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Case Series

Brilliant Blue Dye Phototoxicity Accentuated by Intraoperative Oxygen Supplementation

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Abstract

Aim: To report four cases of outer retinal macular phototoxicity following uncomplicated 25-gauge vitrectomy with internal limiting membrane (ILM) peeling, and to investigate the potential pathological role of high intraoperative oxygen levels and choriocapillary loss in this injury.

Methods: A retrospective case series was conducted on four patients (three with idiopathic macular holes and one with an epiretinal membrane) who underwent uncomplicated 25-gauge vitrectomy. Standard surgical safety protocols were strictly followed, including routine operating time, controlled dye contact time, and safe endoilluminator placement. Brilliant blue G (0.05%) was used for ILM staining, and a 20% SF6 gas endotamponade was injected. All patients were intraoperatively exposed to 100% oxygen for 25–30 minutes during the procedure for respiratory insufficiency.

Results: Despite standard intraoperative precautions, all four eyes developed macular phototoxicity characterized by macular degeneration that predominantly affected the outer retina. In one representative case, the retinal degeneration was accompanied by a noticeable loss of the choriocapillaris.

Conclusion: Macular phototoxicity involving the outer retina can occur after vitrectomy even when standard endoillumination and dye precautions are maintained. Intraoperative hyperoxia (100% oxygen delivery) may act as a critical synergistic risk factor that accelerates phototoxic damage. Additionally, choriocapillary loss may play a key role in the underlying pathological process of this unusual complication.

Keywords: Internal Limiting Membrane (ILM); Pigmentation

Introduction

Advances in vitreoretinal surgical techniques and the use of vital dyes have improved the success of macular hole surgery [1]. However the use of dyes especially ICG have been reported to have detrimental effects on the RPE and even choroid [2]. Though brilliant blue is believed to be a safer dye [3], cases of macular toxicity following brilliant blue G-assisted macular hole surgery has been demonstrated in few reports [4,5]. Whether these cases represent dye based toxicity or photo toxicity induced by light

source has not been ascertained clearly and it appears that they could both be contributory. Though factors like proximity of light source to the retina and increased duration of surgery have been implicated there could still be other mechanisms at play. Here we report 4 cases of brilliant blue dye phototoxicity following macular surgery possibly enhanced by intraoperative oxygen supplementation.

Case 1

A 67 years old bilaterally pseudophakic lady with left eye full thickness macular hole (Vision CF2m) of basal diameter 1055 micron underwent a standard uncomplicated 25 G pars plana vitrectomy with PVD induction, brilliant blue staining (Ocublue Plus 0.05%w/v, Aurolab) with contact time of 1 minute under saline and 20% SF6 injection with 1 week of prone positioning. The duration of surgery was 90 minutes. During surgery she had difficulty breathing with fall in SPO2 and needed 100% oxygen by nasal prongs for a period of 25 minutes. Post operatively at 3 weeks the macular hole was closed, but fundus showed pigmentary mottling temporal and inferior to fovea with characteristic OCT (Figure 1B) and FAF findings (Figure 1C). No significant progression of the changes were noted at 6 months (Figure 1D) and the final BCVA remained at CF 2m.

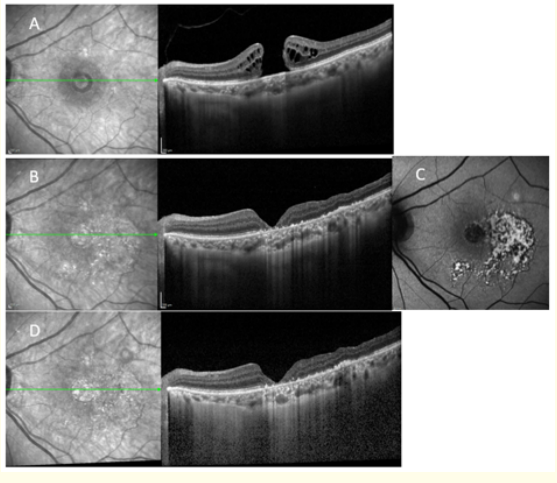


Figure 1: Case 1-A. Preop SDOCT shows a large full thickness macular hole with surrounding intraretinal cysts. B. Two weeks postop SD-OCT showing closed hole with thinning of outer nuclear layer, discontinuity of the external limiting membrane, ellipsoid zone and RPE focal clumps corresponding to the parafoveal area of altered AF mottling noted on blue peak FAF image (C). Also notice the choroidal hypertransmission in this area. The SD OCT changes remain status quo at 6 months with no increase demonstrable (D).

Case 2

A 74 years old lady with a history of peripheral iridectomy in right eye and pseudophakia both eyes presented with left eye full thickness macular hole of 973 micron basal diameter and mild epiretinal membrane. She underwent a standard uncomplicated 25 G pars plana vitrectomy with brilliant blue staining (Ocublue Plus 0.05%w/v, Aurolab) and 20% SF6 injection with 1 week of prone positioning. The duration of surgery was 75 minutes. During surgery she complained of breathlessness with significant fall in SPO2 and needed 100% oxygen with nasal prongs for a period of 30 minutes. 3 weeks postoperatively Type 1 closure of macular hole was noted with pigmentary alteration superior and temporal to the fovea corresponding to outer retinal atrophy on SDOCT (Figure 2B) and abnormal FAF on OCT (Figure 2C). at 6 months, no progressive changes were noted (Figure 2D) and the final BCVA was 6/36.

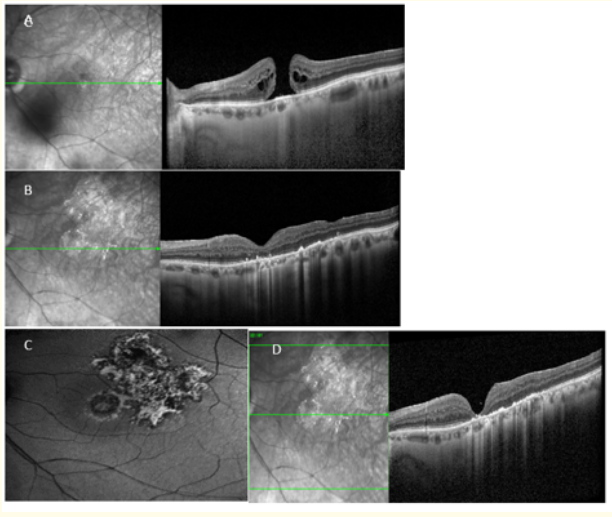


Figure 2: Case 2-A. Preop SDOCT shows a full thickness macular hole with surrounding intraretinal cysts. B. Four weeks postop SD-OCT showing closed hole with discontinuity of the external limiting membrane, ellipsoid zone and RPE focal clumps corresponding to the parafoveal area of altered AF mottling noted on blue peak FAF image (C). Also notice the hypertransmission in this area. The SD OCT changes remain status quo at 6 months with more evident central atrophy (D).

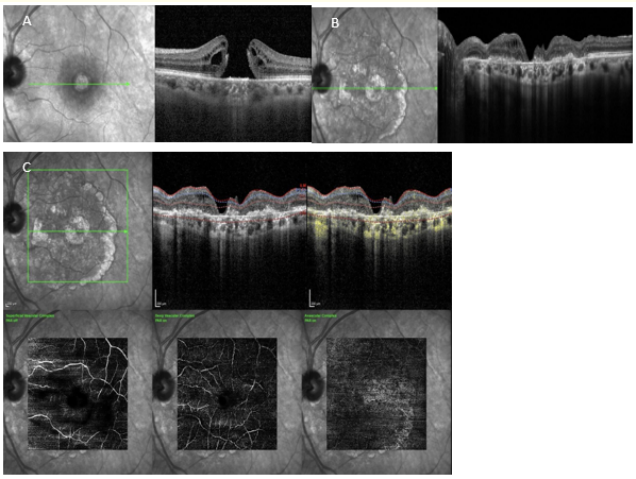
Case 3

A 77 years old lady with both eye pseudophakia and mild nonproliferative diabetic retinopathy and full thickness macular hole in left eye of basal diameter 1296 microns since 6 months. She had a history of surgery for vitreomacular traction in the left eye. Best corrected visual acuity was 6/6 and 6/24p in the right eye

and left eye respectively. She underwent surgery in the left eye with 25G vitrectomy with internal limiting membrane staining with brilliant blue dye (Ocublue Plus 0.05%w/v, Aurolab) followed by peeling and tucking of the flap. Internal tamponade done with 14% C3F8 gas. During the surgery, the patient felt difficulty in breathing and SPO2 was falling down so 100% oxygen supplementation was given for 20 minutes. Total time taken in the procedure was 60 minutes. In the postoperative period, macular hole was closed but RPE degenerations were seen in the macular area. On followup visits, OCT showed a large area of RPE atrophy and ellipsoid zone disruption justifying the poor visual outcome. The final visual outcome in the left eye was CF1m and phototoxic scar was seen in the involved area.

Case 4

A 63 years old gentleman with pseudophakia both eyes presented with right eye grade 3 epiretinal membrane (Figure 4A, 4B). He underwent a standard uncomplicated 25 G pars plana vitrectomy with brilliant blue staining (Ocublue Plus 0.05%w/v, Aurolab) and 20% SF6 injection. The duration of surgery was 55 minutes. During surgery was given 100% oxygen for 20 minutes due to breathlessness with significant fall in SPO2. 4 weeks postoperatively pigmentary alteration temporal to the fovea corresponding to outer retinal atrophy on SDOCT (Figure 4C). OCTA to the corresponding area showed no flow signal (Figure 4D) and abnormal FAF (Figure 4E). After 18 months, chronic pigmented scar was seen (Figure 4F) and outer retinal tubulations and RPE atrophy were noted with normal fovea on OCT (Figure 4G). The final BCVA was 6/6.



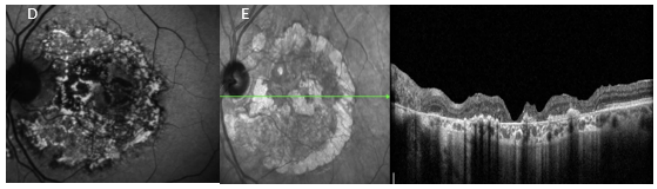


Figure 3: Case 3- A. Preop SD-OCT shows a full thickness macular hole with intraretinal cysts. B. Postop 6 months SD-OCT showing type 2 closure of the hole with discontinuity of the external limiting membrane, ellipsoid zone and RPE thinning with focal clumps, OCTA showing lack of flow signals in involved retinal area (C) that also corresponds to the area of altered AF mottling noted on blue peak FAF image (D). The SD OCT changes remain status quo at 1 year (E) with prominence of RPE clumps and increased choroidal hypertransmission.

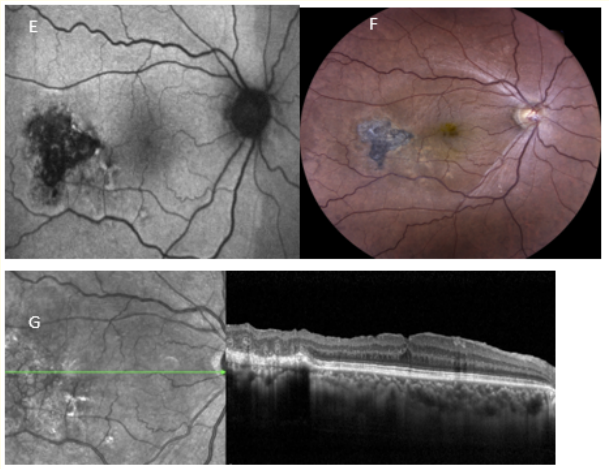


Figure 4: Case 4- (A) Fundus picture and Preop SD-OCT shows grade 3 ERM (B). Postop 4 weeks SD-OCT showing disruption of EZ and RPE layer with focal clump (C), OCTA showing lack of flow signals in involved retinal area (D) that also corresponds to the area of altered AF mottling noted on blue peak FAF image (E). The fundus picture (F) and SD OCT changes remain status quo at 1.5 year (G) with prominence of RPE clumps with black shadowing and outer retinal tubulations in the involved area.

Discussion

Retinal damage following MH and ERM surgery have been related to increased surgical time, vital dye toxicity and endoilluminator

blue light phototoxicity [5-7]. The technique of peeling in all cases in this series was a pinch and peel technique with ILM forceps and initiated in the superotemporal quadrant in case 1,3 and inferotemporal to fovea in case 2,4 and was done by the same surgeon. All the cases needed restaining with an additional contact time of 1 minute. Xenon endoilluminator light pipe was used in all cases with an intensity of 75% maintained approximately 5-10 mm away from the retinal surface and the total operative time was not significantly longer. In spite of the standard precautions macular toxicity was noticed in all the eyes.

Vital dyes possibly penetrate the retina and produce phototoxic free radicals due to changes in emission spectrum after absorption of Xenon light causing damage to the outer retina. However under uniform conditions of staining and light exposure it is difficult to explain why some eyes manifest toxicity and others don't. Lesions related to light toxicity appear away from the fovea with relative sparing of the fovea due to protection aided by the concentrated xanthophylls as was the finding in all our cases. During our analysis of intraoperative events in these patients compared to other cases done during the same period we realised that intraoperative oxygenation was a unique event in all these cases. All patients received 100% intraoperative oxygen for a period of 25-30 minutes during the procedure.

The role of intraoperative oxygenation on macular toxicity has been studied in animal eyes and oxygenation is known to potentiate the light damage demonstrable both clinically and histologically. Lesions produced with 99% FiO2 were up to 7 times larger than the corresponding lesions formed with 21 % FiO2 [8]. Ham et al reported that lesions produced under conditions of high O2 had evidence of severe damage to the RPE and pigmentation [9]. It has been suggested that the harmful effects of oxygen may be mediated through the production of reactive species including singlet oxygen and free radicals which may be strongly dependent on the concentration of oxygen [9,10]. Choriocapillaries being a rich source of oxygen and responsible for the outer retinal perfusion may have had higher concentrations during 100% oxygen therapy thereby potentiating the light based or dye based toxic manifestations even during standard duration of exposure in our cases.

To the best of our knowledge, cumulative BBG and xenon light toxicity with oxygen therapy has not been reported in literature in human eyes and needs a more elaborate analysis. Routine use of oxygen for intraocular surgery under local anaesthesia is the practice in most surgical set ups. Though rare, the possibility of dye toxicity under oxygenation has to be kept in mind and unnecessary use of oxygen should be avoided.

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