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Allogeneic anterior lens capsule transplantation (ALCT) for the management of HSV neurotrophic keratitis

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A R T I C L E I N F O	A B S T R A C T
Keywords: Anterior lens capsule transplantation ALCT HSV Neurotrophic Keratitis Keratopathy Ulcer	<i>Purpose</i> : To report a case of allogeneic anterior lens capsule transplantation (ALCT) for the management of HSV neurotrophic epithelial keratitis. <i>Observations</i> : An 81-year-old man was referred to our department due to neurotrophic keratitis in the left eye that he had been suffering from over the past 3 months. He had recurrent episodes of HSV keratitis in the left eye over the past 3 years and despite multiple previous treatments, there was no improvement. At the time of presentation, corrected distance visual acuity (CDVA) was 20/200 in the right eye and no light perception (NLP) in the left eye. Slit-lamp examination revealed a corneal epithelial defect with underlying stromal thinning and concomitant scarring. An allogeneic anterior lens capsule (ALC) was placed over the epithelial defect to act as a biological dressing, anchored with a droplet of fibrin glue. A bandage contact lens (BCL) was placed over to prevent the slippage of the ALC. No intra or postoperative complications were observed. Two weeks later, the ALC was removed revealing complete epithelial healing, while two months later the epithelium remained completely healed with a significant reduction of corneal scarring. <i>Conclusions and importance:</i> Anterior Lens Capsule transplantation (ALCT) seems to be a promising new treatment option for the management of corneal neurotrophic keratitis.

1. Introduction

Neurotrophic keratitis (NK) is a corneal disease related to reduced or nonexistent corneal sensitivity. This condition results in the breakdown of the corneal epithelium, reduced healing processes, and eventually leads to the formation of corneal ulcers, melting, and perforation. The most common cause is HSV and VZV keratitis, accounting for 30 % of all NK causes.¹ According to the "Mackie Classification", Grade I is characterized by corneal epithelial irregularity, Grade II by persistent epithelial defects and Grade III by corneal ulceration and stromal melting.² Management of severe cases is challenging and primarily focuses on the prevention of corneal melting and perforation. Numerous treatments are used in clinical practice such as bandage contact lenses, autologous serum, nerve growth factors (NGF), insulin drops and amniotic membrane transplantation (AMT).^{3,4}

The anterior lens capsule (ALC), otherwise known as the anterior capsule of the crystalline lens, is the thickest basement membrane in the

human body and possesses unique physiological characteristics.⁵ It has been considered an excellent substrate for the development and multiplication of various ophthalmic cells. The application of the ALC in recurrent ulcers has been carried out in rabbit models; all eyes treated demonstrated faster epithelialization than the control eyes.⁶ The ALC promoted the reformation of hemidesmosomes that were identical in size to hemidesmosomes of the healthy cornea,⁷ which assisted in epithelial apposition to the underlying stroma. Moreover, it is readily available in ophthalmology clinics as its removal is necessary in every cataract surgery.

Herein, we describe a novel method for the management of HSV neurotrophic keratitis using an allogeneic ALC.

2. Case report

The study was approved by the institutional ethics committee (No.12065), while written consent was obtained from both the donor

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and the recipient. This report followed the tenets of the Declaration of Helsinki. An 81-year-old man was referred to our department due to a prolonged, painless corneal epithelial defect in his left eye for the past 3 months. Corrected distance visual acuity (CDVA) at presentation was 20/200 in his right eye (OD) and no light perception (NLP) in his left eye (OS). His ophthalmological history included phacomorphic angle closure glaucoma in the OS which was managed with lensectomy and IOL implantation 10 years ago, resulting in NLP vision since then. Moreover, he had been suffering from several incidents of Herpes Simplex Virus (HSV) keratitis in the same eye over the preceding three years. Despite multiple treatments (epithelial debridement, bandage contact lens, topical autologous serum, oral doxycycline, oral valacy-clovir) during the last 3 months, the epithelial defect remained unresponsive to treatment.

Slit-lamp examination revealed a paracentral corneal epithelial defect in the left eye (Fig. 1). The defect was accompanied by moderate stromal thinning, marked scarring and significant intrastromal neovascularization (Mackie, Grade III). Evaluation of corneal sensitivity with a Cochet-Bonnet aesthesiometer indicated a significant reduction in corneal sensitivity, whereas corneal scrape cultures yielded negative results. The clinical diagnosis of corneal neurotrophic keratitis was confirmed. Due to the prolonged corneal defect, the resistance to previous treatment, and the reluctance of the old patient to undergo a laborious surgery, we implemented a new technique to manage the corneal defect and restrain any additional stromal thinning, using an ALC.

An allogeneic anterior lens capsule was obtained from a cataract surgery and inserted in a sterile vial containing a balanced salt solution (BSS), secured for the next surgery. A complete serology test of the donor patient was performed the day before the surgery, turning back all values negative. According to the medical standards of Eye Bank Association of America (EBAA) the required testing for corneal transplants includes: anti-HIV-1, anti-HIV-2, HBsAg, anti-HCV, syphilis.⁸ We complied with the above tests and tested for HSV-1, HSV-2, VZV, CMV, EBV. The ALC was placed with the epithelium facing down (onlay) on the top of our patient's cornea. During the capsulorhexis, the ALC was torn into 2 pieces which later aided us to locate its epithelial side, by joining the sections in a unique way. The epithelium surrounding the defect was scrapped away (Fig. 2a) to ensure that no overlapping epithelium remains and the edges of the ALC were meticulously adjusted to cover the whole extent of the damaged area (Fig. 2b). The adhesion of the capsule to the cornea was achieved by applying a portion of blood (Fig. 2c) produced during the epithelium debridement due to the neovascularization, then the cornea was dried out with an eye spear (Fig. 2d) and a droplet of fibrin glue was instilled over the ALC (Fig. 2e). Finally, a bandage contact lens was placed (Fig. 2f) to prevent the capsule dislocation during blinking [video].

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Postoperatively the patient received chloramphenicol + dexamethasone, (Dispersadron-c Laboratoires, Thea) and moxifloxacin (Vigamox, Alcon) eyedrops 4 times a day for the following 14 days with a gradual tapering of the dexamethasone (one drop every 10 days). Oral valacyclovir 500mg two times daily was also prescribed.

After the operation slit lamp examination confirmed that the ALC was attached (Fig. 3a).

Two days postoperatively, the ALC was centered and perfectly attached to the area of the epithelial defect (Fig. 3b). Anterior segment OCT (ASOCT) depicting the ALC is in place (Fig. 3c).

Two weeks later, the ALC was still attached to the cornea (ASOCT, Fig. 3d) with underlying epithelium. Forceps were used to remove the ALC (Fig. 3e). Fluorescein confirmed a completely healed epithelium (Fig. 3f).

During the follow-up period during the next 2 months, the corneal epithelium remained intact with a significant reduction of corneal scarring (Fig. 3g).

3. Discussion

Neurotrophic keratitis (NK) is a degenerative eye condition characterized by diminished or absent sensitivity in the cornea, leading to the degradation of the corneal epithelium, impaired healing abilities, the development of corneal ulcers, stromal melting, and ultimately, perforation. Herpes Simplex Virus (HSV) and Varicella-Zoster Virus (VZV) keratitis are the most frequent causes, responsible for 30 % of NK incidences.¹ A range of treatments are utilized in practice for neurotrophic keratopathy, with nerve growth factors and amniotic membrane transplantation being among the most effective. However, NGF treatments can be prohibitively expensive,⁹ and amniotic membranes may not always be available in eye care facilities.

Surgical treatments like AMT have been used for the management of neurotrophic keratitis. However, in comparison with the AMT, the ALC does not contain stroma tissue, making the ALC a more transparent and suitable tissue for transplantation. It is composed of collagen type IV and is the thickest basement membrane of the human body.⁵ Allogeneic anterior lens capsule transplantation has been performed in rabbit eyes for the management of persistent, mechanically induced, epithelial ulcers.^{6,7} The eyes that underwent ALC allotransplantation demonstrated faster re-epithelialization than the control eyes.⁶ Moreover, at an ultrastructural level, it contributed to healthy hemidesmosome formation, resulting in a more robust attachment of epithelial cells to the underlying stroma in areas where the epithelial basement membrane was



Fig. 1. Pre-operative slit-lamp examination depicting the neurotrophic epithelial defect accompanied by marked scarring (white arrows).



Fig. 2. Surgical technique, (a) removing the epithelium surrounding the defect, (b) adjusting the ALC to fully cover the epithelial defect, (c) applying a portion of blood over the ALC to attach it to the underlying stroma, (d) drying out the area of epithelial defect, (e) fibrin glue instillation, (f) bandage contact lens placed on the cornea. ALC: Anterior Lens Capsule.



Fig. 3. (a) After the operation slit lamp examination confirmed that the ALC was attached. **(b)** Two days postoperatively, the ALC was centered and perfectly attached to the area of the epithelial defect. **(c)** ASOCT two days postoperatively, depicting the ALC (green arrow) is in place (note the yellow arrow, showing the edges of the ALC and the surrounding epithelium). **(d)** ASOCT two weeks post-operatively, confirming that the ALC was still attached to the cornea with underlying epithelium (blue arrow). **(e)** Forceps were used to remove the ALC (red arrow), **(f)** a completely healed epithelium was revealed. **(g)** Slit-lamp image 2 months postoperatively, the cornea remained clear without any signs of corneal epithelial defect. ALC: Anterior Lens Capsule ASOCT: Anterior Segment OCT. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

absent due to chronic trauma.⁷ The preceding cases were performed in avascular corneas and included inlay transplantation (epithelium facing up) techniques. In inlay transplantation, the reabsorption of the graft is related to the extent of the neovascularization before surgery,¹⁰ as a result in cases with marked neovascularization, onlay transplantation is preferred. In our case, due to the extent of the neovascularization, we proceeded with onlay ALCT to avoid the membrane's rapid reabsorption and let the ALC act as a biological bandage. In clinical practice, the ALC has been utilized in phacotrabeculectomy, placing the capsule under the scleral flap instead of using mitomycin-c with comparable outcomes.¹ In addition, it has been used in macular hole closure, Chen & Yang¹² managed to treat 20 eyes with persistent macular holes that had undergone standard surgery previously. In human corneas, the ALC has been used as a biological drape to secure corneal perforations with favorable outcomes.¹³

In this case report we present a case of ALCT in a patient with HSV neurotrophic epithelial keratitis resistant to previous treatments. It seems that the ALC served as a scaffold to facilitate corneal epithelialization, thereby aiding the healing process. A major advantage of ALC is that it is an easily available biological membrane (can be obtained during cataract surgery) being a viable solution for patients who are reluctant or unable due to medical conditions to have multiple visits or to undergo a more laborious surgery.

4. Conclusions

Allogeneic anterior lens capsule transplantation successfully managed refractory HSV neurotrophic keratitis, resistant to multiple previous treatments. To the best of our knowledge, this is the first reported case of using ALCT for the management of neurotrophic keratitis in the human eye.

CRediT authorship contribution statement

George D. Kymionis: Writing – review & editing, Data curation, Conceptualization. Dionysios G. Vakalopoulos: Writing – original draft, Data curation, Conceptualization. Marina S. Chatzea: Writing – original draft, Formal analysis. Konstantina A. Togka: Writing – original draft. Vasileios A. Tsagkogiannis: Writing – review & editing, Validation. Petros C. Petrou: Writing – review & editing, Supervision.

Patient consent for publication

Informed consent was obtained from the patient for the publication of the data included in this case report.

Disclosures

The authors have nothing to disclose.

Compliance with ethics guidelines

The study was approved by the institutional ethics committee, while written consent was obtained from both the donor and the recipient. This case report followed the tenets of the Declaration of Helsinki.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://do i.org/10.1016/j.ajoc.2025.102292.

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