Retinal pigment epithelial atrophy following indocyanine green dye-assisted surgery for serous macular detachment

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To report subretinal migration of indocyanine green dye (ICG) and subsequent retinal pigment epithelial (RPE) atrophy during macular surgery for serous macular detachment. A 65-year-old woman presented with residual epiretinal membrane and serous detachment of the macula following vitreoretinal surgery for epiretinal membrane. She underwent resurgery with ICG-assisted internal limiting membrane peeling and intraocular tamponade. Intraoperatively a large area of subretinal ICG was seen with subsequent RPE mottling and atrophy of the macula in the area involved during follow-up. This case demonstrates that subretinal migration of ICG is possible and can be toxic to RPE.

Key words: Indocyanine green, macular hole, retinal pigment epithelial atrophy, serous macular detachment

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Indocyanine green (ICG) dye has contributed immensely to the understanding and imaging of choroidal pathology. Its use has also extended to macular hole and epiretinal membrane surgery. It has been shown that internal limiting membrane (ILM) peeling in macular hole improves surgical outcome. Indocyanine green has also been implicated in causing potential toxicity to the retinal pigment epithelium (RPE) in definite doses and osmolality concentrations. There is evidence to suggest that ICG can cause adverse functional changes in the RPE and glial cells following macular hole surgery. We report a case of inadvertent subretinal migration of ICG dye during surgery for serous macular detachment secondary to epiretinal membrane surgery.

Case Report

A 65-year-old woman presented to us five months after epiretinal membrane surgery, with a complaint of decreased vision in her left eye. Her past history suggests that she underwent uneventful cataract surgery with intraocular lens implantation in the left eye following which her visual acuity (VA) was 20/400. She was diagnosed to have vitreomacular traction with neurosensory detachment which was confirmed on optical coherence tomography (OCT). Based on the diagnosis, she underwent pars plana vitrectomy, epiretinal membrane peeling and fluid gas exchange in the left eye one month later. Four weeks following surgery, her VA was 20/200 in the left eye.

On examination, the best corrected visual acuity (BCVA) was 20/20 in the right eye and 20/160 in the left eye. Anterior segment examination was within normal limits. Intraocular pressure was 12 and 14 mm Hg in the right and left eye respectively. Fundus examination of the right eye was unremarkable. The left eye showed serous elevation of the macular area with cystoid changes and a thin foveal roof. Residual epiretinal membrane...
was also seen [Figure 1A]. Optical coherence tomography of the left eye confirmed the findings [Figure 2]. There was no evidence of a macular hole. Retinal vasculatures were within normal limits. Fundus fluorescein angiography (FA) showed neither leakage nor any evidence of choroidal pathology. She was advised ICG-assisted ILM peeling with silicon oil injection in left eye. The reason for ILM peeling was serous detachment persisting for five months following surgery, raising the possibility of a missed small macular hole.

Intraoperatively, 0.5% ICG was injected in the vitreous cavity using a double cannula and after a 30-sec gap, the ICG was aspirated. Though an obvious retinal hole or tear was not seen in the macula and other retinal area, we noted subretinal presence of ICG during aspiration. Internal limiting membrane peeling was done up to the arcades. The subretinal presence of ICG was noted prominently after removal of the ILM. An attempt was not made to remove the ICG as there was no gross evidence of hole and ICG binds to RPE immediately. Fluid air exchange was performed and the macula was flat following which silicone oil was injected. On postoperative Day 1, BCVA was counting fingers (CF) at 1/2 meter in the left eye and fundus examination showed subretinal ICG in the superior half with a flat macula [Figure 1B]. At one week, her BCVA was CF at 1/2 meter with an extensive area of RPE alteration in the macula [Figure 1C]. Optical coherence tomography of left eye showed foveal thinning (83 micron) with inferior shallow neurosensory elevation [Figure 3]. After three months, her BCVA was counting fingers at 1.5 meters in the left eye. Fundus examination showed RPE atrophy with pigment stippling in the superior half of the macula within the arcades [Figure 1D]. She underwent silicone oil removal in the left eye. Four months after silicone oil removal, her BCVA was CF 2.5 meters in the left eye which was maintained till 12 months of follow-up. Optical coherence tomography at this time showed foveal thickness of 80 microns.

**Discussion**

This case demonstrates that ICG can be toxic to the RPE. The toxicity resulted in extensive area of RPE mottling and macular atrophy seen on OCT [Figures 1D and 3]. The unique features of this case include the lack of evidence of a macular hole along with subretinal migration of ICG dye and RPE toxicity. Uemoto et al.,9 reported a chart review of 31 patients who underwent macular hole surgery with 0.5% ICG ILM staining. Of these, three cases developed RPE changes with foveal atrophy (74, 80 and 60 microns) and markedly worse postoperative VA. This may be possible in an evident macular hole where RPE can have direct contact with the dye, unlike in the present case. Similarly, a single case report of unintentional introduction of subretinal ICG also showed RPE atrophy and visual field defect in the area of contact.8

Animal studies in rabbits have shown that injection of 0.1 ml of ICG (5 mg/ml) into the vitreous cavity of non-vitrectomized eyes causes reversible changes as seen in electroretinograms and in the cellular ultrastructures.10 In vitrectomized eyes, no abnormalities were observed in the RPE and photoreceptors when ICG was injected on the retinal surface. However, a
subretinal injection showed angiographic findings of RPE window defects while histology exhibited pyknosis of the outer nuclear layer and damage to photoreceptor inner segments, photoreceptor outer segments and RPE. This suggests that ICG is toxic when directly in contact, as in our case, with RPE and the outer retina [Figure 1B].

Author uses a double-bore cannula to inject the ICG which allows gradual injection with equal egression of fluid through the other bore. Forceful injection as can occur with single-bore cannula would create a visible macular hole. It may be speculated that the presence of a micro-macular hole (centric or eccentric) may have caused this situation. It may have also been possible that the preoperative presence of a microhole on the thin fovea might have been missed on OCT.

Injection of the dye in the extrafoveal zone, use of non-toxic agents to coat the macular hole, low concentration (0.1%) of ICG dye or even use of other dyes like trypan blue or infracyanine green may reduce adverse events during macular surgery for primarily macular hole.

Hence, subretinal migration of ICG [Figure 1B] is possible in macular surgeries, even where there is no direct evidence of a macular hole surgery.

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