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Br J Ophthalmol published online May 14, 2010
doi: 10.1136/bjo.2009.159913

BJO Online First, published on May 14, 2010 as 10.1136/bjo.2009.159913

Fluorescein angiography and optical coherence tomography concordance for choroidal neovascularisation in multifocal choroidtis

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Accepted 31 January 2010

ABSTRACT

Purpose To compare the utility of fluorescein angiography (FA) and optical coherence tomography (OCT) as diagnostic adjuncts in evaluating symptomatic patients with choroidal neovascularisation (CNV) due to multifocal choroiditis (MFC).

Methods Patients with CNV due to MFC were retrospectively evaluated in a consecutive fashion. Fundus photography, FA, OCT and biomicroscopy were used to establish the diagnosis. Primary outcome measures included CNV classification (type 1 or occult and type 2 or classic) location and the associated FA and OCT findings.

Results Twenty eyes from 17 patients were included in the study. In 19 eyes (95%) the FA revealed CNV type 2; in one eye (5%) the type of CNV was indeterminate due to a subretinal haemorrhage that covered the lesion. The OCT images revealed a hyper-reflectance beneath the neurosensory retina in all 20 eyes but only 53.8% of them revealed evidence of subretinal fluid (SRF) or intraretinal cystic abnormalities.

Conclusions The CNV in MFC is virtually always type 2, or so-called classic CNV, with vessels beneath the neurosensory retina. Except when blocked by subretinal blood, the neovascularisation is clearly demonstrated by FA. In contrast, only 53.8% of these eyes showed clear evidence of actively proliferating neovascularisation on OCT. Therefore, eyes suspected of having CNV in MFC should be evaluated with FA.

INTRODUCTION

Fluorescein angiography (FA) was for decades the standard diagnostic adjunct for studying macular diseases and their manifestations, especially choroidal neovascularisation (CNV). Recently, optical coherence tomography (OCT) has emerged as a non-invasive alternative for diagnosing chorioretinal diseases, with enhanced specificity and sensitivity, particularly for vitreoretinal interface and exudative macular abnormalities. However, studies have shown that leakage demonstrated with FA, cannot always be detected with OCT.[1 2]

We evaluated patients with CNV secondary to multifocal choroiditis (MFC) with FA and OCT, and characterised the nature of the CNV and the concordance between these two diagnostic modalities in detecting it.

METHODS

We conducted a retrospective analysis of consecutive, symptomatic patients with MFC in a referral practice. The objective of the study was to evaluate the clinical characteristics and nature of CNV in this idiopathic inflammatory retinal condition and to compare the utility of the diagnostic adjuncts, FA and OCT. The patients were either evaluated at the Vitreous-Retina-Macular Consultants of New York or at the First Department of Ophthalmology of the Medical School of Athens University, between May 1999 and March 2008. Fundus photography, FA, OCT and slit-lamp biomicroscopy were used to establish the diagnosis of MFC based on the characteristic retinal morphology of multiple punched-out, chorioretinal atrophic spots located in the posterior pole or mid-periphery in association with signs or clinical history of vitreous and anterior chamber inflammation. Supplemental serological studies were employed as clinically indicated to exclude other systemic medical diseases with similar ocular inflammatory presentations.

Only patients with a diagnosis of MFC who exhibited acute visual deficits and clinical manifestations of active CNV were included in the study. The active CNV was diagnosed by biomicroscopy and the typical findings seen on FA such as early hyperfluorescence with late dye leakage. Disciform scars at separate sites than the active CNV, in the same or fellow eye, were not included. Other exclusion criteria were: features of other neovascular maculopathies such as age-related macular degeneration; hereditary retinal disorders or idiopathic CNV; previous therapeutic interventions such as submacular surgery, laser photocoaguation, photodynamic therapy (PDT) or anti-vascular endothelial growth factor (anti-VEGF) pharmacotherapy; and underlying ocular or systemic inflammatory or infectious diseases such as presumed ocular histoplasmosis (POHS,) tuberculosis and sarcoidosis.

Each patient received a comprehensive ophthalmic examination which included Snellen distant visual acuity measurement to determine best-corrected visual acuity (BCVA), intraocular pressure, slit-lamp biomicroscopy, indirect ophthalmoscopy and FA and OCT findings. OCT imaging was carried out using a Stratus OCT camera (Carl Zeiss Meditec, Dublin, California, USA) or a Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany). Primary outcome measures included CNV classification (type 1 or occult and type 2 or classic), location and the associated FA and OCT findings, specifically alterations of the retinal architecture and existence of subretinal fluid (SRF) or intraretinal cysts.

RESULTS

Twenty eyes from 17 patients were included in the study. There were 14 women and three men

Table 1 Visual acuity, fluorescein angiography and optical coherence tomography (OCT) findings of patients with choroidal neovascularisation (CNV) due to multifocal choroiditis

Case	Visual acuity	Location of CNV	Type of CNV	OCT findings
1	20/25	Juxtafoveal	Classic	No fluid
2	20/60	Juxtafoveal	Classic	NA
3	20/70	Juxtafoveal	Classic	NA
4	20/25	Juxtafoveal	Classic	NA
5	20/25	Juxtafoveal	Indeterminate	NA
6	20/70	Subfoveal	Classic	No fluid
7	20/25	Juxtafoveal	Classic	NA
8	20/20	Extrafoveal	Classic	NA
9	20/60	Juxtafoveal	Classic	NA
10	20/200	Subfoveal	Classic	SRF
11	20/200	Juxtafoveal	Classic	No fluid
12	20/25	Juxtafoveal	Classic	No fluid
13	10/400	Subfoveal	Classic	SRF
14	20/30	Extrafoveal	Classic	Cysts
15	20/30	Extrafoveal	Classic	No fluid
16	20/70	Subfoveal	Classic	Cysts
17	20/40	Subfoveal	Classic	Cysts
18	20/40	Extrafoveal	Classic	SRF
19	20/40	Juxtafoveal	Classic	SRF, cysts
20	20/40	Juxtafoveal	Classic	No fluid

NA, not available; SRF: subretinal fluid.

ranging in age from 29 to 78 years with a mean age of 42.7 years. The BCVA ranged from 20/25 to 10/400 with a mean of 20/100 and the mean spherical equivalent ranged from −1.50 to −16.00 with a mean of −7.3 dioptres (for five eyes the spherical equivalent data was not available). Eleven cases revealed a history of corticosteroid therapy: oral medication (nine), subtenon's injection (one) and intravenous medication (one). Additionally, seven eyes showed old CNV scars in the same or fellow eye without evidence of active leakage with FA and these lesions were excluded from analysis.

In five eyes (25%) the active choroidal neovascularisation was subfoveal, in 11 (55%) juxtafoveal and in four (20%) extrafoveal (table 1).

In 19 eyes (95%) the early phase of FA revealed a well-demarcated area of hyperfluorescence indicative of type 2 or classic CNV followed by late dye leakage (figure 1). In one eye (5%) the type of CNV was indeterminate due to a subretinal haemorrhage which obscured most of the lesion.

OCT data was available for 13 eyes (12 patients). In all eyes, the OCT imaging of the active CNV lesions revealed an area of hyper-reflectivity beneath the neurosensory retina (figure 2). Only 53.8% of these eyes revealed subretinal fluid (SRF) or intraretinal cystic changes. Three eyes (23%) developed intraretinal cysts without SRF, four eyes (31%) developed SRF without intraretinal cysts and one eye (7.7%) developed SRF and intraretinal cysts. In six eyes (46%) no evidence of fluid accumulation was observed (figure 3).

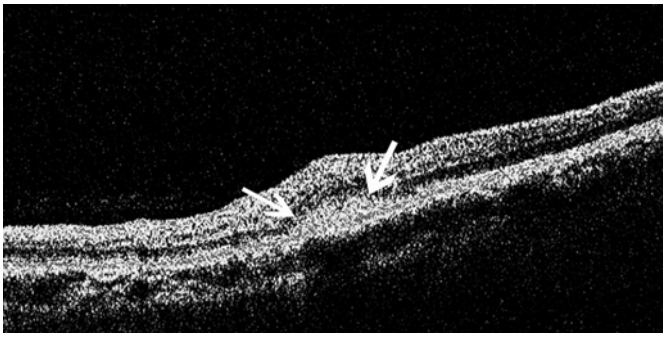

Figure 2 Optical coherence tomography (OCT) image of the lesion shown in figure 1, reveals a highly reflective area beneath the neurosensory retina (arrows). No signs of fluid accumulation are observed.

DISCUSSION

In virtually all of our acute MFC cases (19 of 20), the clinical and angiographic findings demonstrated type 2 neovascularisation or so-called classic CNV. The one exception was indeterminate because of a subretinal haemorrhage which obscured the lesion. Our findings are in accordance with other studies involving CNV in MFC.[3 4] In type 2 CNV, as introduced by Gass, the neovascular membrane proliferates beneath the neurosensory retina rather than beneath the retinal pigment epithelium (RPE).[5] An explanation for the development of this type of CNV in MFC is inherent in the inflammatory nature of the abnormality. The lesions in MFC are located at the level of the RPE and inner choroid leading to disruptions of the choriocapillaris—Bruch's membrane—RPE complex; in some cases there is infiltration of the retina, essentially a chorioretinal inflammatory spot. These lesions are focal or multifocal but not diffuse as in ARMD. Bruch's membrane remains attached to the pigment epithelium and prevents the choroidal vessels from proliferating beneath the RPE.[5]

Accordingly, new vessels have ready access to the subretinal space and they penetrate from the choriocapillaris—Bruch's membrane—RPE complex anteriorly and laterally. The hypothesis is also supported by the observation of type 2 CNV in other inflammatory conditions such as serpiginous choroiditis and POHS[5 6] Non-inflammatory focal neovascular maculopathies

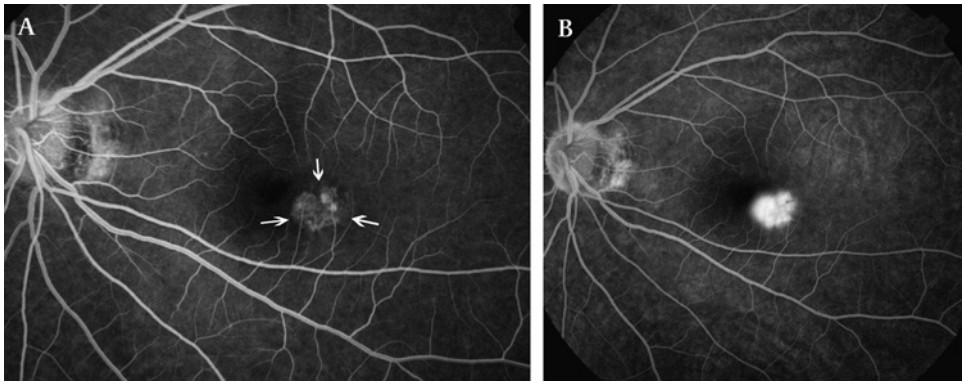

Figure 1 Early (A) and late (B) phase of fluorescein angiography (FA) of a patient with multifocal choroiditis shows a well-demarcated area of hyperfluorescence (arrows) and late leakage, indicative of type 2 or classic choroidal neovascularisation (CNV).

Kotsolis AI, Killian FA, Ladas ID, *et al*. *Br J Ophthalmol* (2010). doi:10.1136/bjo.2009.159913

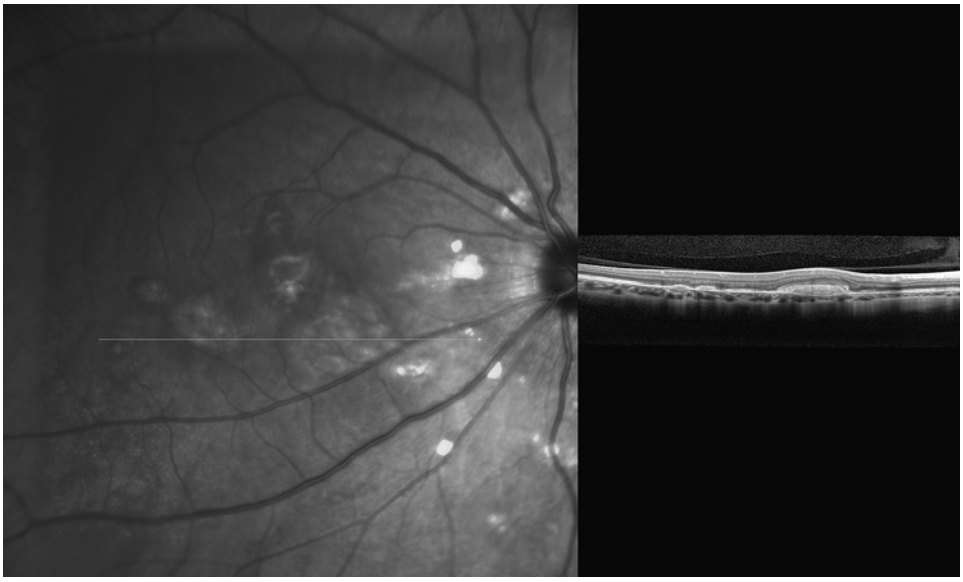

Figure 3 Spectralis HRA+optical coherence tomography (HRA+OCT) image of a symptomatic patient with multifocal choroiditis shows subretinal areas of hyper-reflectivity without signs of subretinal fluid (SRF) or intraretinal cysts.

may also develop type 2 CNV from a mechanical disruption of the choriocapillaris—Bruch's membrane—RPE complex. This is prevalent in pathological myopia via lacquer cracks, in pseudoxanthoma elasticum via angioid streaks and in trauma via ruptures of the choroid and RPE where the neovascular membrane may have access to the subretinal space.[5 7]

Type 1 CNV in inflammatory diseases most probably represents recurrences where neovascularisation has appeared and regressed spontaneously or been subjected to therapy such as laser photocoagulation or pharmacological intervention. In these cases, the regressed portion of the neovascularisation most likely constitutes type 1 neovascularisation, and the recurrent actively proliferating neovascularisation once again is the type 2 form.

Our study has shown that FA is more sensitive in detecting CNV in patients with MFC. This finding is not surprising as previous studies of patients with neovascular ARMD who were treated with PDT showed that leakage with FA is not always associated with obvious anatomical correlates captured by OCT imaging.[1 2] Eter *et al* proposed two explanations for this discrepancy: first, it is possible that the OCT image did not register areas that were noted to be leaking during the FA; and second, leakage with FA may not always be associated with subretinal or intraretinal bulk flow of fluid.[2] These explanations may also be the reason for the absence of detectable subretinal or intraretinal fluid seen with OCT in our cases.

We propose a third possible explanation which relates to the characteristics of the overall neovascularised lesion in MFC. The inflammatory-related CNV beneath the neurosensory retina leads to accumulation of blood and proteinaceous exudate in the subretinal space. The inflammatory debris produces a homogeneous cellular mass which fills the subneurosensory space surrounding the CNV. Consequently, this highly reflective, serosanguineous material gives a false impression of attachment between the RPE and the retina with OCT imaging. The usual silent or vacuous reflectance indicative of detachment is absent, whereas the FA demonstrates intense vascular hyperfluorescence within the blood and exudates.

The study has obvious limitations such as its retrospective, non-controlled nature and the limited number of cases. However, it clearly demonstrates that CNV secondary to inflammatory conditions like MFC is indeed type 2 neovascularisation and that FA is more reliable in documenting actively proliferating neovascularisation than OCT. In conclusion, we recommend that FA be used in the evaluation of eyes suspected of having active CNV in MFC and in any other diseases exhibiting inflammatory-related neovascularisation of the macula.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed

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