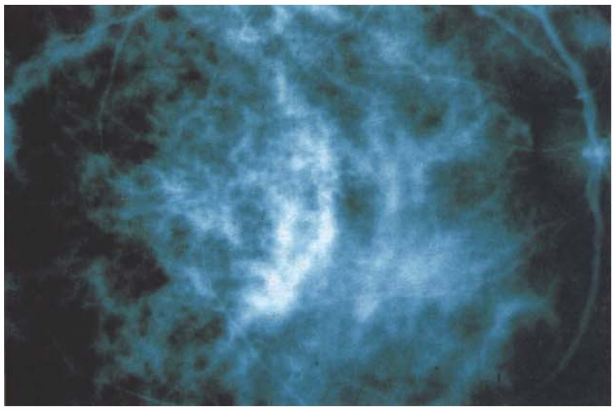


(f)

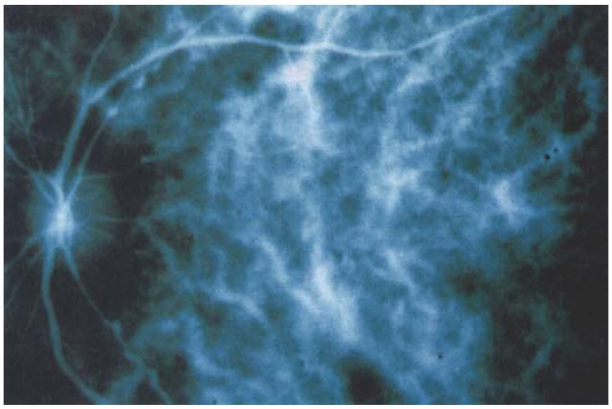


(g)

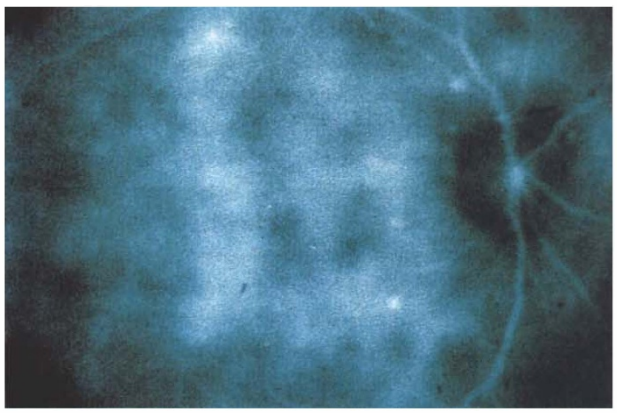
Fig. 1. (a) Right eye. Red-free image. Fundus appearance at the time of presentation. (b) Left eye. Red-free image. Fundus appearance at the time of presentation. (c) Right eye. Early-phase fluorescein angiogram. Note the aneurysmal changes along the retinal arterioles. A cluster of leaking aneurysms was present in the foveal region. (d) Left eye. Early-phase fluorescein angiogram. Note the aneurysmal changes on the optic nerve head. (e) Right eye. Late-phase fluorescein angiogram. The aneurysmal changes were still detectable by late fluorescein pooling and staining. (f) Left eye. Late-phase fluorescein angiogram. Note the optic disc hyperfluorescence. Diffuse dye leakage into the retina coming predominantly from the retinal venous vessels was observed. (g) Left eye. Late-phase fluorescein angiogram. Extensive capillary dropout was found in the peripheral fundus.



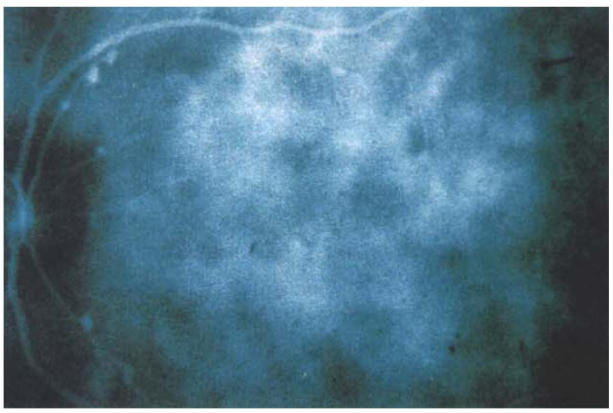
(a)



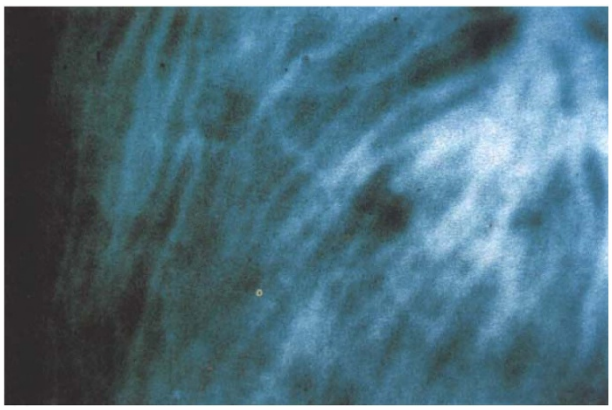
(b)



(c)



(d)



(e)

Fig. 2. *(a) Right eye. Early-phase ICG angiogram. Dilated choroidal vessels associated with choroidal hyperfluorescence were observed in the posterior pole. (b) Left eye. Early-phase ICG angiogram. Note the areas of focal hyperfluorescence at the level of the retinal aneurysmal changes. (c) Right eye. Intermediate-phase ICG angiogram. Diffuse choroidal hyperfluorescence was present. (d) Left eye. Intermediate-phase ICG angiogram. Note how retinal arterial aneurysmal changes were still well defined. (e) Right eye. Late-phase ICG angiogram. Patchy hypofluorescent areas of choroidal hypoperfusion were noted in the peripheral fundus.*

medical history was unremarkable and she denied any recurrent oral or genital ulceration as well as the occurrence of any atypical skin lesions.

On examination visual acuity was 20/30 in the right eye with a refractive error of 1.5 dioptres of myopia and 20/20 in the left eye with a refractive error of 1 dioptre of myopia. Both anterior segments were normal. There was no evidence of an afferent pupillary defect. There were +1 vitreous cells and posterior vitreous detachment in both eyes. Results of fundus examination showed the presence of aneurysmal dilatations along the first- and second-order retinal arteries associated with diffuse retinal thickening bilaterally and circinate exudation in the right posterior pole (Fig. 1a, b). Automated visual field testing demonstrated three paracentral relative defects in the right eye; the field was full in the left. Fluorescein angiography demonstrated the aneurysmal changes on the retinal arteries and the optic nerve head with dye leakage and diffuse intraretinal oedema involving the fovea. Dye leakage along the retinal venous vessels associated with phlebitis was also demonstrated in the posterior pole and in the mid-periphery bilaterally (Fig. 1c–f). Extensive areas of peripheral capillary non-perfusion were present in both eyes (Fig. 1g).

On ICG study choroidal hyperfluorescence and dilated, leaking, large choroidal vessels were present bilaterally in the posterior pole and in the mid-periphery. They were particularly evident in the early (Fig. 2a, b)

and intermediate phases (Fig. 2c, d). During the retinal arterial transit phase ICG began to stain the retinal arterial aneurysms with focal hyperfluorescence that persisted until late phases without leakage. In addition, patchy hypofluorescent areas were noted bilaterally, in the peripheral region, from the intermediate to the late phases of angiography, with a choroidal perivascular distribution (Fig. 2e).

The following laboratory investigations were requested: full blood count, routine blood chemistry, specific index of inflammation, haemoglobin electrophoresis, prothrombin time (PT), partial thromboplastin time (PTT), serum protein electrophoresis, urinalysis, blood and urine culture, vaginal tampon, Venereal Disease Research Laboratory (VDRL), fluorescent treponemal antibodies (FTA-ABS), purified protein derivative (PPD), Lyme titres, antibody titres for human immunodeficiency virus, C3, C4, antinuclear antibody (ANA), anti-double-stranded DNA antibody titre (anti ds-DNA), antiphospholipid antibodies (APS) including anticardiolipin (ACA) and lupus anticoagulant (LAC) antibodies, rheumatoid factor, anti-neutrophil cytoplasmic antibody (ANCA), cryoglobulins, subpopulations of lymphocytes, pathergy test, angiotensin converting enzyme (ACE test), serum lysozyme, chest radiographs, electrocardiogram, echocardiogram, colour flow Doppler imaging of carotid arteries, HLA typing and magnetic resonance imaging of the head.

The patient was not anaemic but microcytic erythrocytes were present consistent with thalassaemia trait. There were no other laboratory abnormalities except for the presence of human leucocyte antigen B51. A diagnosis of IRVAN was made. A short course of pulsed high-dose intravenous methylprednisolone and oral steroids were administered with no appreciable clinical improvement.

Results of ocular examination of the patient's father, mother and twin sister were all normal.

Comment

Idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) is a very rare syndrome. Previous fluorescein angiographic studies have demonstrated the involvement of the retinal and optic nerve head vasculature.

ICG angiography of this patient showed choroidal vascular abnormalities which were not evident either on fundus examination or on fluorescein angiography. Dilated, leaking, large choroidal vessels on the early to the intermediate phase of ICG angiography may indicate an associated choroidal vasculitic component with vessel wall damage and abnormal diffusion of the ICG molecule. Peripheral patchy areas of ICG hypofluorescence on the intermediate to the late phase of angiography may be caused by an impairment of physiological ICG diffusion from the fenestrated choriocapillaris because of vascular obstruction. Alternatively they may represent either whole-thickness, space-occupying inflammatory choroidal lesions or choroidal stromal atrophy with an intact, undamaged retinal pigment epithelium, both preventing physiological ICG staining of the choroidal stroma.

In addition, ICG angiography proved to be useful in the detection of the retinal aneurysmal dilatations that have been shown to remain well delineated throughout the examination as focal areas of retinal hyperfluorescence without leakage. On the contrary on fluorescein angiography the retinal arterial aneurysms became progressively less defined because of dye leakage on the intermediate to late phases.

Aetiological considerations include inflammatory vascular diseases that, as in our case, primarily affect arteries. Among systemic disorders collagen vascular diseases, coagulopathies, cardiac emboli, infections, Behçet disease, Buerger disease, Takayasu arteritis, sarcoidosis and multiple sclerosis should be considered.[6] As in the other cases reported in literature no systemic manifestations were found in our patient, despite extensive medical investigation. HLA typing demonstrated the presence of HLA B51, although no clinical evidence of Behçet disease was found.[7] Among primary ocular vasculitides, Eales' disease bears some resemblance to IRVAN. Eales' disease, however, typically affects young men and frequently is associated with tuberculin hypersensitivity. In addition, the vascular inflammation in Eales' disease is more pronounced in the peripheral veins than the arteries.[8]

Despite the apparent inflammatory nature of IRVAN, systemic corticosteroids either intravenously or orally administered have been shown to have little effect on the progression of the disease.[1] We avoided photocoagulation of the ischaemic retina because no evidence of neovascularisation was present. Laser photocoagulation along both sides of the retinal aneurysms to reduce macular oedema, as suggested by others,[9] was not performed in this case because the amount of retinal exudation and visual loss did not justify this approach.

References

1. Chang TS, Aylward GW, Davis JL, Mieler WF, Oliver GL, Maberley AL, et al. The Retinal Vasculitis Study Group. Idiopathic retinal vasculitis, aneurysms, and neuro-retinitis. Ophthalmology 1995;102:1089–97.
2. Karel I, Peleska M, Divisova G. Fluorescein angiography in retinal vasculitis in children's uveitis. Ophthalmologica 1973;166:251–64.
3. Kincaid J, Schatz H. Bilateral retinal arteritis with multiple aneurysmal dilatations. Retina 1983;3:171–8.
4. Malan P, Ciurana AJ, Boudet C. Artérite rétinienne bilatérale avec dilatations anévrysmales multiples. J Fr Ophtalmol 1986;9:23–8.
5. Owens SL, Gregor KJ. Vanishing retinal arterial aneurysms: a case report. Br J Ophthalmol 1992;76:637–8.
6. Sanders M. Duke-Elder lecture. Retinal arteritis, vasculitis and autoimmune retinal vasculitis. Eye 1987;1:441–65.
7. International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's disease. Lancet 1990;335:1078–80.
8. Schubert HD. Eales' disease. In: Guyer DR, editor. Retina, vitreous, macula. Philadelphia: WB Saunders, 1999:415–20.

9. Brancato R, Vergani S, Ciardella AP. The rheumatic retinal diseases. In: Guyer DR, editor. Retina, vitreous, macula. Philadelphia: WB Saunders, 1999:527–34.

Magda Gharbiya ✉
Francesco Bozzoni Pantaleoni
Massimo Accorinti
Paola Pivetti Pezzi
Institute of Ophthalmology
University 'La Sapienza' of Rome
Viale del Policlinico, 155
I-00161 Rome, Italy
Tel: +39 6 490296
Fax: +39 6 4457706

Sir,

Stable pigmentary retinopathy in a child with 3-hydroxyacyl-CoA dehydrogenase deficiency

Deficiency of long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD),[1,2] an enzyme involved in mitochondrial beta-oxidation of fatty acid, has been shown to be associated with hypoketotic hypoglycaemia, hepatic steatosis, cardiomyopathy, rhabdomyolysis, peripheral neuropathy and retinopathy.[1–3] Prognosis of life and vision in these patients is poor. The natural course of the disease can be alleviated by a low-fat high-carbohydrate diet along with carnitine and docozahexanoic acid (DHA) supplementation.[4,5] We present a case of stable pigmentary retinopathy in an 8-year-old child with LCHAD therapy on dietary substitution of carnitine and DHA therapy.

Case report

A 3-year-old emmetropic boy was referred to the ophthalmology unit for fundus evaluation following detection of pigmentary retinopathy. The child, a known case of LCHAD deficiency, was on dietary therapy with DHA (65 mg/day) and carnitine supplementation.

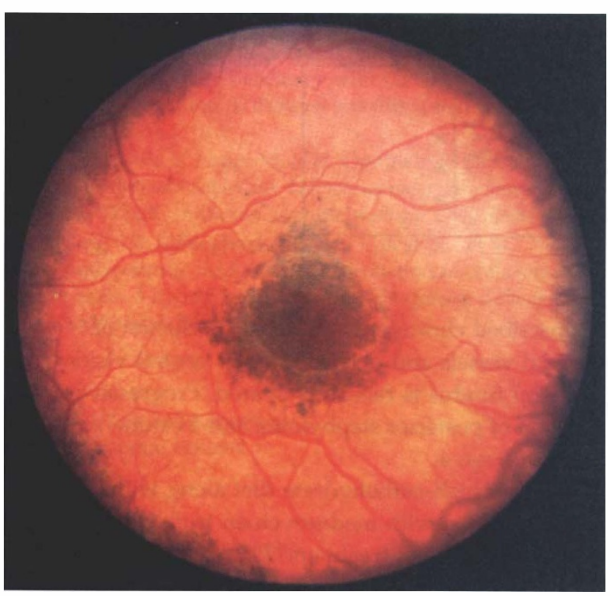


Fig. 1. *Fundus photograph of the right eye showing pigmentary maculopathy.*

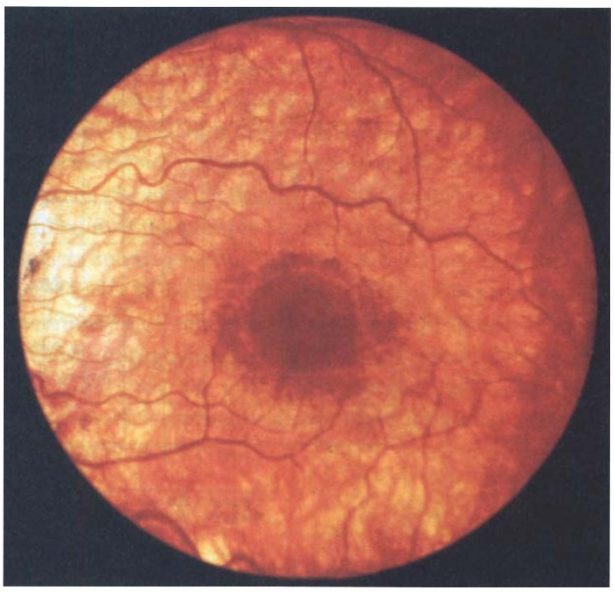


Fig. 2. *Fundus photograph of the left eye showing pigmentary maculopathy.*

Ocular examination revealed a best corrected Snellen visual acuity of 6/9 in the right and 6/6–4 in the left eye. The child was emmetropic and orthophoric with normal ocular motility. Anterior segment was essentially normal. Fundus evaluation revealed bilateral foveal pigmentary retinopathy and secondary retinal pigment epithelium atrophy (Figs. 1, 2). An impression of bimacular pigmentary retinopathy secondary to LCHAD was made.

The child was followed yearly in the clinic for 5 years to assess the progression of disease. However, his ocular condition and visual acuity remained near stable during this period. At his last follow-up his best-corrected visual acuity was 6/9 in both eyes. Fundus evaluation revealed no progression of retinopathy. The child had full Goldmann fields. Threshold visual fields showed scattered scotomas not conforming to any pattern. Electrophysiology performed at this visit revealed normal visual evoked potentials (VEP); flash electroretinogram (ERG) amplitudes were near the lower limit of normal, and pattern ERG was of poor amplitude (Fig. 3).

Comment

Long chain 3-hydroxyacyl-CoA activity is found in the mitochondrial trifunctional protein (MTP). Its deficiency, a result of G1528C mutation, leads to deficiency in beta-oxidation of fatty acids[2] and is characterised by low activity of LCHAD with normal levels of immunoreactive MTP.[6] Although analysis of serum carnitine[4] can be used as a screening test, LCHAD deficiency can be detected by measuring the enzyme activity or by detection of G1528C mutation in blood or tissue samples. Prenatal diagnosis is also possible by chorionic villous biopsy. Urine analysis in patients with LCHAD deficiency shows increased levels of 3-hydroxylated carboxylic acids.[5]