Indocyanine green angiographic findings in idiopathic choroidal neovascularisation

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CLINICAL STUDY

Abstract

Purpose **The authors report the cases of two patients affected with idiopathic choroidal neovascularisation studied with combined fluorescein angiography and indocyanine green (ICG) angiography. In particular the presence of choroidal abnormalities at ICG angiography which could not be detected by fluorescein angiography was studied.**
Methods **Both patients underwent a complete systemic and ocular assessment. Fluorescein angiography and ICG angiography were performed in a routine fashion at the time of presentation in both cases and after 14 months in the second patient.**
Results **Results of the systemic investigations were unremarkable. A distinct dark rim surrounding the choroidal neovascular net was evident until the late phases of ICG angiography despite the presence of subretinal blood. Dilated choroidal vessels were observed beneath the neovascular membrane in both cases. In the first patient a hyperfluorescent area beyond the primary lesion was detected in the affected eye and a distinct leaking subfoveal choroidal venous vessel was found in the fellow eye. The second patient never showed other angiographic alterations either in the affected or in the fellow eye.**
Conclusions **ICG angiography has proved to be useful, both to better define and follow up the true extent of the pigment halo (healing response) around the neovascular membrane when subretinal blood and dye leakage at fluorescein angiography prevent its full appreciation, and to rule out other causes of choroidal neovascularisation in young healthy adults associated with either choroidal inflammatory focal lesions or choroidal vascular dynamic or inflammatory alterations.**

Key words Dark rim, Idiopathic choroidal neovascularisation, Indocyanine green angiography, Pigment halo, Serous haemorrhagic choroidopathy of the young

A subretinal neovascular membrane, located in the macular zone, is not frequent in patients under 50 years of age. There exists a distinct subset of young patients in whom choroidal neovascularisation (CNV) develops in the absence of any detectable primary ophthalmic or systemic disease which has been recognised to cause submacular neovascular membranes.[1–3] When no apparent cause or association can be determined, the subretinal neovascular membrane in patients younger than 50 years of age is classified as idiopathic (ICNV).[4–12]

Few cases of ICNV studied with combined fluorescein angiography and indocyanine green (ICG) angiography have been reported.[13,14] We report the cases of two patients with macular subretinal neovascular membranes which were diagnosed as idiopathic at fluorescein angiography and in which ICG angiography demonstrated abnormalities of the choroidal vasculature.

Case reports

Case 1

A healthy 30-year-old woman noted sudden, painless blurring of vision in her right eye. Medical, surgical and ocular history was unremarkable and she was taking no medications. There was no family history of eye disease.

On examination 1 week after the onset of symptoms, visual acuity was 20/60 in the right eye and 20/20 in the left eye with a refractive error of 1.75 dioptres of myopia in both eyes. An Amsler grid test was altered in the right eye and normal in the left eye. There was no evidence of an afferent pupillary defect. Results of anterior segment examination were normal in both eyes. Results of dilated fundus examination of the right eye showed a grey submacular lesion surrounded by subretinal blood and an overlying neurosensory retinal detachment; the optic disc and retinal vessels were normal (Fig. 1a); the overlying vitreous was clear. The left fundus was normal, except for the presence of a pinpoint area of retinal pigment epithelium (RPE) atrophy in the macular region (Fig. 1b). At fluorescein angiography the lesion showed an early net-shaped hyperfluorescence which

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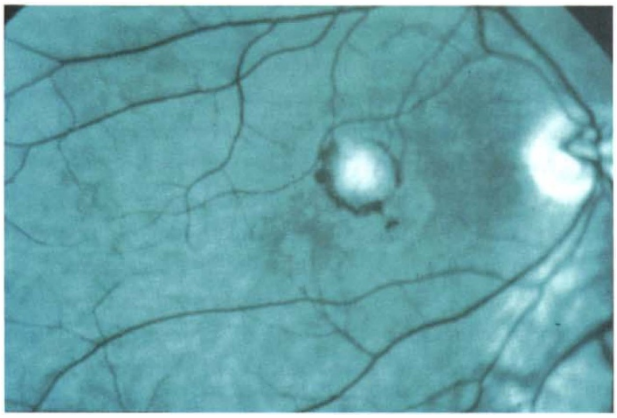

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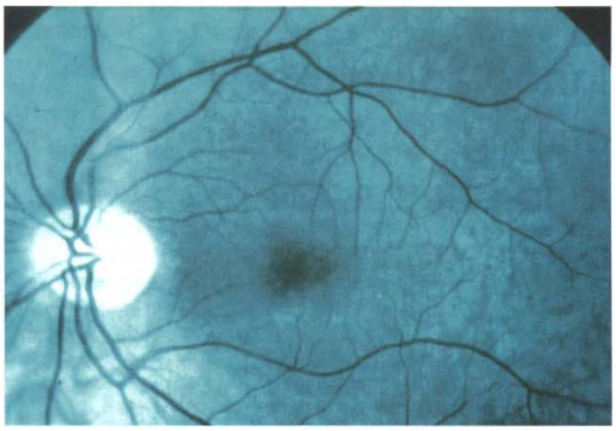

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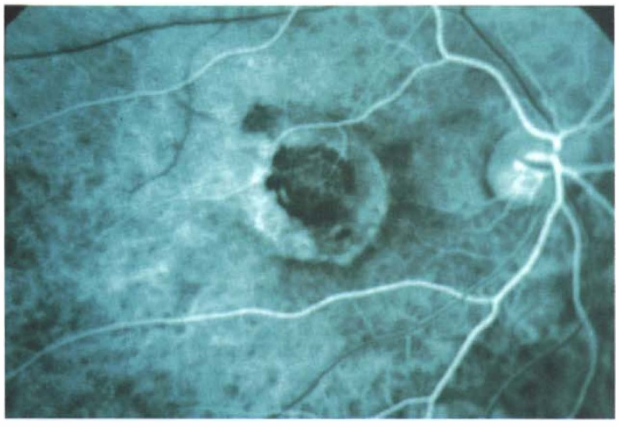

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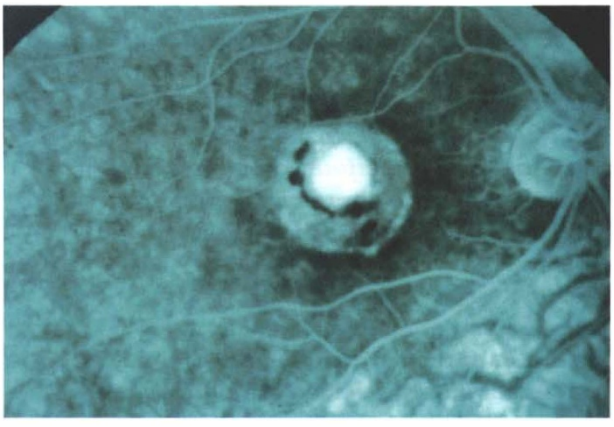

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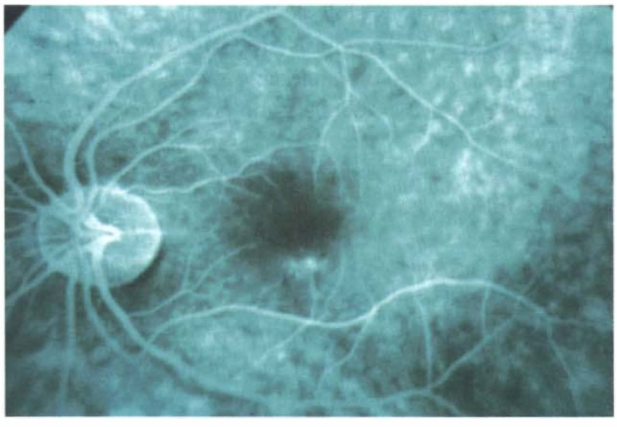


(e)

Fig. 1. *Case 1. (a) Red-free image. Right eye. Fundus appearance at time of presentation. (b) Red-free image. Left eye. Fundus appearance at time of presentation. (c) Right eye. Early phase fluorescein angiogram. Note the incomplete hypofluorescent halo surrounding the neovascular lesion and masking due to associated haemorrhage. (d) Right eye. Late phase fluorescein angiogram. Dye leakage from the neovascular membrane completely obscures the dark rim. (e) Left eye. Late phase fluorescein angiogram. A hyperfluorescent spot of retinal pigment epithelium atrophy was observed in the macular region.*

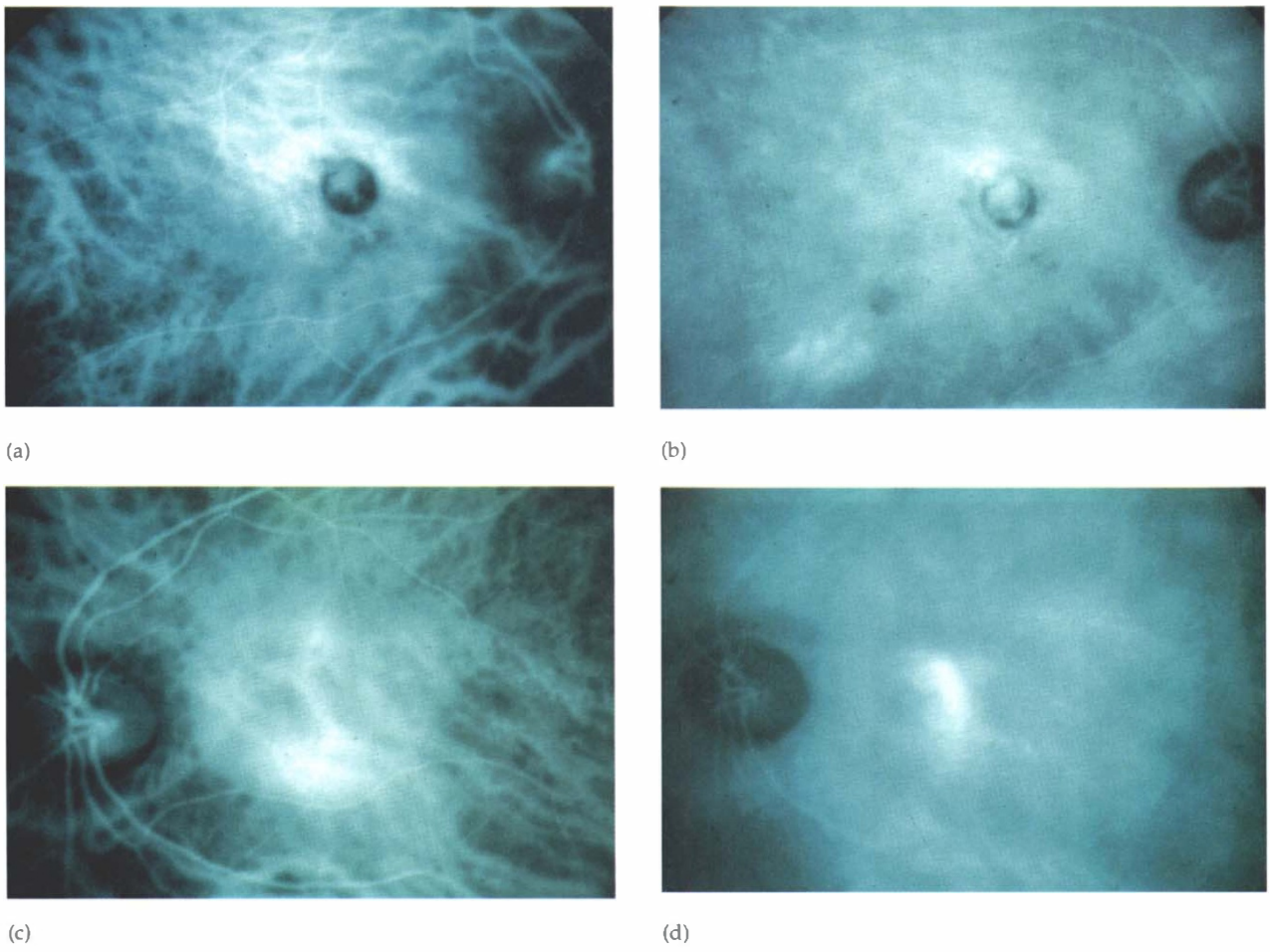


Fig. 2. *Case 1. (a) Right eye. Early phase indocyanine green (ICG) angiogram. Choroidal hyperfluorescence and dilated choroidal vessels were observed beneath the neovascular membrane. (b) Right eye. Late phase ICG angiogram. Note the complete dark rim surrounding the neovascular membrane and the area of choroidal hyperfluorescence inferior to the macula. (c) Left eye. Early phase ICG angiogram. Note the roundish area of diffuse hyperfluorescence centred on an underlying dilated choroidal vein in the macular region. (d) Left eye. Late phase ICG angiogram. A roughly linear hyperfluorescent area of staining was observed along the venous choroidal vessel.*

increased in the late phases, retaining sharply defined borders throughout the examination. In the early phases an incomplete dark rim was present around the neovascular net partially masked by subretinal blood, and became progressively obscured by dye leakage from the choroidal membrane. The optic disc was normal (Fig. 1c,d). In the left eye a hyperfluorescent spot in the macular region which remained unchanged throughout the examination was diagnosed as an area of RPE atrophy (Fig. 1e).

At ICG angiography the network structure of choroidal neovascularisation emerged in the early phases as a faint hyperfluorescent area surrounded by a distinct dark rim that remained well defined throughout the examination (Fig. 2a). In the early phases dilated choroidal vessels associated with faint choroidal hyperfluorescence that persisted until the late phases were observed beneath the membrane. A distinct area of choroidal hyperfluorescence was detected inferior to the fovea in the late phases (Fig. 2b). In the left eye a roundish area of diffuse hyperfluorescence involving the macular region appeared in the early phases centred on an underlying leaking choroidal vein (Fig. 2c). In the late phases a roughly linear hyperfluorescent area of staining along the venous choroidal vessel was observed (Fig. 2d).

A complete immunological assessment, antibody titres for bacterial, viral and parasitic pathogens, PPD, ACE test, serum lysozyme, chest radiographs, blood and urine culture, full blood count, specific index of inflammation and vaginal tampon were all negative. Laser treatment of the choroidal neovascular membrane was not recommended because of the subfoveal localisation. On the grounds of the ICG study demonstrating vascular abnormalities in both eyes, thought to be related to an underlying inflammatory vascular process, systemic corticosteroid therapy was administered. The patient was started on oral prednisolone 1 mg/kg body weight daily for 3 weeks with no visual and angiographic changes. Steroids were discontinued but unfortunately she was lost to follow-up.

Case 2

A 24-year-old woman suffered a sudden decrease in central vision in her left eye 2 weeks before presentation. Past ocular and medical history was non-contributory. The patient was in good general health. On examination visual acuity was 20/20 in the right eye and 20/40 in the left eye. An Amsler grid test was normal in the right eye and altered in the left eye. Results of anterior segment

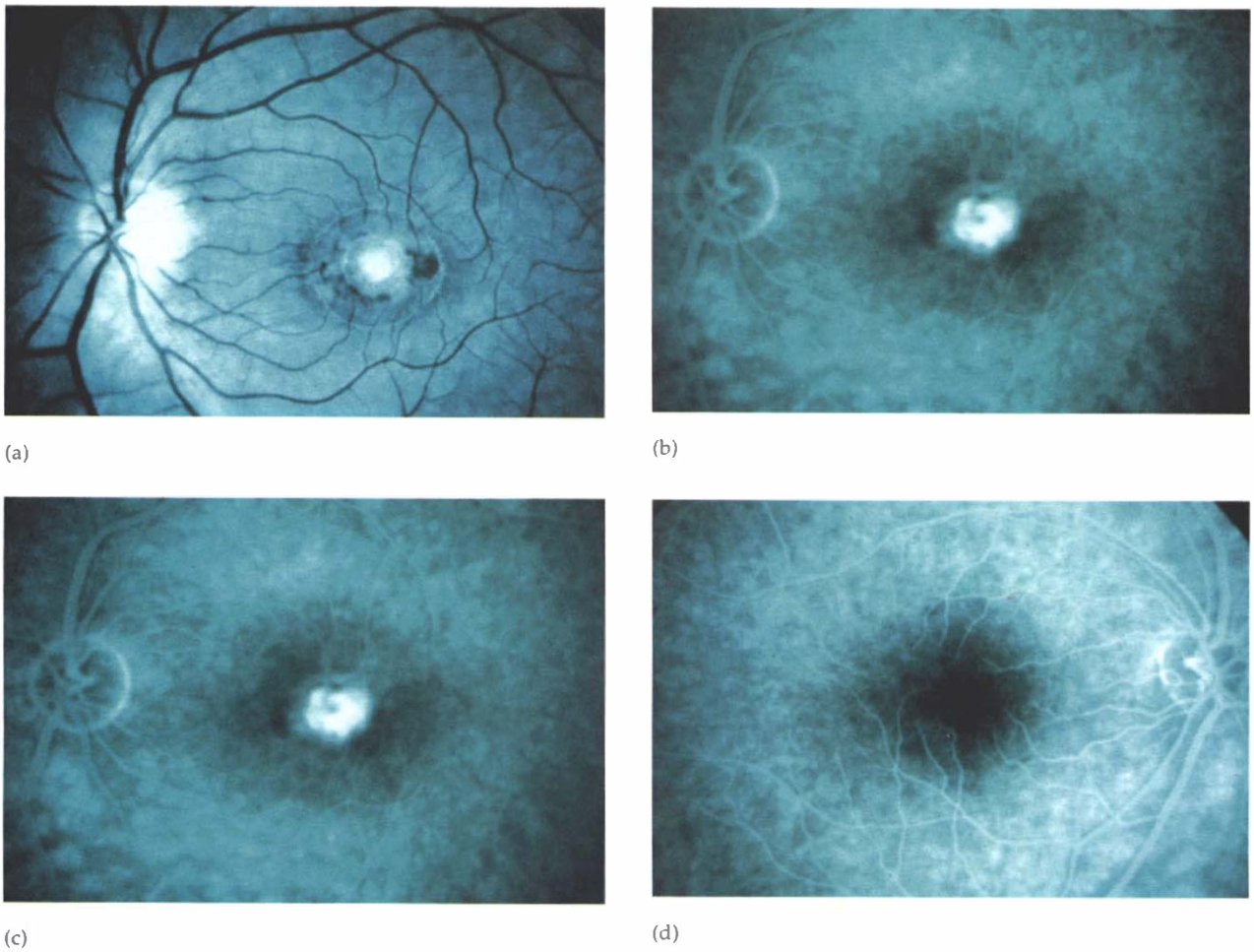


Fig. 3. *Case 2. (a) Left eye. Red-free image. Fundus appearance at time of presentation. (b) Left eye. Early phase fluorescein angiogram. Note the hypofluorescent halo around the neovascular net. (c) Left eye. Late phase fluorescein angiogram. Dye leakage from the neovascular membrane masked the dark rim. (d) Right eye. Late phase fluorescein angiogram. No alterations were found.*

examination were unremarkable in both eyes. No evidence of vitritis was present. A discrete greyish subfoveal elevation with associated subretinal fluid and subretinal haemorrhage was present within the left macula (Fig. 3a). The right fundus was normal.

Fluorescein angiography confirmed the subfoveal neovascular membrane in the left eye. In the early phases the lesion appeared surrounded by a complete hypofluorescent halo (Fig. 3b) which was progressively masked by fluorescein leakage coming from the neovascular net (Fig. 3c). Fluorescein angiography did not show abnormalities in the right eye (Fig. 3d). The optic disc was slightly hypofluorescent in both eyes. In the left eye ICG angiography demonstrated an early hyperfluorescent island corresponding to the neovascular membrane surrounded by a well-defined dark rim. The lesion appeared within an area of early faint hyperfluorescence associated with dilated choroidal vessels (Fig. 4a) which faded in the late phases (Fig. 4b). In the right eye ICG angiography did not demonstrate any abnormalities (Fig. 4c).

Results of a complete immunological assessment, antibody titres for bacterial, viral and parasitic pathogens, PPD, ACE test, serum lysozyme, chest radiographs, blood and urine culture, full blood count, specific index of inflammation and vaginal tampon were unremarkable. ICG study did not show any alterations in the fellow eye. The patient was then started on a periocular steroidal therapeutic regimen but no visual improvement was obtained.

Fourteen months later she returned to our observation complaining of an episode of transient blurred vision occuring 2 days previously in the fellow eye. Visual acuity was unchanged in both eyes. Results of fundus examination were unremarkable for the right eye; in the left eye the lesion was almost unchanged in size, with a glial appearance (Fig. 5a). Fluorescein angiography was normal in the right eye (Fig. 5c); in the left eye the lesion appeared almost unchanged in its fluorescence pattern and a well-defined outer granular hyperfluorescent halo of pigmentary changes was present (Fig. 5b). ICG angiography findings were unchanged in both eyes (Fig. 6a,b). To date no further changes have occurred.

Discussion

ICNV, or serous haemorrhagic choroidopathy of the young, is now a well-defined clinical entity characterised by: its appearance in young subjects (below 50 years of age); sudden onset of symptoms related to submacular neovascular membrane (i.e. decreased acuity, metamorphopsia); foveal or juxtafoveal localisation

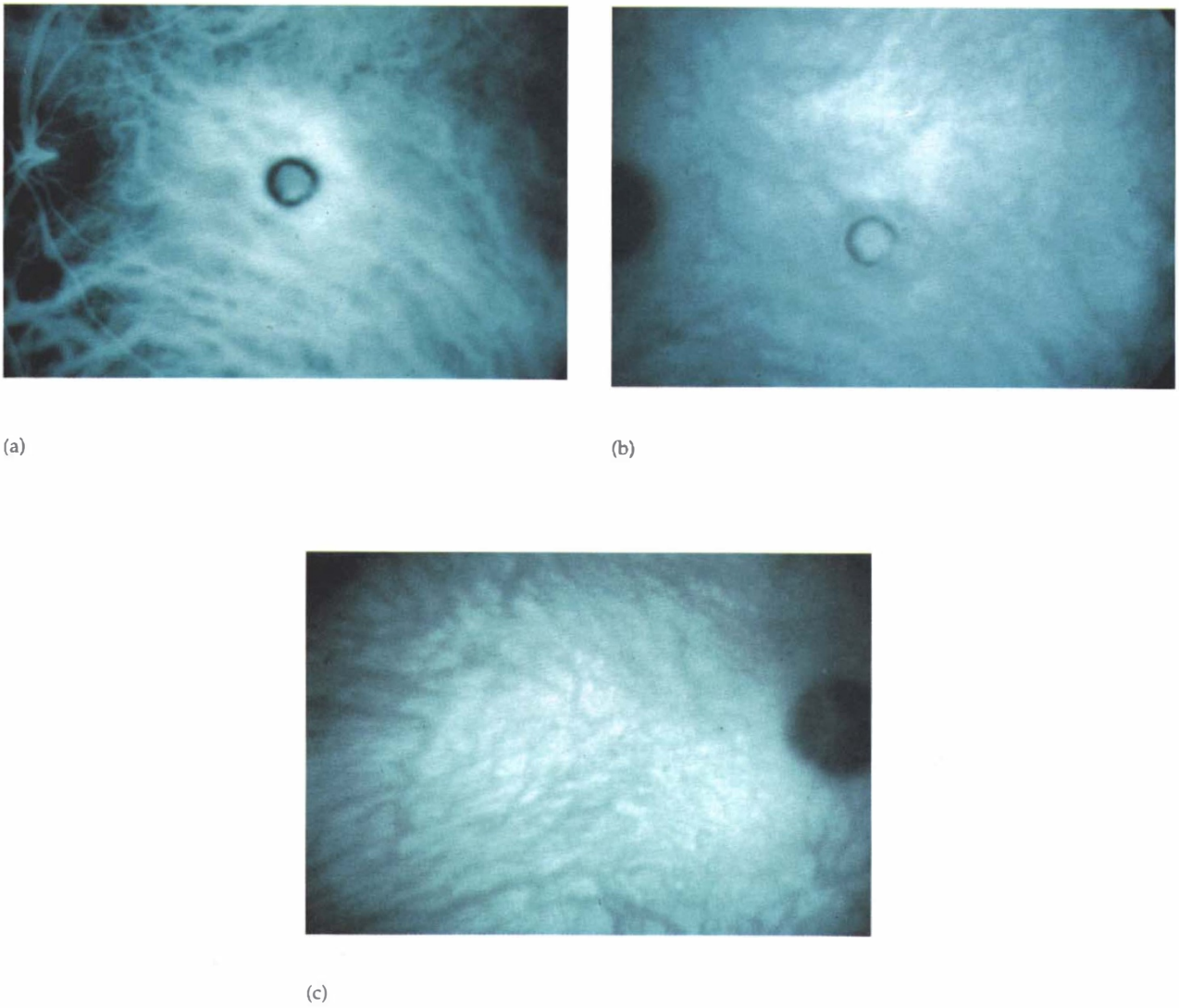


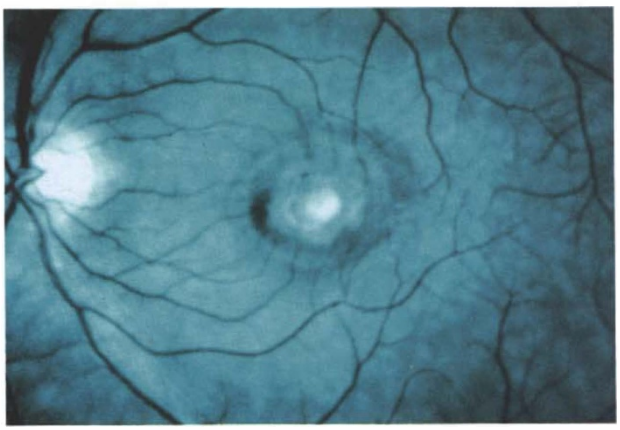
Fig. 4. *Case 2. (a) Left eye. Early phase ICG angiogram. Choroidal hyperfluorescence and dilated choroidal vessels were observed beneath the neovascular lesion. (b) Left eye. Late phase ICG angiogram. Note the prominent dark rim around the neovascular membrane. (c) Right eye. Late phase ICG angiogram. No alterations were found.*

usually associated with a serous and/or haemorrhagic detachment of the overlying neurosensory retina; unilateral involvement in 86–100% of cases;[9,11] absence of any detectable primary ocular or systemic disease; and spontaneous involution into a fibroglial scar slightly larger than the initial active lesion with a more favourable visual outcome if compared with submacular membranes in age-related macular degeneration (AMD) and ocular (OHS) or presumed ocular histoplasmosis syndrome (POHS).[11]

The introduction of ICG angiography into clinical practice has enabled the observation of alterations that could not be detected either with ophthalmoscopy or with fluorescein angiography in many conditions.

In our patients ICG angiography was not essential for the imaging of the CNV, which was already well delineated by fluorescein angiography. No detectable signs of choroidal hypoperfusion were observed, either in the affected or in the fellow eyes. In both our cases a distinct dark rim surrounding the choroidal neovascular membrane was evident until the late phases. This hypofluorescent halo was only partially visible in the early phases of fluorescein angiography because of masking by subretinal blood, and became almost completely obscured by dye leakage from the neovascular core in the late phases. Most previous clinicopathological reports[14,15–18] have indicated that the dark rim observed clinically correlates with multiple layers of reactive hypertrophic/hyperplastic pigment epithelial cells enveloping the outer margin of the neovascular membrane and represents a favourable healing response. The presence of an association between young age, a surrounding pigment ring and spontaneous involution of subfoveal neovascular membrane has been described.[14,15,18,19]

Several interpretations have been proposed to explain this singular clinical appearance: the RPE of younger subjects may be more effective in enveloping CNV and a more effective source of local neovascular inhibitors;[11,20,21] Gass[15,18] correlated these clinical



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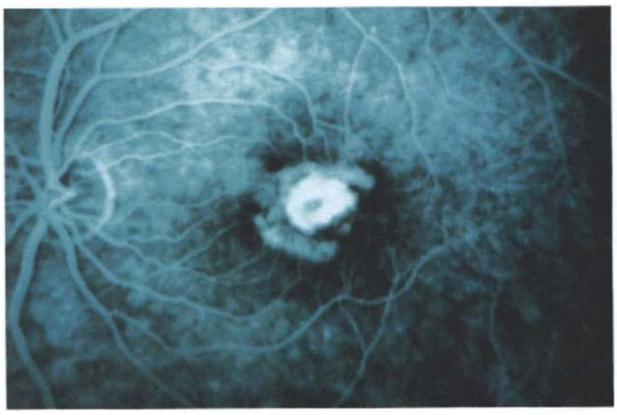

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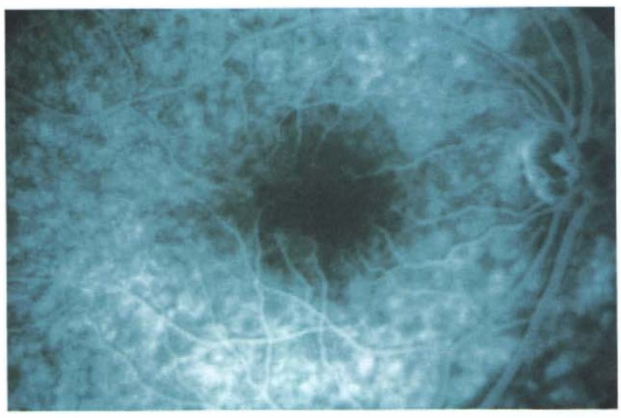

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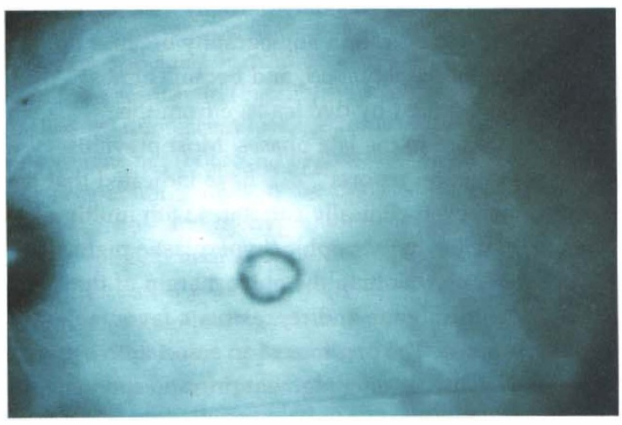
Fig. 5. *Case 2. Fourteen months after presentation. (a) Left eye. Red-free image. (b) Left eye. Late phase fluorescein angiogram. The lesion appeared unchanged in size and surrounded by a granular hyperfluorescent halo of pigmentary changes. (c) Right eye. Late phase fluorescein angiogram. No abnormalities were present.*



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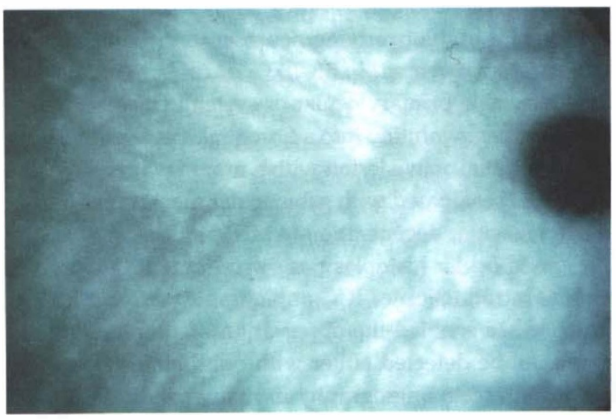

(b)

Fig. 6. *Case 2. Fourteen months after presentation. (a) Left eye. Late phase ICG angiogram. No changes were observed. (b) Right eye. Late phase ICG angiogram. No alterations were present.*

features with a distinct subsensory retinal growth pattern of CNV (type 2 membrane) that is associated with focal damage to the Bruch's membrane/RPE complex.

ICG angiography proved to be useful for identifying the hypofluorescent halo even when both ophthalmoscopy and fluorescein angiography failed to detect its true extent because of masking by subretinal blood and dye leakage.

As a diagnostic adjunct ICG angiography would be most useful for identifying distinct features that would assist in differentiating ICNV from other known conditions associated with secondary choroidal neovascularisation in young healthy subjects. Among these POHS, punctate inner choroidopathy (PIC) and multiple evanescent white dot syndrome (MEWDS) need to be considered. These diseases are known to occur in young women and are characterised by the absence of anterior chamber and vitreous inflammation. ICG angiography may give us clues to make the distinction between these entities and ICNV, although this is usually feasible on the basis of the clinical and fluorescein angiographic picture. Patients with POHS usually show hyperfluorescent spots in the posterior pole in the mid- and late phases of ICG study.[22,23] Hypofluorescent spots clustered in the posterior pole have been shown to be present in PIC.[24–26]

Hypofluorescent dots clustered and fused in the posterior pole and around the optic disc, and scattered in the peripheral region, have been observed in MEWDS.[27-29] Neither hyperfluorescent nor hypofluorescent spots were identified in our cases or in the series reported by Iida and associates.[14]

In our patients ICG angiography demonstrated choroidal vascular abnormalities either posterior to the choroidal membrane (both cases), distant from it (case 1) or even in the asymptomatic fellow eye (case 1). Choroidal hyperfluorescence and dilated choroidal vessels were observed beneath the neovascular membrane in both patients. In case 1 a hyperfluorescent area far from the primary lesion was detected in the affected eye and a distinct leaking choroidal venous vessel was detected in the fellow eye. These findings may be related to choroidal hyperpermeability and somewhat resemble what is observed in central serous chorioretinopathy but without any associated RPE alterations typical of this disease.[30,31] They may result from an underlying inflammatory vascular process involving large choroidal vessels which ultimately leads to focal damage to the Bruch's membrane/RPE complex and secondary choroidal neovascular membrane formation.

The second patient never showed angiographic alterations apart from those detected in the foveal region of the affected eye, either at her initial presentation or in the following 2 years. Iida and associates[14] found choroidal hyperfluorescent areas separate from the neovascular membrane in 6 of 16 patients; in 2 of them they observed choroidal hyperfluorescent areas also in the fellow eye. There were still a significant percentage of patients in whom the ICG angiography did not demonstrate choroidal alterations apart from the site of the submacular neovascular membrane. Although they apparently shared the same clinical and fluorescein angiographic appearance our patients showed a clearly different expression of the disease on the basis of ICG findings in both the affected eye (multifocal versus unifocal disease) and the fellow eue (bilateral versus unilateral disease). The question is whether their disease truly shares the same aetiology.[12]

No significant histopathological differences have been found among the excised neovascular membranes from patients with different underlying disease. This has led to the concept that choroidal neovascular membranes, regardless of the aetiology, represent a stereotypic healing response similar to granulation tissue proliferation.[17,32]

Among idiopathic cases of choroidal neovascularisation ICG angiography might be useful in identifying those with associated distinct choroidal vascular abnormalities either in the affected eye or in the fellow eye that may represent a subgroup or probably a distinct group with a difference course and a different underlying aetiology.

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