

Sutureless amniotic membrane transplantation following excision of ocular surface neoplasia

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Dear Sir,

Success of surgical management of conjunctival neoplasias primarily depends on the complete excision of the mass and eradication of tumor cells from the ocular surface [1-3]. Especially in cases that extensive resections are required, primary closure may not be feasible; so ocular surface reconstruction can be a challenging problem for the surgeons. For conjunctival tissue defects different surgical techniques have been reported in the literature. These include conjunctival autografting, limbal transplantation, conjunctival flap transposition and mucosal graft transplantation [4,5]. However in cases with wide defects, excessive harvest of these tissues may result in complications at the donor and recipient site that may cause cosmetic problems, patient discomfort and even visual dysfunction [5,6].

Human amniotic membrane has been used for ocular surface reconstructions since it was introduced to ophthalmology. It is used for the treatment of conditions requiring conjunctival repair such as pterygium surgery, chemical burns, symblepharon release, conjunctivochalasis and cicatricial disorders. It is also used for the treatment of many corneal epithelial disorders. Fresh or preserved it is an ideal coating material that acts as an antiangiogenic, antiinflammatory and antifibrotic substrate [4]. It also provides the advantage of closing the defects with any size, thus amniotic membrane transplantation (AMT) has been frequently preferred surgical procedure for reconstructions of wide ocular surface defects.

In previously conducted studies AMT has been shown to be an effective technique for the management of ocular surface reconstructions following the excision of conjunctival tumors [2,4,7-9]. Besides all advantages, prolonged operating time, postoperative patient discomfort, suture-related complications such as granuloma formation, papillary conjunctivitis and suture abscesses are the most common disadvantages when amniotic membrane is fixated to the adjacent conjunctiva and underlying sclera with sutures [10]. Whereas attaching amniotic membrane with tissue adhesives reduces the surgery time and avoids complaints related to sutures. In recent years fibrin glue became a good alternative to sutures in surgeries of various ocular surface diseases such as pterygium, conjunctivochalasis and limbal stem cell deficiency [11-13]. There are limited number of cases reported in the literature that sutureless technique is used for amnion membrane fixation after tumor removal. In this study we present the results of 8 cases underwent AMT using fibrin glue following conjunctival tumor excision.

From March 2011 to October 2013, eight eyes of 8 consecutive patients with ocular surface neoplasias who underwent tumor excision and AMT using fibrin glue were participated in this study. The study was conducted according to the principles outlined in the Declaration of Helsinki. A complete ophthalmologic examination was performed and digital anterior segment photography was taken preoperatively and at each visit after the operation. Clinical data concerning age, sex, tumor size and location were collected; histopathologic diagnoses were reported. Postoperative follow-up examinations were done at day 1, weeks 1, 2 and 4, month 3 and at 3mo intervals thereafter. Postoperative patient comfort, surface healing, tectonic and cosmetic success were evaluated, possible complications such as graft dehiscence, inflammation, scarring, symblepharon and recurrence were monitored.

All surgeries were performed under retrobulbar block by the same surgeon after written informed consents were obtained from the patients. Tumors were resected carefully with a 3-4 mm lesion free margin with the "no touch" technique. In cases with corneal involvement, a superficial keratectomy was performed. This was followed by perilesional

cryotherapy to the conjunctival margins until an ice ball extended 2 mm onto the healthy conjunctiva with double freeze technique. Resected specimens were sent to the pathology department for histopathologic diagnosis.

The cryopreserved amniotic membrane was trimmed to fit the denuded surface. Fibrin glue (Tisseel[®], Baxter Inc., Deerfield, IL, USA) was applied onto the bare sclera and margins of recessed healthy conjunctiva. Then amniotic membrane was placed over the surgical defect with the epithelial side facing up and firmly attached to the underlying sclera and adjacent conjunctiva. After instillation of a drop of topical ofloxacin 0.3%, the patient's eye was pressure-patched approximately for 24h.

Eight patients, 2 women and 6 men, with ocular surface neoplasia had a mean age of 53.38 ± 19.38 (range 20-78y). The mean duration of ocular surface mass before the surgery was 11.75 ± 10.3 (range 2-36mo). Only one patient (case 8) had a previous mass excision history with a histopathologic diagnosis of nevus. Bulbar conjunctiva was involved in all cases. Tumor invaded limbal area (Figure 1A) in three, both limbus and cornea (Figure 2A) in three and medial canthus (Figure 3A) in two patients. The mean area of tumor involvement was 37.5 (range 14-56) mm². Histopathologic examination revealed carcinoma *in situ* in two eyes, conjunctival squamous cell carcinoma in one eye, malignant melanoma in one eye, conjunctival epithelial dysplasia in two and conjunctival nevus in remaining two patients. The surgical margins were tumor free in all patients.

No complications were observed during surgery. At the first postoperative day, amniotic membrane was firmly attached in all eyes (Figures 1B, 2B, 3B). Patients with corneal involvement reported mild discomfort that was thought to be related with superficial keratectomy, and it disappeared after corneal epithelization. Other patients had no significant subjective complaints such as pain, itching, watering or burning. One patient (case 8) was instructed to use topical interferon alpha 2b as adjuvant therapy after the histopathologic examination of his conjunctival mass revealed malignant melanoma. It was applied as eye drops (1 million IU/mL) four times a day for three months and no complications related to this treatment were observed.

The mean follow-up after surgery was 25.63 ± 7.48 (range 18-37mo). During this period examinations revealed complete conjunctival epithelial healing with a smooth and stable ocular surface in all cases. No adverse effects due to fibrin glue application were observed. Complications such as inflammation, immunologic reaction, infection, graft retraction, scarring or symblepharon were not observed. All

patients had satisfactory final cosmetic appearance in early and late postoperative periods (Figures 1C, 2C, 3C) without any recurrent lesions.

The utilization of human amniotic membrane in ophthalmology was first reported by De Rotth^[14] in 1940 for the treatment of conjunctival tissue defects. Since then it has been used in widespread ophthalmic applications. AMT has been shown to be an effective technique for ocular surface reconstructions in various conjunctival and corneal disorders. It covers and protects underlying ocular structures as a biological bandage; serves as basement membrane allowing migration of epithelial cells; produces several growth factors, cytokines and mediators that facilitate healing^[3,4]. Furthermore it has a transparent appearance, low immunogenicity and no size limitation. These properties make amniotic membrane an ideal patching material for closure of ocular surface defects and provide superiority to its alternatives.

Complete excision of the mass with lesion-free margins is the most important point in the surgical management of conjunctival neoplasias. The excision of a large tumor results in an extensive defect. AMT has been a preferable procedure for closing defects following conjunctival tumor removal and a number of studies have been conducted on the use of amniotic membrane for conjunctival repair after excision of ocular surface neoplasias^[2-4,7-9,15,16]. Most of the authors have reported favourable outcomes with this technique, except a few cases. Espana *et al*^[2] stated that one case developed pyogenic granuloma in their study which they reported 16 patients that underwent excision of conjunctival tumor and AMT. Gündüz *et al*^[3] reported minimal fibrosis and symblepharon formation that was not significant in one eye of 10 patients with ocular surface neoplasias. Asoklis *et al*^[4] demonstrated only one eye with a clinically insignificant symblepharon after the ocular surface reconstruction of 9 patients. In a recent study with 21 patients and a mean follow-up of approximately 30mo, ocular surface healing was achieved in all cases with limbal stem cell deficiency in three and a mild symblepharon in one eye^[17]. Paridaens *et al*^[9] also reported symblepharon after AMT following wide excision, but this resulted in restricted ocular motility and they pointed out that in extensive ocular surface defects, especially involving the fornix and palpebral conjunctiva, the success of AMT might be limited. In our case series two patients had tumors involving medial canthus, but fornix or palpebral conjunctiva was not involved in any eyes and we did not observe symblepharon formation.

The major disadvantages of AMT are prolonged operating time and suture related complications such as abscess,

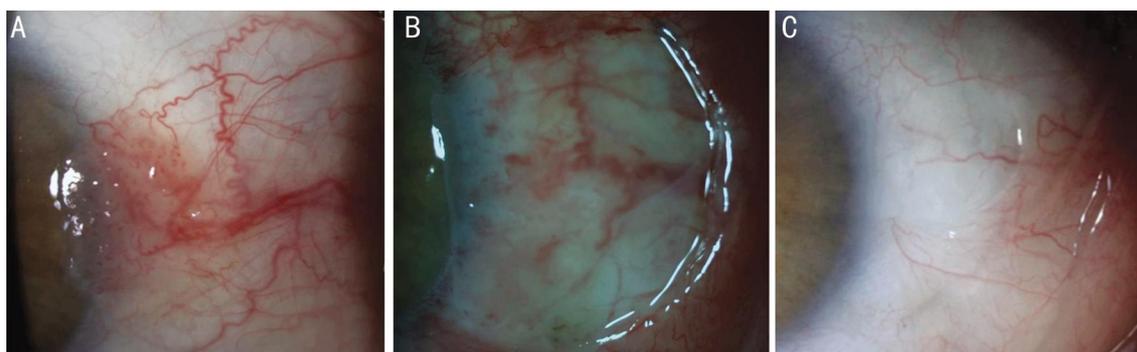


Figure 1 Anterior segment photographs of case 3 A: Preoperative anterior segment photograph of case 3 with conjunctival mass (epithelial dysplasia) involving limbus and bulbar conjunctiva; B: Postoperative view of the same eye showing firmly attached amniotic membrane 1d after the surgery; C: Postoperative second year appearance of the same patient showing successfully healed ocular surface.



Figure 2 Anterior segment photographs of case 5 A: Preoperative anterior segment photograph of case 5 with ocular surface neoplasia (*in situ* carcinoma) involving limbus, cornea and bulbar conjunctiva; B: Postoperative view of the same eye showing the amniotic membrane firmly covering the conjunctival defect 1d after the surgery; C: The same patient 2y after the surgery without any sign of complication.



Figure 3 Anterior segment photographs of case 7 A: Preoperative anterior segment photograph of case 7 showing her nevus involving bulbar conjunctiva and medial canthus; B: Postoperative view of the same eye showing firmly attached amniotic membrane 1d after the surgery; C: Anterior segment photograph of the same patient showing the successful cosmetic and functional outcome 2y after the operation.

granuloma and papillary conjunctivitis when sutures are used to secure the amniotic membrane. Also sutures are the most common causes of patient complaints such as stinging and discomfort. Tissue adhesives have recently gained acceptance for attaching grafts to the recipient site to eliminate all these problems. This sutureless technique is reported as a successful procedure for ocular surface reconstructions in pterygium surgery, conjunctivachalasis excision and limbal dermoid removal [10-12,18,19]. It is indicated that using fibrin glue instead of sutures shortens the operating time, promotes postoperative patient comfort and cosmetic results, obviate suture related complications^[11,12,18]. Graft dehiscence may be a problem in this sutureless procedure but pressure-patching the eye for 24h enables a tight graft adherence and

attachment. Kheirkhah *et al* [12] noted focal inflammation of host conjunctiva adjacent to amniotic membrane and pyogenic granuloma in cases who underwent AMT using fibrin glue for conjunctivachalasis, but all had completely resolved after subconjunctival steroid injection. A disadvantage of commercially available fibrin glue is being a rather expensive substrate compared to sutures. Taylan Sekeroglu *et al* [18] reported that the tissue adhesive used in their study for pterygium surgery was less expensive and easier to obtain compared to commercially available equivalents.

This study offers an alternative surgical management for ocular surface neoplasias. Following excision of the mass, using fibrin tissue adhesive for covering conjunctival defects

with amniotic membrane provides shorter surgery time, improved cosmetic outcomes and enhanced patient comfort.

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