Combined use of a novel dried cross-linked amniotic membrane and tissue adhesive to conjunctival defect following multiple trabeculectomy

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Abstract
A 74-year-old woman underwent trabeculectomy with mitomycin C in the left eye. A large conjunctival defect with aqueous leakage suddenly developed 2 days postoperatively. The patient had undergone extracapsular cataract extraction and five previous trabeculectomy procedures in the left eye. Amniotic membrane dried by a new method (Hyper-dry), then cross-linked by glutaraldehyde was inserted underneath the conjunctival bleb through the conjunctival defect site and 2-octyl cyanoacrylate adhesive was applied to the surrounding area inside the conjunctival defect edge to secure the amniotic membrane to the conjunctiva. The bare surface of the transplanted amniotic membrane was gradually covered with conjunctival epithelia and the defect was completely sealed 14 days later. The dried, cross-linked amniotic membrane did not dissolve during the 24-month follow-up period. This procedure may become a superior method of treating conjunctival defect following trabeculectomy and the novel dried cross-linked amniotic membrane appears to be a useful therapeutic material for glaucoma surgery.

Key words: cross-linked, amniotic membrane, hyper-dry, bleb leaks, glaucoma, trabeculectomy

Introduction
Multiple ocular surgeries induce conjunctival shrinkage and subconjunctival fibrous scar formations. It is difficult to perform trabeculectomy following the development of these ocular conditions. Spoerl et al.1 reported that amniotic membrane cross-linked by glutaraldehyde was a useful material for surface reconstruction of the cornea and that the cross-linked amniotic membrane was not dissolved by ocular enzymatic digestion. Toda et al.2 recently reported a dried amniotic membrane that was processed by a “Hyper-dry” device. We developed a novel dried cross-linked amniotic membrane (HDCL-AM) by combining Toda's and Spoerl's methods1,2. Using this HDCL-AM, we treated a large conjunctival defect developed after trabeculectomy with mitomycin C in a patient with multiple failed trabeculectomy.

Case report
A 74-year-old woman was referred to our clinic because of elevated intraocular pressure of the left eye. The patient complained of headache and ocular discomfort in the left eye. The patient had previously undergone extracapsular cataract extraction and five failed trabeculectomy procedures during the past 15 years. On examination, her left intraocular pressure was 36 mmHg despite treatment with topical instillations of antiglaucoma drug and oral acetazolamide. Left visual acuity was 0.09, while the right visual acuity was no light perception due to optic atrophy following primary open-angle glaucoma. The patient underwent trabeculectomy with 0.04% mitomycin C. Two days postoperatively, a large conjunctival tear (4 × 3 mm) with aqueous leakage developed at the center of filtering bleb. The intraocular pressure of her left eye was 2 mmHg. The patient received a HDCL-AM

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Preparation of a hyper-dried cross-linked amniotic membrane

This study was approved by the Ethics Committee of the University of Toyama, and informed consent of the patients was obtained. Fresh human amniotic membrane was obtained from seronegative donors undergoing caesarian sections at Toyama University Hospital. The amniotic membrane was washed with sterile phosphate buffer saline. According to the method described by Spoerl et al.\textsuperscript{1}, the fresh amniotic membrane was cross-linked by 0.1\% glutaraldehyde. The cross-linked amniotic membranes were dried using a Hyper-dry device (Sakura, Nagano, Japan)\textsuperscript{2}. The hyper-dried cross-linked amniotic membrane (HDCL-AM) was cut into 5 cm squares and packaged, then sterilized by gamma-ray (25 kGy) irradiation (Fig. 2).

Surgical procedure for repair of the conjunctival defect

The HDCL-AM was cut 7 mm by 7 mm, and the dried membrane was inserted through the conjunctival defect underneath the conjunctival bleb. After drying with a cellulose sponge, tissue adhesive (2-octyl cyanoacrylate) was applied to the surrounding area inside the conjunctival defect edge. By pressing the lesion with a cellulose sponge, the tissue adhesive was dried.

Discussion

Our patient had previously undergone multiple filtering surgeries and suddenly developed a large conjunctival defect with aqueous leakage 2 days after

patch with the use of tissue adhesive. The bare surface of the HDCL-AM patch was gradually covered with conjunctival epithelia, and 2 weeks later, completely covered (Fig. 1a, b). There was no further aqueous leakage. Left visual acuity was 0.2. The intraocular pressure was 14 mmHg in the left eye. During the 24-month follow-up period, there were no remarkable changes.
the most recent trabeculectomy with mitomycin C. This history of multiple ocular surgeries seemed to be responsible for the weakness of the conjunctival tissue. Leaking filtering bleb is an emergency situation that can result in serious ocular complications such as hypotony, maculopathy, choroidal detachment and endophthalmitis. Several surgical techniques to repair the leaking bleb have been described, including application of tissue adhesive, autologous blood subconjunctival injection, suturing of free conjunctival patch or amniotic membrane graft, and advancement of conjunctival flap. None the less, the treatment of bleb leak remains a challenging management problem. We successfully treated a patient with combined application of our HDCL-AM and tissue adhesive (2-octyl cyanoacrylate). Kim et al. reported that 2-octyl cyanoacrylate has a minimal histotoxic effect in ocular tissue. In our patient, there have not been any apparent adverse effects of the tissue adhesive.

We consider that our HDCL-AM may possess several advantages for ophthalmic use. Our dry-state amniotic membrane is easy to handle and cut to the desired size and shape with scissors before application. Because it can be preserved in dry state at room temperature, it is convenient to use. On hydration, it becomes flexible. Spoerl et al. reported that cross-linking of amniotic membrane by glutaraldehyde could increase the resistance to collagenase on the ocular surface and the patch was not dissolved for months after transplantation onto the ocular surface. In our patient, the implanted HDCL-AM was not dissolved for 24 months, as shown on anterior segment OCT. There was no adverse effect induced by the implanted HDCL-AM. The long-term durability and minimal toxicity of HDCL-AM may make it available as an implant for glaucoma surgery.

Burman et al. reported that amniotic membrane possesses properties that promote re-epithelialisation. In our patient, conjunctival re-epithelialisation over the HDCL-AM was noted. Further investigation of conjunctival wound repair using our HDCL-AM is needed.

In the present study, we successfully treated a case showing a large conjunctival defect with bleb leaks, using a combination of a single layer HDCL-AM inlay and tissue adhesive. This simple easy technique may be a promising alternative method to manage a large conjunctival defect with leaking bleb after trabeculectomy.

REFERENCES