



## Combination of Repeat Penetrating Keratoplasty with Amniotic Membrane Transplantation for Graft Failure with a Persistent Epithelial Defect after Infectious Keratitis

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Here we report the successful management of corneal transplant failure with a persistent epithelial defect by using combined penetrating keratoplasty (PK) with amniotic membrane transplantation (AMT). A 75-year-old woman who had an exacerbation of pseudophakic bullous keratopathy in her left eye had been treated by PK 4 years before. One year after the surgery, endothelial graft rejection with graft failure developed despite intensive topical corticosteroids being prescribed. Unfortunately, severe corneal ulceration in the graft with an anterior chamber reaction was noted 2 days prior to her visit to our department. The results from corneal scrapings showed *Pseudomonas* infection. After 2 weeks of fortified antibiotics treatment, the corneal ulceration was controlled but a persistent epithelial defect remained unhealed. Repeat PK combined with AMT was performed to rescue her vision. Three weeks after the combined procedure, the amniotic membrane patch was absorbed. Corneal transparency was maintained and complete healing of the epithelium without recurrences of infection was noted. Vision improved to 6/20 during 5 months of follow up. AMT may play an adjuvant role in the management of high-risk repeat corneal transplantation.

**Key words:** aminotic membrane transplantation, infectious keratitis, penetrating keratoplasty, persistent epithelial defect, pseudophakic bullous keratopathy

### INTRODUCTION

Corneal diseases are the major causes of blindness and visual impairment in developing countries<sup>1</sup>. Penetrating keratoplasty (PK) remains the choice to rehabilitate patients with corneal blindness; however, although 80%-90% of low-risk grafts succeed, between 50% and 70% of high-risk grafts fail, mainly due to immune rejection. The original diagnosis, preoperative peripheral anterior synechiae, postoperative neovascularization, and regrafting are common risk factors for graft failure. Therefore, proper diagnosis and the institution of appropriate medical therapies to correct the underlying cause, to suppress untoward inflammation, and to augment tissue healing, may improve graft survival.

Human amniotic membrane transplantation has been a means of treatment of corneal epithelial defects<sup>2</sup>. In ophthalmology, amniotic membranes are a biological tissue that has been used as a graft for corneal and conjunctival reconstruction in a variety of ocular surface diseases. Previous studies have shown that amniotic membrane transplantation (AMT) facilitates epithelialization and reduces inflammation, vascularization, and scarring<sup>3</sup>. There is also anecdotal evidence that applying a patch of amniotic membrane onto surgical grafts helps to lessen the risk of rejection.

In this case report, we used PK combined with AMT to successfully manage corneal transplant failure with a persistent epithelial defect.

### CASE REPORT

A 75-year-old female patient underwent extracapsular cataract extraction with intraocular lens implantation in her right eye in September 2000. Unfortunately, two years after cataract surgery, pseudophakic bullous keratopathy with glaucoma developed, with her visual acuity decreasing to light perception only. Medical treatments were prescribed, but the transparency of the cornea decreased

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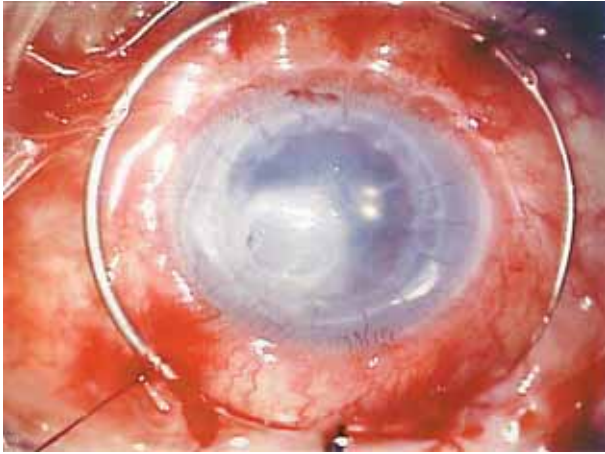


Fig. 1 Slit-lamp photograph of the patient's right eye revealed controlled corneal ulceration with persistent epithelial defects between the 6 and 9 o'clock-hours in the graft.

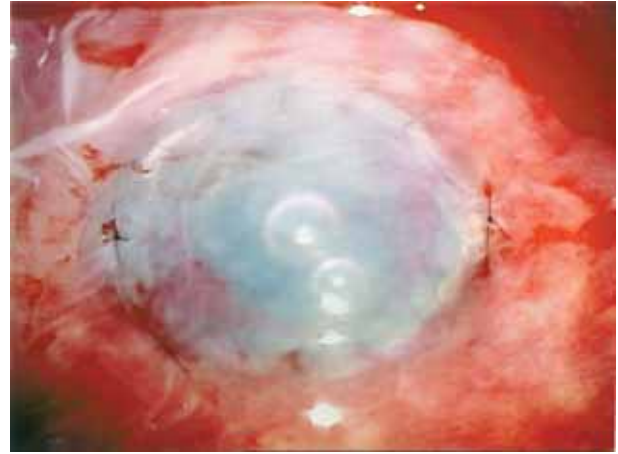


Fig. 2 Slit-lamp photograph of the patient's right eye showed that the amniotic membrane was sutured with the interrupted 10-0 nylon to the sclera before trimming the extra edges.

continuously, with worsening corneal edema. On September 29, 2002, PK was performed to improve optical performance. However, endothelial graft rejection with corneal failure developed.

On February 1, 2006, she presented to our department with severe corneal ulceration of the corneal graft, with an anterior chamber reaction. After admission, corneal scrapings were collected for bacterial culture, and aggressive medical treatment with fortified cefazolin (Veterin; Veterans Pharmaceutical Plant, Taipei, Taiwan) and 0.3% norfloxacin (Baccidal; Kyorin Pharmaceutical Company, Tokyo, Japan) was given hourly. Corneal scrapings were taken for bacterial and fungal cultures, and the cultures showed *Pseudomonas aeruginosa* infection, which was susceptible to both cefazolin and norfloxacin. After two weeks of medical treatment, the corneal ulceration had been controlled but a persistent epithelial defect was noted (Fig. 1). Repeat PK combined with amniotic membrane transplantation was performed with four interrupted cardinal sutures and 16 interrupted sutures in total. At the end of the surgery, cryopreserved amniotic membrane was applied over the corneal graft, with the epithelial side down. The amniotic membrane was sutured to the edge of the limbus with 10-0 nylon purse-string sutures (Fig. 2). Topical 0.3% norfloxacin and 1% prednisolone acetate eye drops every two hours, preservative-free artificial tears six times per day, and 1% atropine eye drops twice per day were prescribed. Three weeks after the combined procedure, the amniotic membrane patch was absorbed totally. The patient's preoperative visual acuity was 6/60. The patient



Fig. 3 Slit-lamp photograph of the patient's right eye showed maintained corneal transparency with no anterior chamber reaction 12 months postoperatively.

was followed-up for 12 months and her visual acuity improved to 6/20 in her right eye. Corneal transparency was maintained and there was no anterior chamber reaction. There was moderate ciliary congestion between the 6:00 to 1:00 positions and we will continue surveillance for further rejection (Fig. 3).

## DISCUSSION

In this report, we successfully used repeat PK combined with AMT to treat graft failure with a persistent epithelial defect. We demonstrated the effectiveness of AMT in facilitating the treatment of a persistent epithelial defect.

The result is comparable to those obtained in previous studies using amniotic membrane to treat ocular surface diseases, corneal ulcers, and corneal perforations<sup>2-6</sup>.

Persistent corneal epithelial defects with ulceration can be effectively managed by being covered with a layer of preserved human amniotic membrane. The amniotic membrane contains a thick basement membrane and an avascular stromal matrix<sup>7</sup>, features we thought important to successful transplantations. The basement membrane promotes the migration, adhesion, and differentiation of epithelial cells, while preventing epithelial apoptosis<sup>8</sup>. The use of AMT does not affect the penetration of antibiotic eye drops. All these actions allow the amniotic membrane to effectively permit rapid epithelialization.

In addition, the degree of postoperative pain and inflammation might be decreased via the use of amniotic membrane. This might be explained by the anti-inflammatory function of the amniotic membrane. The stroma of the amniotic membrane stimulates apoptosis of inflammatory cells<sup>9</sup>, suppresses cytokines (interleukin-1 $\alpha$  interleukin-1 $\beta$  interleukin-2, interleukin-8, interferon  $\gamma$  and tumor necrosis factor  $\alpha$ )<sup>10</sup>, and contains various proteinase inhibitors<sup>11</sup> and anti-inflammatory proteins<sup>12</sup>.

PK is one of the most common and successful tissue transplants used worldwide. Although there have been many advances in corneal transplantation surgery, graft failure is still one of the leading indications for PK<sup>13</sup>. Risk factors for repeat PK include rejection episodes, patient age and gender, the original diagnosis leading to corneal transplantation, the presence of preoperative peripheral anterior synechiae, intraoperative anterior vitrectomy, and postoperative corneal neovascularization<sup>14</sup>. In this case, one year after the primary PK, this patient developed endothelial graft rejection with stromal and epithelial edema. These signs are comparable with those in previous studies, and this patient belonged to a high-risk group for graft failure. Therefore, we used combined repeat PK with AMT for graft failure with a persistent epithelial defect.

However, some limitations of PK combined with AMT should be considered. The use of AMT makes it difficult to observe the epithelialization and transparency of the corneal graft. Further, commercial preparations of amniotic membranes are expensive and several brands exist. The quality of the amniotic membrane also varies with supplier and some preparations require special storage.

The results in this case suggest that the combination of penetrating keratopathy with amniotic membrane transplantation may allow successfully management of corneal transplant failure with a persistent epithelial defect. This case report is based on the augmented ideas of our

predecessors. More studies are required to evaluate the effectiveness and the safety of PK combined with AMT to treat graft failure with persistent epithelial defects.

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