ICG STAINING OF THE INNER LIMITING MEMBRANE FACILITATES ITS REMOVAL DURING SURGERY FOR MACULAR HOLES AND PUCKERS

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SAMENVATTING

Een maculair gaatje is een idiopathische aandoening gekenmerkt door een onderbreking op het niveau van de neuroretina ter hoogte van de fovea. Tangentiële tractie door de lamina limitans interna zou aan de basis liggen van het ontstaan van een maculair gaatje. Het verwijderen van de lamina limitans interna leidt in de meeste gevallen tot het sluiten van het maculair gaatje. Aangezien de lamina limitans interna echter een doorschijnende epiretinale structuur is, kan een totale verwijdering soms moeilijk zijn. Ook bij puckervorming, waarbij epiretinaal weefsel op de macula groeit en metamorfopsie veroorzaakt, kan verwijdering van de lamina limitans interna verdere visusverbetering veroorzaken.
Dit artikel beschrijft hoe de lamina limitans interna gekleurd kan worden met indocyanine groen om deze volledig te kunnen verwijderen.

ABSTRACT

Formation of a macular hole is an uncommon idiopathic disease whereby a disruption of the neural retinal layer is formed at the foveal area. It has been suggested that tangential traction of the inner limiting membrane (ILM) on the neuroretina may contribute to the formation of a macular hole. Removal of the ILM has been associated with very high closure rates in macular hole surgery. However, since the inner limiting membane is a transparent layer, it can be difficult to achieve complete removal from the underlying neural retina. Also in surgery for macular pucker formation, whereby growth of epiretinal tissue induces metamorphopsia, removal of the ILM may play a beneficial role.
This paper describes a method facilitating the removal of the inner limiting membrane by staining it with indocyanine green.

RÉSUMÉ

Le trou maculaire est une maladie idiopathique caractérisée par une interruption de la rétine neurale au niveau de la fovéa. Une traction de la membrane limitante interne (MLI) contribue probablement à la formation d'un trou maculaire. Le pelage de la MLI a été associé à la fermeture des trous maculaires. La MLI est une structure transparente, ce qui peut rendre le pelage difficile. Aussi pour la chirurgie de fibrose prémaculaire l'usage d'ICG peut aider à atteindre une vision postopératoire optimale.
Cet article montre une nouvelle méthode pour opacifier la MLI en utilisant le vert d'indocyanine et pour ainsi faciliter son pelage.

KEY-WORDS

Inner limiting membrane, macular hole, indocyanine green, staining

MOTS-CLÉS

Membrane limitante interne, trou maculaire, vert d'indocyanine, opacification

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INTRODUCTION:

Formation of a macular hole (MH) is an uncommon idiopathic disease whereby a disruption of the neural retinal layer is formed at the foveal area. Risk factors of macular hole formation are female gender and increasing age. Patients with this disease may present with blurred vision, metamorphopsia or a small central scotoma, causing reading problems. Some patients spontaneously cover the affected eye to facilitate reading. Many cases however are discovered only after incidental closure of the fellow eye or at the time of routine ophthalmologic examination. On an Amsler chart patients often describe a central scotoma surrounded by a ring of metamorphopsia.

The disease is usually unilateral, but the incidence of developing a macular hole in the fellow eye has been estimated to be 16% over 5 years in the absence of a posterior vitreous detachment. When the disease involves both eyes, reading vision can be dramatically impaired.

During ophthalmoscopy, the macular defect can be observed as a circular or slightly oval hole in the fovea, usually less than one third of a disk diameter in size. Based on ophthalmoscopic findings, four categories of macular holes have been described. Stage I MH (or impending macular hole) is observed as a small yellow spot in the fovea with a loss of the normal foveal depression, with no apparent retinal defect. Analysis of the foveal area with optical coherence tomography (OCT) usually shows the formation of a small retinal cyst (8,11,13). A stage II MH occurs when the retinal layer is partly disrupted from the retinal pigment epithelial layer, but remains partly attached to the adjacent retinal layer. OCT analysis reveals the traction on this operculum by the posterior vitreous cortex. A stage III MH is found when the retinal operculum is completely detached from the retinal pigment epithelial layer, with the posterior vitreous still attached to the retina. When the posterior vitreous cortex is detached from the retina, a stage IV MH is formed.

It has been suggested that centrifugal tangential traction or anteroposterior traction around the fovea causes the formation of a macular hole. During the past years, this theory has been substantiated by OCT findings.

It has been suggested that the inner limiting membrane (ILM) of the neuroretina may contribute to this tangential traction and removal of the ILM has been associated with very high closure rates in macular hole surgery. In this procedure, following vitreous removal, the ILM is carefully peeled off in the macular area, and the eye is filled either with an air/gas mixture (SF6 or C3F8) or silicone oil. Subsequently, in case of gas filling, the patient is instructed to remain in a face-down position for several days or even weeks. It has been shown that anatomical closure of the macular hole is correlated with increased visual acuity postoperatively (10,12).

Epiretinal membrane formation in the macular area not infrequently occurs in the population over 50 years of age. The membranes develop as a result of proliferation of cells and deposition of collagen on the retinal surface. The exact cellular origin of the epiretinal tissue is somewhat controversial. Some authors consider the Müller cells as source of the newly formed membranes, while others suggest that fibroblasts from the vascular connective tissue, epithelial cells from the ciliary body, retinal pigment epithelial cells, inflammatory cells, or retinal glial cells are the cells of origin.

In the initial stage, the ophthalmoscopic appearance is characterized by a mild sheen and hyperreflectivity in the macular area, called ″cellophane maculopathy″. In more advanced stages, increased tortuosity of the temporal arcade vessels can be observed, as well as striae and folds in the underlying neural retina. Prolonged traction from the epiretinal membranes can induce macular edema, macular cyst formation, and even small hemorrhages.

Because of its transparency, removal of the ILM is a difficult step in macular surgery, in spite of recent improvements in instrumentation and techniques such as incising the ILM to aid the peeling. Therefore, peroperative staining of the ILM with a non-toxic dye would significantly facilitate the surgery. This paper describes the use of infracyanine green (ICG) to stain the ILM for this purpose.

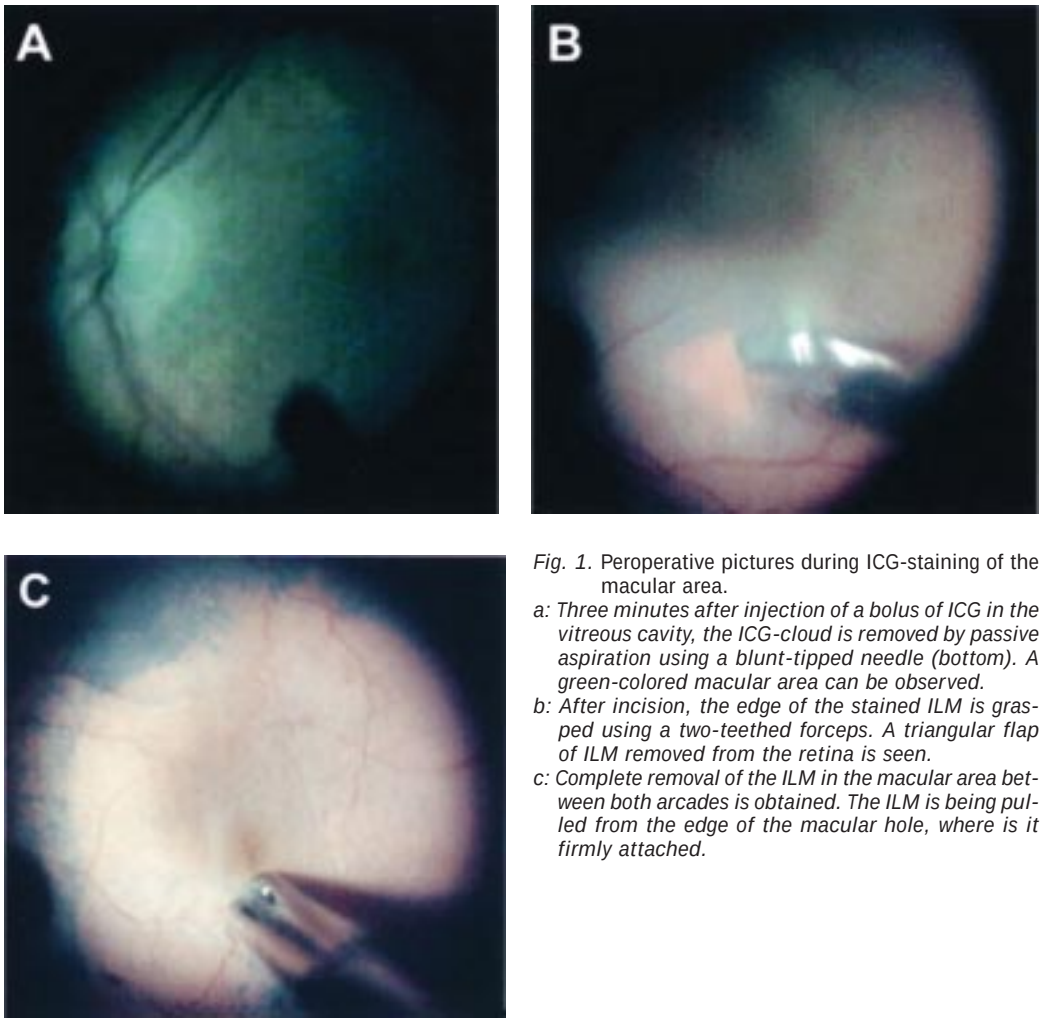

Fig. 1. Peroperative pictures during ICG-staining of the macular area.
a: Three minutes after injection of a bolus of ICG in the vitreous cavity, the ICG-cloud is removed by passive aspiration using a blunt-tipped needle (bottom). A green-colored macular area can be observed.
b: After incision, the edge of the stained ILM is grasped using a two-teethed forceps. A triangular flap of ILM removed from the retina is seen.
c: Complete removal of the ILM in the macular area between both arcades is obtained. The ILM is being pulled from the edge of the macular hole, where is it firmly attached.

MATERIALS AND METHODS

In five patients, peeling of the ILM was performed after staining with ICG. In four patients, surgery was performed because of idiopathic stage III or IV macular hole. In one patient, wrinkling of the ILM (cellophane maculopathy) was present, causing metamorphopsia.
Infracyanine green (Laboratoires SERB, Paris, France) was prepared as follows: under a laminar flow system, the 25 mg stock solution was divided into 5 mg aliquots and stored in 1.5 ml rocket tubes. At the time of surgery, 1.5ml glucose 5% was added to the aliquot ICG and shaken vigorously. The liquid is then aspirated in a 2 ml syringe, connected to a blunt-tipped needle (DORC, Zuidland, The Netherlands, catalogue #1281A) with a micropore sterilization filter (Sartorius Minisart). With the needle opening close to the retinal surface, approximately 0.1 - 0.3 ml of ICG is sprayed over the macular area, while the infusion line is closed. The instruments (light fiber and blunt-tipped needle) are kept in the eye or the sclerotomies are temporarily closed using scleral plugs, in order to minimize intraocular fluid movements. This allows the ICG dye to remain in contact with the ILM in the macular area. After 3 minutes, the infusion line is reopened and the ICG cloud is removed by passive aspiration using a blunt-tipped needle mounted on a backflush

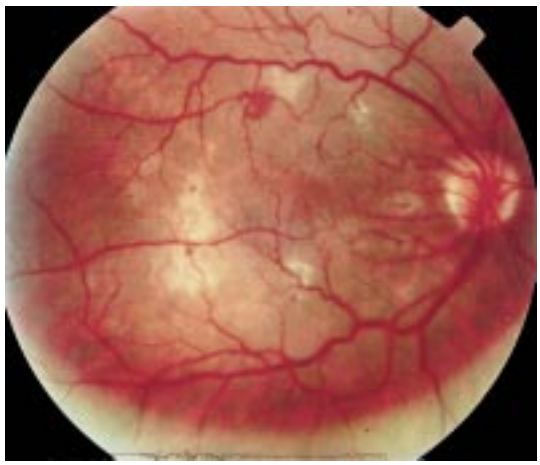

Fig 2. Fundus photograph 24 hrs after removal of the inner limiting membrane during surgery using ICG staining.

handpiece. After the removal of ICG from the vitreous cavity, a homogenous dark-green staining of the inner retinal layer can be observed (figure 1a).

The following technique is then used to remove the ILM: using a 20G sclerotomy knife (Alcon, Forth Worth, USA), the stained superficial membrane is incised close to and parallel with the retinal arcade over a distance of 2-3 disk diameters (figure 1a). A two-teethed retinal forceps is then used to grasp the edge of the incised membrane at the central side of the incision and the membrane is removed in a rhexis-like manner from the macular area (figure 1b). In all patients, a circular or oval rhexis was obtained extending from upper to lower retinal vascular arcade (figure 1c).

In one patient, the stained membrane was fixated in glutaraldehyde for electron-microscopical evaluation.

In three patients that underwent surgery for macular hole, the eye was filled with a 15% SF_6 /air mixture; the fourth eye was filled with silicone oil. In the patient with cellophane maculopathy, no air, gas or silicone oil was used.

RESULTS

In all five patients, the stained ILM had a pistachio-green color where the ICG-cloud had been in contact with the retina. No staining of the more peripheral ILM could be observed. The underlying retinal layers were not stained and contrasted clearly with the green ILM, resulting in an excellent visual control of the extent of the peeling of the ILM (figure 1).

DISCUSSION

This technique simplifies the incision, grasping and removal of the ILM compared to cases that were treated similarly, but without ICG staining. The depth of the incision could be easily controlled because a curling of the edge of the ILM appeared at the site of the incision, as is observed in capsulorhexis. Subsequently, fewer attempts were needed to grasp the ILM, reducing the chances of trauma to the underlying neuroretina and retinal pigment epithelium.

It is difficult to ensure that a complete ″rhexis″ of the ILM on the macular area is obtained when the ILM is not stained. Using this new technique, remnants of the green stained membrane indicated incomplete removal. Such remnants, some of which had a triangular aspect with their tip attached to the foveal area, could be grasped individually and removed from the retinal surface to ensure a complete ILM removal (figure 1c).

In all patients, the pistachio green staining of the ILM remained visible throughout the procedure. However, on the first day postoperatively, no remnant of the green dye could be observed ophthalmoscopically (figure 2).

In one patient with a MH, the green-stained membrane was immediately fixed in 2.5% glutaraldehyde, 0.1M phosphate buffer. After postfixation in 1% $Os0_4$ 0.1M phosphate buffer the specimen was further prepared as for routine electron microscopy.

On electron microscopy single layers of elongated Müller glia-like cells with slender bipolar cytoplasmic processes were found. The cells had an oblong nucleus with rather dense heterochromatin pattern and their cytoplasm contained numerous profiles of rough endoplasmic reticulum (R.E.R.). These Müller glia-like cells were surrounded by an amorphous layer of medium dense extracellular matrix components and a pale staining elastic lamina (figure 3).

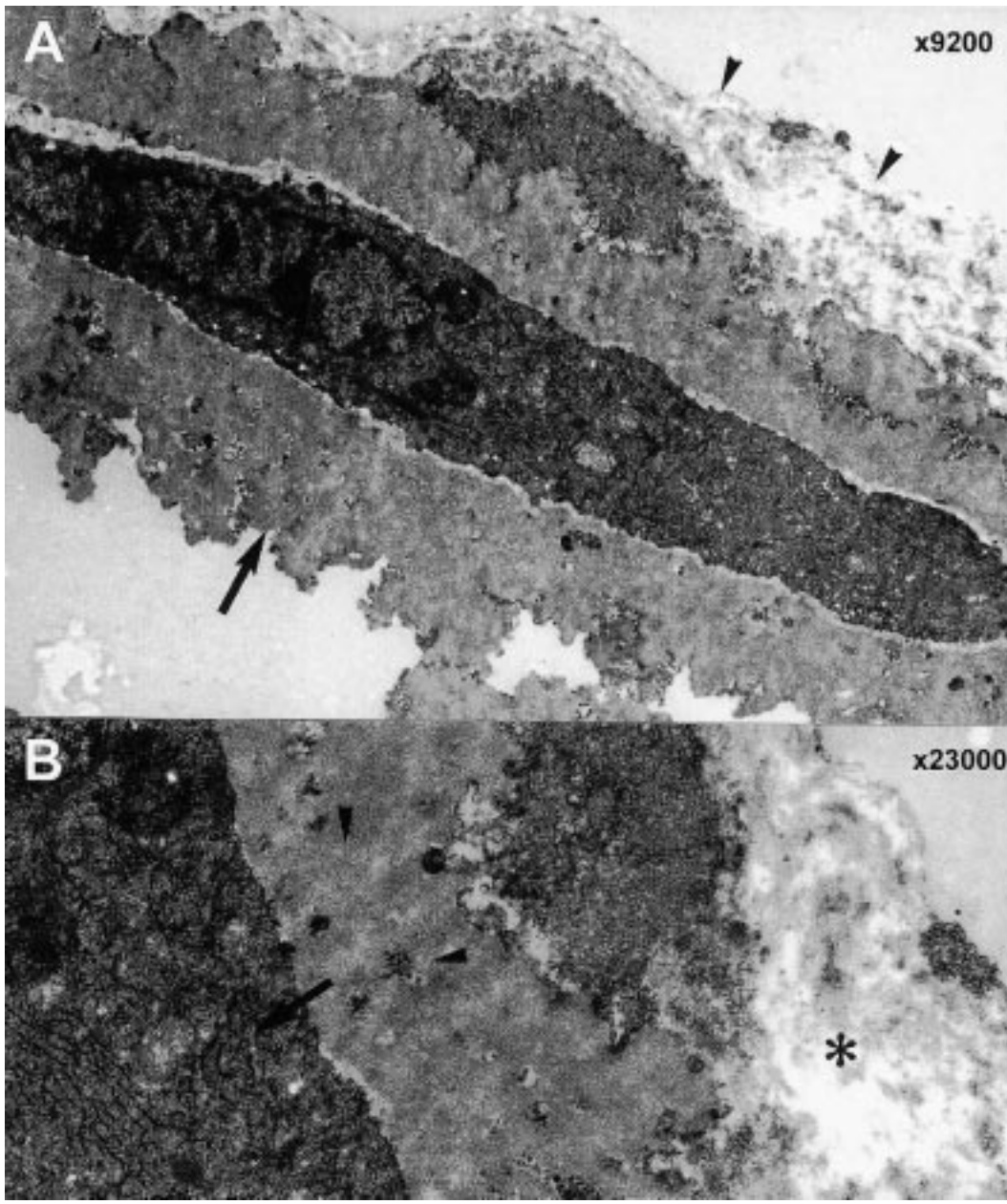

Fig. 3. Electron micrograph of inner limiting membrane.
a: An oblong Müller glia-like cell is surrounded by amorphous extracellular matrix material (arrow), and an elastic lamina (arrowhead). Magnification: x9.200
b: (Detail) Part of the cytoplasm of a Müller glia-like cell with R.E.R. cisternae (arrow); amorphous extracellular components (arrowhead); elastic lamina (asteriks). Magnification: x23.000

CONCLUSION

This pilot study in five patients shows that staining of the ILM with ICG is technically feasible and facilitates the achievement of the surgical goals in macular surgery for MH or cellophane maculopathy: a complete removal of the ILM with less trauma to the underlying neuroretina and retinal pigment epithelium. Although the staining of the ILM is visible throughout the procedure, no remnants of the dye could be seen one day postoperatively and no side effects were observed in the postoperative period.

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