Choroidal neovascularisation

Choroidal neovascularisation and atrophy

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There is a lack of knowledge about why and how atrophy spreads over time

Choroidal neovascularisation (CNV) and geographic atrophy (GA) of the retinal pigment epithelium (RPE) are the two forms of advanced age related macular degeneration (AMD), the major cause of severe central visual loss in white people aged 60 and older.[1] Clinical and histopathological studies in the 1970s laid the foundation for our understanding that CNV and GA are both part of the same basic disease process.[2–4] The two conditions share similar ophthalmoscopic risk factors for their development. Both are more likely in eyes with large drusen or many intermediate drusen, and in eyes with pigmentary abnormality. There may be overlap of the two conditions within patients and sometimes within a single eye. Patients may have CNV in one eye and GA in the fellow eye. They may have GA in an eye and then develop CNV in that eye.[5–7] They may have CNV in an eye, which on involution takes on the appearance of GA.[8–10] They may have an evanescent form of CNV which leaves what appears as ''pure'' GA in its wake.[7 11] Histopathologically, there is often CNV present in cases that have been diagnosed as having ''pure'' GA.[3 12]

In this issue of the *BJO*, Sarks and co-authors (p 442) report their findings, in 20 eyes of 18 patients, of the development of progressive atrophy of the RPE around disciform scars from CNV associated with AMD. Once the scar had become stable, they began measuring the progressive atrophy surrounding it. The final area of the atrophy was a mean of 2.4 times as large as the actual scar it surrounded. The mean rate of enlargement of the atrophy measured 5.1 mm^2 for the first 2 years, a rate that is twice the rate of enlargement of GA in the absence of CNV.[13] The rate slowed after this so that there was a lower mean rate of 2.4 mm^2/year measured over the entire period of follow up, with mean follow up 7.3 years. While early papers noted the presence of atrophy surrounding disciform scars,[3] such large atrophic regions surrounding the scar, and their natural course, have not previously been reported. This considerably larger total area of involvement, compared with the area of the stable scar itself, has implications in terms of visual function. The authors suggest that unlike the expectation that visual function will remain stable with a stable CNV scar, patients with this sort of progressive atrophy surrounding the scar are likely to have further worsening of reading speed and other visual functions.

There are a number of interesting questions raised by this paper. There have been reports of expansion of atrophy around laser scars following treatment,[14 15] but none reported such large areas of subsequent atrophy. The authors specifically excluded patients with high myopia, in whom atrophic spread is more extensive. They included patients who underwent a number of different treatments or who were untreated, so that the cause of the progressive atrophy cannot be attributed to spread of a laser scar alone. The paper does not discuss how common this sort of extensive progressive atrophy is in eyes with stable scars from CNV.

> It may be that ultimate treatment for CNV will include both antiangiogenic agents to address the neovascular process and trophic factors to promote RPE survival and limit progressive atrophy

The authors acknowledge that the only visual function measure assessed was visual acuity, which itself might not be sensitive to enlargement of atrophy once the visual acuity is already severely reduced. They did not assess whether the areas that appeared as GA were truly scotomatous. A number of studies have shown that an atrophic appearance does not necessarily mean an absence of function. One paper reporting expansion of laser scars in CNV associated with ocular histoplasmosis noted that in a case in which the apparent atrophy progressed through the fovea there was not a concomitant loss of visual acuity.[15] Likewise, in some patients who have undergone submacular surgery for choroidal neovascularisation (again, generally younger, non-AMD cases), there are atrophic appearing areas that retain function when measured by scanning laser ophthalmoscope (SLO) macular perimetry.[16] Presumably, what has occurred in these atrophic appearing areas is attenuation and hypopigmentation of the RPE cells rather than complete atrophy. Fundus autofluorescence cannot reliably differentiate total atrophy from RPE attenuation,[17] so it cannot replace functional measures in assessing the visual impact of this expansion. This study should spur macular perimetry using a fundus perimeter such as the Rodenstock SLO (Rodenstock Instrumente GmbH, Munich, Germany) or the Nidek MP-1 (Nidek Technologies SRL, Padua, Italy) to determine the function of these atrophic appearing lesions. Assuming that there is GA and loss of photoreceptors in the regions of progressive atrophy (as found in the authors' histopathological study), there would be an impact on reading rate, since reading rate is inversely related to the size of the central scotoma in eyes that have lost foveal vision.[18]

This paper also highlights the lack of knowledge available regarding why and how atrophy spreads over time. From their histopathological cases, the authors propose that there is preferential shunting of choroidal blood through neovascular vessels, leading to relative ischaemia of the surrounding area, with subsequent RPE atrophy. However, as the external border of the atrophy becomes more remote from the CNV scar, this mechanism would no longer be operant; further spread would then have to be explained by another mechanism. In GA associated with AMD without evidence of CNV, atrophy of the RPE leads to loss of the overlying photoreceptors and of the underlying choriocapillaris. It is still unclear whether there is a vascular component that antedates the development of atrophy itself, though delayed choroidal perfusion has been seen in eyes that went on to develop GA.[19] It is presumed that the RPE surrounding the atrophic region is stressed and laden with lipofuscin and is thus susceptible to atrophy, which leads to progressive enlargement of the atrophic region. Whether this is the mechanism in the instance of expansion of atrophy around scars is not known. The authors point out that in this expansion of atrophy surrounding scars, one does not see a hyperpigmented rim surrounding the atrophy, unlike many cases with GA where this appearance is attributed to hyperpigmentation and possibly

migration of RPE. It appears, however, that, like GA, the atrophy surrounding the scars does not progress indefinitely, and the factors in the more peripheral retina that make it more resistant to the atrophic process in the cases discussed here, and in GA in general, remain to be clarified.

Attention is just now beginning to focus on possible treatments to slow the progression of GA over time. The AREDS study had an insufficient number of patients with GA to show a statistically significant outcome related to the study medication.[20] Since GA is a degenerative disorder, a progression which continues chronically over time, it is likely that medication will have to be supplied on a regular basis, whether systemically, periocularly, or intraocularly. It is possible that the ultimate treatment for CNV will include both antiangiogenic agents to address the neovascular process and trophic factors to promote RPE survival and limit progressive atrophy.

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Retinal tumours

Vasoproliferative retinal tumour

B Damato

Brachytherapy requires further evaluation

Vasoproliferative retinal tumour is an enigmatic disease, characterised by one or more retinal nodules, which are usually located preequatorially and inferotemporally, and which cause retinal exudates, macular oedema, and epiretinal membranes. Numerous single case reports and several case series have been published, with the disease described using a variety of terms.[1–4]

The tumour in question consists mostly of glial cells interlaced with a fine capillary network and dilated, hyalinised blood vessels, some of which are occluded.[5–7] Exudates, macrophages, and foreign body giant cells are also present. The histology does not indicate a ''vasoproliferative'' tumour. The term ''reactionary retinal glioangiosis'' has been proposed.[5]

Approximately 75% of cases are idiopathic and 25% are secondary to other ocular diseases, such as retinitis pigmentosa, uveitis, retinal detachment, congenital toxoplasmosis, and Coats' disease.[3 8] Multiple lesions occur in about 6% of patients without predisposing disease and in 41% of patients with pre-existing ocular disease.[3] Multiple lesions can be bilateral, even in the absence of any apparent underlying ocular disease, especially in females.[3] Bilateral vasoproliferative tumours have been reported in a pair of monozygotic twins.[9] There is no sex preponderance. The condition can present at any age but is usually detected between the ages of 40 years and 60 years. A rare, diffuse variety of vasoproliferative tumour exists, which is relatively aggressive and which tends to occur in young females (mean age 19 years).[3]

Patients tend to present with visual loss, floaters, and/or photopsia. On ophthalmoscopy, the tumour has the appearance of a yellow or pink, intraretinal mass associated with adjacent hard exudates and occasionally retinal and vitreous haemorrhages. The hard exudates tend to extend posteriorly, eventually involving the fovea. There may also be macular oedema and exudative retinal detachment, which can become total. In advanced stages, there can be neovascular glaucoma. Epiretinal membranes may also develop, which can cause retinal distortion. The natural course of this disease varies from patient to patient, progressing slowly or not at all in some but causing severe ocular complications in others.

Fluorescein angiography shows a rich capillary network and/or telangiectatic blood vessels within the tumour. These leak profusely so that the entire lesion is hyperfluorescent in the late stages of the angiogram. On ultrasonography, vasoproliferative tumours vary in size from 1.0 mm to more than 5 mm, averaging about 3 mm. The internal acoustic reflectivity varies from one tumour to another and can be low, medium, or high. Tumour biopsy may be needed in some patients.