

Commentary

Submacular surgery for choroidal neovascularisation

The leading cause of irreversible blindness in the Western world after the age of 55 is age-related macular degeneration (ARMD). We have no effective intervention, either medical or surgical, for the most common variant of this disease – the non-exudative (dry) form. Although many would claim laser photocoagulation as an effective therapy for the exudative (wet) form of ARMD, it is at best a 'poor' therapy.

The shortcomings of laser treatment relate to the inexorable progression of the disease. Most subretinal neovascular complexes in ARMD originate beneath the fovea so that laser treatment is associated with a permanent loss of foveal vision.¹ Even when the neovascular complex is juxtafoveal or extrafoveal in location and laser treatment of the membrane is performed by retinal specialists, the rate of subsequent persistence or recurrence of the neovascular membrane is disappointingly high. In the Macular Photocoagulation Study 79% of eyes with ARMD with juxtafoveal neovascular complexes treated with laser photocoagulation resulted in persistence and/or recurrence of neovascularisation by 5 years; with a slight improvement to 57% for extrafoveal neovascular complexes.² Although laser photocoagulation remains a therapeutic alternative for this complication of ARMD it is suboptimal.

It is with this background that surgical intervention for subfoveal neovascularisation was investigated. Submacular surgery, in which the objective is to remove the neovascular complex from beneath the fovea without irreversible damage to the overlying neurosensory retina or the underlying Bruch's membrane, proved to be successful in restoration of foveal vision in about 45% of eyes with the presumed ocular histoplasmosis syndrome (POHS) – a recovery rate superior to the natural history of the disease. When a similar approach was used for subfoveal neovascularisation in ARMD visual results were disappointing with less than a 10% recovery of central vision – although there appeared to be a stabilisation of vision which would be superior to both the natural history of the disease as well as subfoveal laser photocoagulation.^{3 4}

Why is there a difference in the results with POHS and ARMD? Firstly, many of the eyes with POHS have residual retinal pigment epithelium (RPE) beneath the fovea after removal of the neovascular complex, probably a consequence of the membrane lying between the RPE and neurosensory retina. In contrast, the neovascular complex in ARMD is intimately associated with the underlying RPE resulting in its consistent removal at the time of surgery. Without subfoveal RPE there will not be recovery of central vision. Secondly, some of the eyes with POHS have RPE removed at the time of surgical extirpation of the neovascular complex but presumably have subsequent regeneration of the subfoveal RPE from adjacent cells.

These eyes exhibit recovery of foveal vision with fixation on an area of neurosensory retina beneath which there is no pigmented RPE. Presumably adjacent RPE has replicated, at which time it is non-pigmented, and migrated across an intact Bruch's membrane to re-establish a supportive relation with the overlying photoreceptors. This capability of RPE has recently been demonstrated in the non-human primate and pig.^{5 6} In eyes with ARMD, in patients who are many years older than in POHS, either senescent RPE and/or a damaged Bruch's membrane does not result in the repopulation of the denuded area of RPE created at the time of surgery. If RPE were able to repopulate this area foveal vision might recover in a substantial number of eyes.

How can we repopulate these denuded areas of RPE in ARMD which are created at the time of submacular surgery? Two approaches are currently being explored: (1) the stimulation of adjacent senescent RPE cells to divide and spread by the application of various growth factors at the time of surgery; (2) RPE transplantation with sheets of RPE cells harvested from younger donors.⁷ Although the latter approach involves the transplantation of tissue into a presumed immunologically privileged site the use of foreign (that is, allogeneic) RPE cells will undoubtedly require immune suppression of the recipient, either systemically or locally, to be successful.

The advent of submacular surgery for choroidal neovascularisation has opened new avenues for the potential treatment of retinal diseases for which there is currently no effective intervention. This new era will probably see the use of pharmacological agents, retinal transplantation, and gene therapy to achieve therapeutic success.

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