

Subretinal migration of trypan blue during macular hole and epiretinal membrane peel: an observational case series. Is there a safer method?

S Ghosh, S Issa, I El Ghrably and K Stannard

Abstract

Purpose To report the inadvertent subretinal migration and effect of trypan blue (TB) during staining of the epiretinal membrane (ERM) for macular pucker, and internal limiting membrane during macular hole (MH) surgery, and to suggest alternative safe methods of injecting TB.

Methods Three cases in which TB migrated to the subretinal space were followed up on day 1, day 7, day 21, and at 3 months following the initial operation. Two of the cases were operated for MH and one patient had ERM peel. Colour fundus and optical coherence tomography (OCT) were performed on day 1 and on each subsequent visit.

Results In both cases of MH the hole was closed postoperatively. The patient with ERM had the membrane peeled successfully as documented by OCT. Clinically, all patients demonstrated chorioretinal atrophy in the area of TB migration. There was thinning of the retina as noted by OCT.

Conclusion It is difficult to prove whether the chorioretinal atrophy was caused by the subretinal TB or by the accidental forceful dye injection, but subretinal TB and contact of TB with the retinal pigment epithelium should be avoided, and precautions should be taken during intravitreal injection. We suggest a more controlled method of dye injection in such cases using the flute needle rather than the syringe technique that is conventionally used.

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Introduction

The standard technique to deal with epiretinal membrane (ERM) and macular hole (MH) is pars plana vitrectomy with ERM peel or internal limiting membrane (ILM) peel. The visualisation and removal of the membranes has been made easier by staining with trypan blue (TB).^{1,2} In this case series, we report the effects of inadvertent subretinal migration of 0.15% TB.

Case reports

All the patients underwent best-corrected visual acuity (BCVA), fundus examination, fundus pictures and optical coherence tomography (OCT) (Stratus OCT, Carl Zeiss Meditec, Dublin, CA, USA). After informed consent the patients underwent surgery. TB (0.15%, 312 mOsm; DORC, Zuidland, The Netherlands) was used to stain the membranes. All the patients were examined at day 1, 7, 21, and 3 months following operation. The main outcome measures were the correlation between the BCVA, fundus picture on examination, and OCT findings.

Case 1

A 66-year-old man with a right MH and BCVA of 6/60 OD and 6/6 OS, respectively,

Department of Ophthalmology, Royal Victoria Infirmary, Newcastle, UK

Correspondence: K Stannard, Department of Ophthalmology, Royal Victoria Infirmary, Queen Victoria Road, Newcastle Upon Tyne NE1 4LP, UK
Tel: +44 0191 282 5315; Fax: +44 0191 282 5446.
E-mail: kevin.stannard@nuth.nhs.uk

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underwent a 23-gauge pars plana vitrectomy and ILM peel guided by TB using the Oertli system (Oertli OS3, Berneck, Switzerland). After fluid–air exchange around 0.3 ml of 0.15% TB was injected through the existing sclerotomy using a 1-ml insulin syringe and a blunt 23-gauge cannula into the posterior pole under air. After air–fluid exchange a subretinal TB collection was noted, about 3 disc diameter in size, inferior to the disc (Figure 1a). A tiny hole was noted in the area of subretinal TB, through which the dye aspiration was tried. The ILM peel was completed and fluid–gas exchange was performed with 14% C3F8 gas. Subretinal TB was present on the first postoperative day, but on the seventh day an atrophic area was documented. Three

weeks later a retinal pigment epithelium (RPE) change (Figure 1b) was documented in the area corresponding to the TB migration area. The BCVA at 3 months was 6/60 OD.

Case 2

A 57-year-old man with a BCVA of 6/24 OD and 6/6 OS and MH in his right eye underwent a 20-gauge pars plana vitrectomy and ILM peeling. TB was injected through the sclerotomy using the prefilled TB syringe and the supplied blunt cannula under air. A jet of TB was noted to cause a subretinal haemorrhage with a bluish hue inferior to the disc. Operation was completed with peeling of ILM. Subretinal haemorrhage along with subretinal TB was noted on the first postoperative day. At 1 week, chorioretinal atrophy with RPE changes was noted (Figure 2a). An OCT scan showed choroidal hyperreflectivity (Figure 2b). Three months after surgery the MH was closed and the BCVA was 6/18 OD.

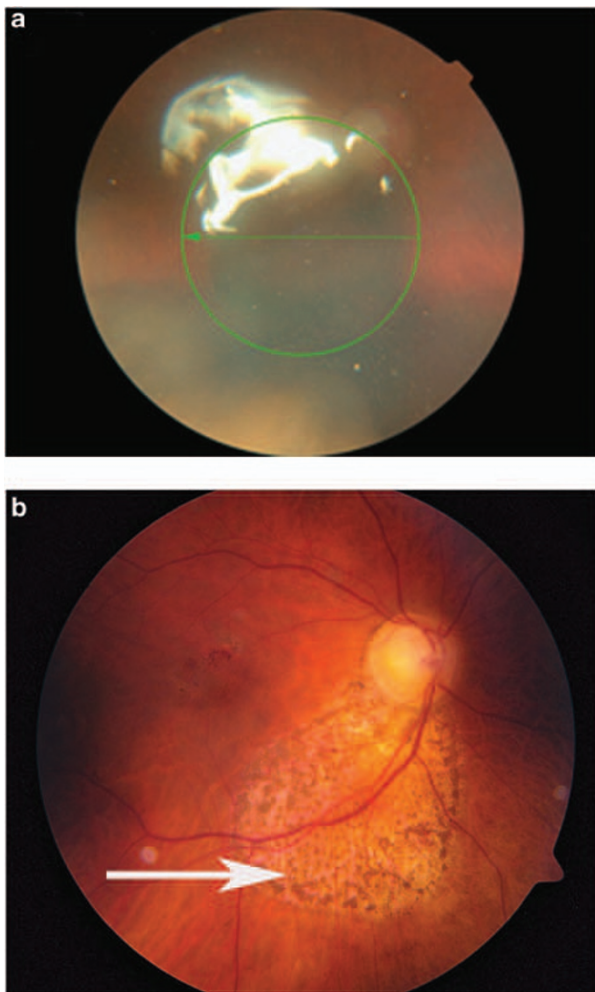


Figure 1 Case 1. (a) Immediate postoperative picture of the patient through the gas bubble showing subretinal migration of TB as a bluish area inferior to the optic disc (reflection from the gas bubble is shown an artefact temporal to disc). (b) Colour fundus picture 3 weeks after the operation. Arrow showing the area of pigment change and chorioretinal atrophy corresponding to the area of dye migration.

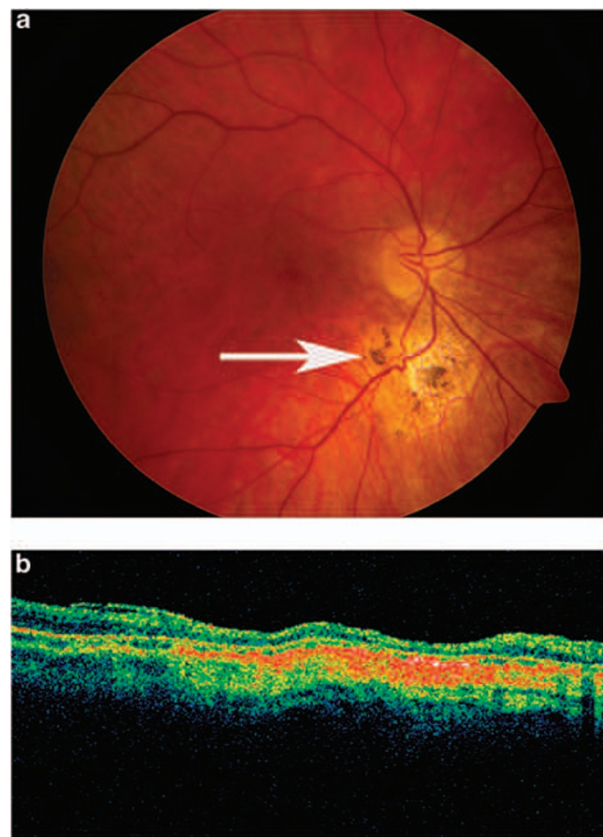


Figure 2 Case 2. (a) One week postoperative picture showing the area of chorioretinal atrophy and RPE change as shown by the solid arrow. (b) OCT scan through the area of dye migration showing hyper-reflectivity due to RPE and choriocapillary atrophy.

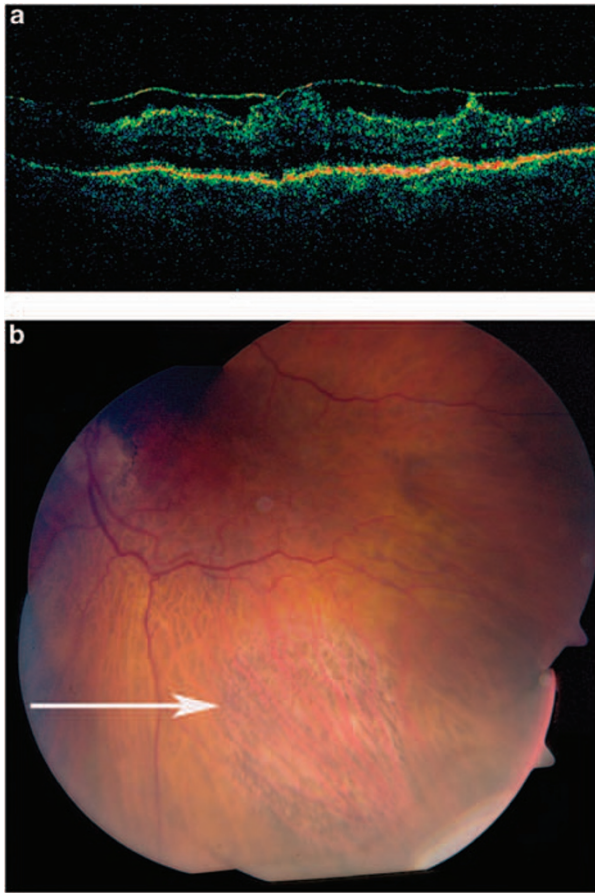


Figure 3 Case 3. (a) OCT scan showing the epiretinal membrane. (b) Postoperative montage colour fundus picture showing the area of chorioretinal atrophy in the area of dye migration as shown by the arrow.

Case 3

An 80-year-old man with a VA of 6/36 OD and 6/60 OS was diagnosed with ERM in both eyes (Figure 3a) and underwent a 23-G vitrectomy with TB-assisted ERM peel. TB was injected through the existing sclerotomy using a 1-ml syringe and a 23-gauge cannula under air. A jet of dye was noted to cause an immediate subretinal bluish hue along the inferior temporal vascular arcade. The operation was successfully completed with an ERM peel. On the first postoperative day subretinal dye was documented. On subsequent follow-up, the patient was noted to have an atrophic area with pigment changes in the area where the dye migrated (Figure 3b). The final BCVA at 3 months was 6/24 OS.

Discussion

Since the introduction of Indocyanine green (ICG) by Kadonosono *et al.*³ for staining of ILM, various dyes have been used to stain ILM and ERM. There have

been reports of toxicity of the retina with ICG.⁴ Accidental subretinal ICG migration has been shown to result in poor visual outcome and RPE atrophy.⁵ TB has been demonstrated to be well tolerated in an animal model study as compared with ICG,⁶ but subretinal migration of TB can cause RPE changes.⁷ Our case series demonstrates similar RPE changes in all the three cases.

The possible mechanism of dye migration in the subretinal space is either through a tiny retinal hole or through the macular hole itself by accidental forceful injection of the dye.^{6,7} Various alternatives have been proposed to prevent direct retinal damage due to dye injection, such as use of perfluorocarbon liquid⁸ and viscoelastic.⁹ Lanzetta *et al.*¹⁰ suggested the use of Infracyanine green (Serb, Paris, France), which is isoosmotic and causes lesser phototoxicity than ICG. Oberstein *et al.*¹¹ suggested the use of heavy TB, prepared by mixing TB with 10% glucose isovolumetrically. Controlled injection of the TB can also be achieved without a fluid–air exchange using Hartmann fluid. Brilliant Peel (Brilliant blue G 0.25 g/l, 306 mOsm/kg H₂O; Geuder, Germany) has a high affinity for ILM but low affinity for ERM, and can be used without the need for fluid–air exchange.¹²

It is possible that the chorioretinal atrophy as documented by our cases and also by Uno *et al.*⁷ could be due to direct trauma of the jet of TB to the retina or by toxicity of the TB itself. There are reports on a small number of patients using subretinal TB for break identification in retinal detachment surgery with successful outcome.¹³ Nevertheless, for MH and ERM surgery it is still important that the macula and the surrounding subretinal area are not damaged in any way to achieve satisfactory visual outcome. We propose an alternative safe and more controlled procedure for dye injection, which is applicable only when undertaking a fluid–air exchange. A flute needle is filled with TB from the TB syringe directly or by aspiration into the flute by pressing on the tubing. Dye injection was done with the prefilled flute after fluid–air exchange, which allowed only drops of TB to be injected. We propose that the controlled drop-by-drop injection of TB allowed good visualisation of the retina throughout the injection process and obviated the need for excess dye injection.

In summary, our series proves that subretinal migration of TB and accidental trauma to the retina during dye injection can cause RPE changes, which can be prevented by more controlled dye injection methods, with the flute technique, after fluid–air exchange, being one of them.

Summary

What was known before

- Trypan blue was safer than Indocyanine green for staining of membranes.
- Subretinal Trypan blue can still cause damage.
- Various methods to prevent toxicity due to retinal dyes used new dyes or complicated procedures.

What this study adds

- Proves the point from three case series that Trypan blue or accidental forceful injection of dye causes chorioretinal atrophy in the area of subretinal dye migration.
- Proposes a new method of dye injection in cases where a fluid–air exchange is done via a flute needle, which is easy to use and safe and prevents this unwanted complication of subretinal dye migration.

Conflict of interest

The authors declare no conflict of interest.

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