SCIENTIFIC REPORT

Macular relocation after photodynamic therapy for recurrent choroidal neovascular membrane: visual results and histopathological findings

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Methods: Histopathological evaluation of the choroidal neovascular membrane (CNV) specimen including immunohistochemical assessment. Results: Microscopy revealed one CNV area that was richly vascular with attached retinal pigment epithelial cell monolayer and another area that was made up of densely collagenous avascular tissue with adherent fragments of Bruch’s membrane and glial elements. Conclusion: The findings suggest that the PDT treated part of the CNV may have been adherent to the neuroretina and may have contributed to the formation of the macular hole. Caution is advised when considering MRS for CNV previously treated PDT.

We considered that photodynamic therapy (PDT)\(^1\) and Macular Relocation Surgery (MRS)\(^2\) not to be mutually exclusive treatments and that in some patients it might be feasible and worthwhile to undertake MRS when PDT has failed.

PATIENT AND METHODS

An 81 years old male patient with bilateral age related macular degeneration (AMD) and a predominantly classic subfoveal choroidal neovascular membrane (CNV) underwent PDT with verteporfin (Visudyne, Novartis Ophthalmics, Duluth, GA, USA) to the right eye according to published treatment guidelines.\(^3\) This eye subsequently developed a predominantly classic subfoveal CNV recurrence (Fig 1A). The patient declined re-treatment with PDT and sought macular relocation surgery. Following counselling, the patient was offered the surgery. Immediate preoperative vision was 20/80 (54 letters at 1 metre on the logMAR chart as measured by TAP study protocol refraction and by accredited optometrist).\(^4\)

The surgery consisted of phacoemulsification, intraocular lens implant, vitrectomy, 360° retinotomy, excision of the choroidal neovascularisation-retinal pigment epithelium (RPE) complex, relocation of the macula superiorly, and the injection of internal tamponade agent (1200 centistokes silicone oil). A 2 mm diameter fragment of subretinal tissue specimen was processed into 10% neutral buffered formalin, dehydrated in ethanol and embedded in paraffin wax. Histopathological evaluation of the specimen revealed that it consisted chiefly of fibrous tissue (Fig 1B). The fibrous tissue could be divided into two distinct parts. In the central thicker part of the specimen there was dense collagen but no blood vessels. The pigment cell layer was fragmented over this part and strips of Bruch's membrane-like material were attached to the membrane. In the peripheral part of the specimen, there were numerous vessels within the fibrous element, which was covered by a pigment cell layer (Fig 1B inset).

Immunohistochemistry confirmed that, in both regions, the fibrous tissue contained fibroblastic RPE cells (cytokeratin positive) (Fig 1C). Staining with the glial marker glial fibrillary acidic protein (GFAP) revealed the presence of glial elements on the surface of the densely collagenous, avascular area of the specimen (Fig 1C inset). Remnants of photoreceptor outer segments were found at several locations around the surface of the specimen.

There was subjective improvement in vision in the early postoperative period with the patient reporting diminution of distortion and clearing of the central scotoma. A repeat protocol refraction at 18 days showed that the vision was 20/132 (44 letters at 1 metre on the logMAR chart).

Eighty four days after the macular relocation surgery, the patient underwent removal of the silicone oil and counter-rotation muscle surgery which consisted on transposition of the superior and inferior oblique muscles. An epiretinal membrane (ERM) overlying the macula was removed and processed for histopathology as described above. The specimen consisted of folded inner limiting lamina type material with attached fibrocellular tissue on the vitreous side. Many of the cells were vacuolated, consistent with the histology of proliferative vitreoretinopathy that had arisen in the presence of silicone oil tamponade, but no neuroretinal fragments were detected (Fig 1D).\(^5\) No macular hole was identified at the time of surgery and no further tamponade was used.

Fourteen days later the patient presented with a retinal detachment secondary to a macular hole measuring approximately 380 µm in maximum diameter. No other retinal breaks were found. The edge of the 360 degree retinotomy was secured by previously applied laser retinopexy. There were no focal epiretinal membranes or other signs of peripheral vascular resistance. Even so, because of the previous epimacular membrane formation, we thought it was appropriate to use a prolonged tamponade to reattach the retina. Further surgery therefore involved a fluid air exchange, the injection of 1200 centistokes silicone oil but without peeling of the epiretinal membranes (Fig 1E).

Thirty four days after this third surgery the retina remained attached and the best corrected vision under silicone oil was 20/126 (45 letters at 1 metre). According to the patient the peripheral vision was restored and there was a small central scotoma.

DISCUSSION

It is relatively rare to obtain histology of CNV treated after PDT. Ghazi et al\(^6\) and Schnurrbusch et al\(^7\) reported the histological findings in surgically excised classic CNV treated with PDT. Ghazi et al studied one specimen by electron microscopy. The authors concluded that PDT causes endothelial cell...
damage, thrombus formation, and vascular occlusion. Schnurrbusch et al studied two recurrent CNV. The authors concluded that the evidence of fluorescein leakage from the CNV and enlargement of the neovascular complex following PDT could be related to new vessel growth and recanalisation of occluded vessels. RPE disturbances were thought to be related to the original pathology or as a result of PDT. Our specimen appeared to lack vessels where the RPE cell layer was fragmented but was vascular where the RPE cell layer was intact. These two regions may correspond to the original (PDT treated) CNV and its recurrence respectively. Bynoe et al have described the non-even distribution of blood vessels and the presence of large areas of avascular elements. 7

We considered the possible causes of the macular hole: it might have occurred as a complication of MRS or as a consequence of ERM peel or it might be related in some way to the previous PDT. The macula in cases of AMD undergoing MRS is often affected by chronic cystoid oedema and exudative retinal detachment. When subjected to the infusion hydrostatic pressure during the induction of the retinal detachment, a macular hole can develop. Fujiy et al reported a 7.8% incidence of macular hole formation as a complication of limited macular translocation in a series of 153 eyes. In this patient, a macular hole was not observed following the MRS. Furthermore, we were not aware that we caused a hole during the ERM peel procedure. Although the ERM specimen did not show any evidence of neuroretinal tissue attached to it, we cannot exclude the possibility that we did cause a tear in the macula during peeling.

We speculate that PDT may have a role in modulating a wound healing-type response at the site of the CNV (thus increasing the chances of a CNV neuroretinal adhesion). PDT has been shown to cause vacuolisation of the cytoplasm of the RPE and its separation from the underlying Bruch’s membrane. Such physical damage could induce RPE cell-mediated repair. It is also conceivable that PDT could induce a glial cell-mediated response. If this was the case, it would explain the presence of glial cells on the CNV. It is interesting that the glial elements were found on the surface of the avascular component of our specimen, consistent with our interpretation that the neuroretina was adherent here.

The notion that one can perform MRS after PDT is dependent on the fact that the injury with the laser is selective and confined to the CNV and that the neuroretina remains intact. If the retina was mechanically weakened in some way by repeated surgery, PDT, and retinal detachment, then pucker peeling might be less feasible. Based on the experience of this case, we would advise caution when considering epiretinal membrane peeling in this situation.

None of the authors have a proprietary interest.

**REFERENCES**


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