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Atrophic changes in the retinal pigment epithelium after macular hole surgery using an indocyanine green dye

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ABSTRACT

Since indocyanine green (ICG) dye was introduced for macular hole (MH) surgery to facilitate visualization of the internal limiting membrane (ILM), successful anatomic closure of MHs has been achieved in almost all cases. However, when only using ICG dye is used atrophic changes of the retinal pigment epithelium (RPE) sometimes occur in the area of the previous MH. There is a possibility that these atrophic changes might be due to the toxicity of the ICG dye. Here we report 2 cases with such atrophic RPE changes after surgery using ICG dye. Moreover, for the first time, we observed the autofluorescence of ICG over time and found that ICG remained in the macular area longer than expected. The similarity between the present 2 cases was that their preoperative visual acuities were less than 20/200. These findings suggest that the RPE cells might be exposed to the ICG dye for a long time and be more affected by the toxicity of ICG the previously thought. Since RPE cells in cases of poor visual acuities become fragile, they might be more susceptive to the toxicity of ICG. We conclude that sufficient care should be taken when ICG is used for MH cases with poor visual acuities. *Ryukyu Med. J., 22(1,2) 29～31, 2003*

Key words: macular hole surgery, indocyanine green dye, retinal pigment epithelium, atrophic change.

INTRODUCTION

Retinal internal limiting membrane (ILM) peeling has previously been described as a useful adjunct treatment for patients with macular hole (MH). Since introducing indocyanine green (ICG) dye use for MH surgery to facilitate visualization of the ILM[1,2], successful anatomic closure of MHs has been achieved in almost all cases. Recently, Engelbrecht and associates reported unusual atrophic changes in the retinal pigment epithelium (RPE) after using ICG dye solution in surgery[3]. We also observed 2 such cases with atrophic RPE changes following the use of ICG dye in surgery. In addition for the first time we observed remnant ICG post-surgery using autofluorescence over time in the above cases. Our findings suggest that the atrophic changes are caused by direct toxicity to the RPE cells within the MH that are exposed to long term contact with the ICG solution. This report describes our experience and calls attention to the use of ICG dye in certain cases.

REPORT OF CASES

Case 1: A 76 year-old man with bilateral full-thickness MH and deteriorated visual acuity in both eyes. His visual acuities were 20/50(RE) and 20/200 (LE). Fundus examination showed stage 3 MH in his right eye and stage 4 in his left eye according to the criteria described by Gass[4] (Fig. 1 A). We performed vitrectomy with the removal of ILM using

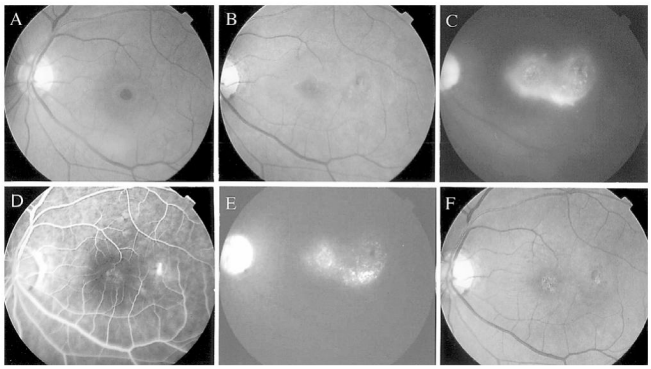

Fig. 1 Case 1. Preoperative fundus photograph (A) shows a stage 4 macular hole with surrounding fluid cuff. One month after surgery shows an anatomical closure of the macular hole and temporal small retinal breaks (B). Retina appears to be edematous and thickened around the macula and the retinal breaks. Postoperative autofluorescence image at 790 nm for ICG angiography is demonstrated in figure C. Mottled high-autofluorescein can be seen at the macula and at the small retinal break together with the nearby retina. Postoperative fluorescein angiogram shows the hyperfluorescence at the retinal hole; hyperfluorescein is seen in the macula (D). Mottled autofluorescein image can be seen at the macula and the injured retina at postoperative 6 months (E). Remarkable RPE changes with pigment clumping and depigmentation in the macula is evident (F).

ICG dye staining in both eyes. Approximately 0.3 ml of aqueous 0.5% ICG dye solution was injected into the posterior vitreous cavity over the macula and then the solution was immediately washed out. After the visualization of ILM by ICG dye staining, the ILM was peeled off and removed, followed by fluid/air exchange. The patient was then instructed to maintain a face-down position for 7 days. During the surgery on his left eye, the retina was touched by the peeling needle along the area of ILM opening. Seven days postoperative fundus examination revealed an anatomical closure of the MH with a small iatrogenic retinal hole in the superotemporal area corresponding to the injured retina during the surgery. At 4 weeks after surgery, the retina appeared thickened around the macula and around the small retinal hole (Fig. 1 B). A faint green ICG dye was also seen in the area of the thickened retina (Fig. 1 B). Autofluorescence imaging at 790 nm for ICG dye was performed with an ICG angiographic camera (TOPCON Co, Tokyo, Japan). Fundus photographs were taken under the filters placed without an intravenous injection of ICG dye.

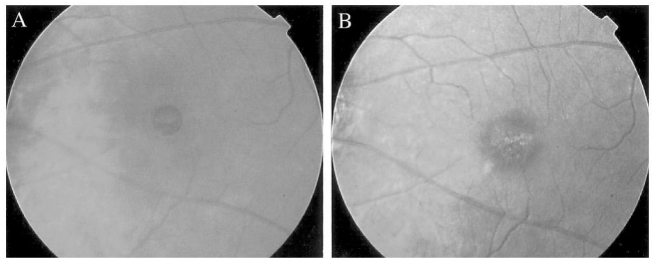

Fig. 2 Case 2. Preoperative fundus photograph (A) shows a stage 3 macular hole with surrounding fluid cuff. Fundus photograph 6 months postoperative (B) shows atrophic pigmentary changes in the area of previous macular hole and surrounding fluid cuff.

Hyperfluorescene was obserbed in the area of thickened retina around the macula 4 weeks after surgery (Fig. 1 C). Six months after surgery fluorescein angiography (FA) showed hyperfluorescence at the retinal hole where pigment epithelia were assumed damaged (Fig. 1 D). Hyperfluoresceince was also seen in the macular area during all the FA phases without any late leakage of the fluorescein dye. FA demonstrated a window defect corresponding to the area of central macula. The retinal thickness gradually decreased and a yellowish white precipitates appeared. Also a mottled hyperfluoresceince of the ICG was seen in the lesion at 6 months postoperative (Fig. 1 E). Nine months after surgery, remarkable RPE changes of pigment clumping was evident in the area where the MH previously was (Fig. 1 F). Two years after surgery the corrected visual acuity was 20/30 in the right eye but 20/200 in the left eye.

Case 2: A 77 year-old woman with a one year history of blurred vision in her left eye. She was diagnosed as having a stage 3 MH with 20/200 visual acuity (Fig. 3 A). Surgical intervention with the removal of ILM using 0.5% aqueous ICG solution was performed. The MH was closed 8 days postoperative. Six months after surgery, unusual atrophic change of retinal pigment epithelium was noted in the area when the MH previously was and surrounding cuffs (Fig. 3 B). In addition when autofluoresceince for ICG was performed with ICG angiographic camera, a mottled hyperfluoresceince pattern in the pre-existing MH was (data not shown). The postoperative best-corrected visual acuity improved transiently to 20/60 and returned to 20/200 eighteen months after surgery.

DISCUSSION

The change in the RPE as described in the present report was not observed until MH surgery was performed using ICG solution. This change was noted in only 2 eyes, out of the 31 on which surgery was performed in our department using this same method. No similar change was observed in 41 cases on which surgery was performed without using ICG. Based on similar observations by others they have suggested that the change might be induced by the toxicity of ICG[3]. In ophthalmology, ICG is used as an angiographic dye, which is intravenously injected mainly in order to examine choroidal circulation. Even if ICG is retained in the eye tissue, it disappears rapidly. The rapid disappearance of ICG is likely the reason why there are no reports of ICG toxicity to the eye. In an animal experiment, when ICG is injected into the vitreous cavity at a very high concentration, retinal degeneration occurs. At clinical concentrations, however, no retinal degeneration is considered to result[5]. It has been reported however that even at normal clinical concentrations, ICG is activated when exposed to light[6]. We observed, for the first time, the autofluorescence of ICG over time in the cases reported have, and found that ICG remained in the macular area for a longer period than expected[7]. This suggests that the RPE cells might be exposed to ICG for a long time. Thus, the RPE cells are considered more affected by the toxicity of ICG.

The similarity between the 2 cases reported have and previously reported cases is that most of their preoperative visual acuities were less than 20/200. Based on the fact that the RPE cells in the fundus of MH became fragile due to diseases in these cases with poor visual acuities, we presume that the RPE cells in such cases might be more susceptive to the toxicity of ICG.

For this reason, we conclude that sufficient care should be taken when ICG is used for MH cases with preoperative visual acuities less than 20/200.

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