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Retinotomy Closure Following Subretinal Stem Cell Transplant with a 30G Needle

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Abstract

The authors report two cases of posterior retinotomy closure following subretinal stem cell transplantation for age-related macular degeneration with a 30-gauge needle — a larger bore needle than those used in prior studies. Partial retinotomy closure was seen on optical coherence tomography within 24 hours in one patient, whereas complete closure occurred by the 5-month and 1-year follow-up visits. A trace retinal hemorrhage occurred in one case, with resolution by 12 weeks. These findings demonstrate the likelihood of uncomplicated, spontaneous retinotomy closure following subretinal stem cell transplantation with a 30-gauge needle.

Introduction

Subretinal injection of human embryonic stem cell-derived retinal pigment epithelium has been shown to improve visual acuity in patients with age-related macular degeneration (AMD).^{1,2} However, subretinal injections require iatrogenic full-thickness retinotomies, the diameter of which depends on the bore of the needle used for transplant. Although smaller bore needles may reduce the size of retinal holes, larger bore needles reduce stem cell shearing, yielding higher cell viability at the time of transplant.

In prior studies, a 25-gauge (0.51 mm) cannula with a small 38-gauge (0.12 mm) tip was used for subretinal injection of human embryonic stem cell-derived retinal pigment epithelium.¹ In this study, a larger 30-gauge (0.31 mm) needle was used. Images acquired with optical coherence tomography (OCT) demonstrate complete closure of the full-thickness retinal hole produced by subretinal transplantation of human central nervous system stem cells (HuCNS-SC) using a larger bore needle.³

Case Report

As part of a phase 1/2 study of safety and preliminary efficacy of subretinal HuCNS-SC (NCT01632527), a 73-year-old man (Figures 1 and 2) and an 83-year-old woman (Figures 3

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and 4) with bilateral advanced AMD causing degradation of vision underwent unilateral HuCNS-SC subretinal transplantation.

Pars plana vitrectomy (PPV) was performed on each subject, after which a macula contact lens was placed on the cornea and a subretinal bleb was created in the superior macula using a 41-gauge needle and balanced salt solution. Next, 1,000,000 HuCNS-SC in 0.1 mL were transplanted into the subretinal space using a 30-gauge needle without complication. Postoperatively, closure of each retinotomy occurred by the 5-month and 1-year follow-up. The retinotomy of the latter subject was not full thickness at 1 day postoperatively, suggesting partial closure within 24 hours. This subject was found to have a trace retinal hemorrhage at the retinotomy site that resolved within 12 weeks.

Discussion

Though use of a larger needle may generate concern for closure of retinotomy sites, these images demonstrate spontaneous closure of the full-thickness retinal defects in both subjects without need for laser. As in the original trials by Schwartz et al., there were no sequential retinal breaks, holes, or retinal detachment identified in either subject.^{2,4} The postoperative retinal hemorrhage in one patient resolved without additional complications.

Retinotomies are often performed to access the subretinal space or drain substances from under the retina. Spontaneous retinotomy closure has been seen following the use of a smaller 41-gauge needle for the subretinal delivery of recombinant tissue plasminogen activator and of air for displacement of submacular hemorrhages.^{5,6} Furthermore, retinotomy closure has been seen following subretinal delivery of viral vectors for gene therapy and after removal of subretinal neovascular membranes.⁷⁻⁹

Thomas et al. first described retinotomy for subfoveal removal of neovascular membranes in ocular histoplasmosis.^{9,10} Retinotomy was initiated with a smaller 36-gauge 130° angled subretinal pick, followed by fluid infusion using a 33-gauge infusion needle, and subsequent removal of subretinal neovascular membrane with 30-gauge subretinal forceps. However, in subretinal neovascular membrane removal, the retinotomy site is often stretched and the resulting retinotomy opening is likely larger than its entry. These retinotomy sites were initially treated with laser, but were subsequently found to be of low risk of retinal detachment and left untreated.¹¹ In most cases of subretinal neovascular membrane removal, retinotomies were found to close within 1 month of the operation.¹²

Posterior draining retinotomies with a tapered 24-gauge extrusion needle and with a 340 µm suture needle have been utilized in retinal detachment repair surgery to drain subretinal fluid.¹³⁻¹⁵ However, several complications have been reported. McDonald et al. reported postoperative subretinal neovascularization, traction macular detachments, and redetachment due to retinotomy opening caused by postoperative drainage site proliferation following posterior draining retinotomies with a tapered 24-gauge extrusion needle.¹³ Raymond et al. reported a 6.4% incidence of hemorrhage greater than two disc diameters following suture needle retinotomy.¹⁴ To reduce the risk of hemorrhage, the authors advised maintenance of

high intraocular pressure, use of sharp sclerochoroidal penetration, and avoidance of large choroidal vessels at the point of penetration.

Importantly, persistence of the retinotomy site is not necessarily associated with an increased risk of complication. Cooper et al. described persistence of an open retinotomy site after submacular removal of choroidal neovascular membranes in five eyes of five patients with ocular histoplasmosis.¹⁶ With a mean follow-up of 47 months, no visual complications or retinal detachments were reported. However, the sample size of this study limits the generalizability of the results.

OCT findings of complete resolution of iatrogenic retinal holes following subretinal HuCNS-SC transplant with a 30-gauge needle can help to reassure providers of the likelihood of spontaneous retinal wound closure following the procedure.

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Figure 1.

Optical coherence tomography images of a 73-year-old man with bilateral advanced dry age-related macular degeneration with foveal atrophy. Horizontal scans centered on the superior retina (right eye) exhibit a closing retinotomy following a 25-gauge pars plana vitrectomy with subretinal injection of stem cells (1,000,000 cells in 0.1 mL) through a 30-gauge needle. Images captured at (A) 1 day, (B) 1 week, (C) 2 weeks, and (D) 5 months postoperatively.

Figure 2.

Fundus photographs of a 73-year-old man with bilateral advanced dry age-related macular degeneration with foveal atrophy. Fundus photographs pre- and postoperatively revealed no complications at the site of the retinotomy (arrow), but a small flame-shaped hemorrhage at an area separate from the retinotomy. Images captured (A) 2 weeks preoperatively and (B) 17 weeks postoperatively.

Figure 3.

Optical coherence tomography images of an 83-year-old woman with bilateral advanced dry age-related macular degeneration with foveal atrophy. Horizontal scans centered on the superior retina (left eye) exhibit a closing retinotomy following a 25-gauge pars plana vitrectomy with subretinal injection of stem cells (1,000,000 cells in 0.1 mL) through a 30-gauge needle. Images captured at (A) 1 day, (B) 1 week, (C) 2 weeks, and (D) 1 year postoperatively.

Figure 4. Fundus photographs of an 83-year-old woman with bilateral advanced dry age-related macular degeneration with foveal atrophy. Fundus photography revealed retinal hemorrhage at the site of the retinotomy (arrow), which resolved spontaneously. Images captured (A) 2 months preoperatively and (B) 1 day, (C) 12 weeks, and (D) 6 months postoperatively.