Living-Related Conjunctival Limbal Allograft

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Indications

The value of a normal limbus in maintaining a normal ocular surface has been well documented on the basis of anatomical and experimental evidence.1–7 The objectives of epithelial stem cell transplantation are to restore phenotypic corneal epithelium to the corneal surface, to promote the barrier function of the limbus, and to improve surface lubrication, thus providing an improved milieu for maintenance of corneal clarity. Depending on the cause, as outlined in earlier chapters, stem cell deficiency may be bilateral and may also involve the conjunctiva with varying severity ranging from subconjunctival scarring, to keratinization, cicatrization, symblepharon formation, and secondary lid abnormalities. In bilateral disease, the only option for stem cell restoration is the use of allogeneic sources.8–10 Procedures available include a cadaveric keratolimbal allograft (KLAL), living-related conjunctival limbal allograft (lrCLAL), and more recently, ex vivo stem cell allograft expansion.

Keratolimbal allograft transplantation has the advantage of providing a complete limbus for transplantation and thus a larger load of stem cells with restoration of a barrier to the whole limbus. The practical disadvantage is that it is almost impossible to obtain immune histocompatibility and, with such highly antigenic tissue transplanted into a highly vascularized recipient bed, there is the potential increase risk of graft rejection.11,12 This risk of rejection may account for the reduced long-term survival of nonmatched keratolimb allografts. Tsubota reported long-term survival of only 51%,13 and Ilari reported 50%.14 Furthermore, depending on cadaver and storage time, there may be a degree of stem cell death, thus reducing the volume of cells transplanted. While there may be limitations on the amount of tissue that can be transplanted in a lrCLAL, there is the advantage of providing some degree of immune histocompatibility,15,16 thereby reducing the dependency on and dosage of systemic immunosuppressive agents. Additionally, cell death is theoretically limited because of the rapidity of transplantation from donor to recipient and the rapid revascularization of grafted material.

Ocular surface reconstruction can be divided into two components, structural reconstruction and surface restoration. Structural reconstruction involves reduction of ankyloblepharon and symblepharon and treatment of lid abnormalities, whereas surface restoration includes establishment of the barrier function at the limbus and epithelialization of the cornea with phenotypic corneal epithelium. Cadaveric KLAL transplantation alone or in combination with amniotic transplantation may accomplish both successful structural reconstruction as well as surface restoration. On a long-term basis, KLAL may fail to maintain phenotypic corneal epithelium even if structural reconstruction is usually maintained without recurrence of symblepharon.10,13,17,18

Since lrCLAL requires a procedure on an individual other than the patient, it is best reserved for eyes in which there is a minimal risk of failure. Eyes that require surface restoration alone are best suited for lrCLAL. Eyes requiring both reconstruction as well as restoration are unsuitable for lrCLAL and are best initially treated by KLAL with amniotic membrane transplant as a first stage, followed by lrCLAL in the event of epithelial failure.

Contraindications and Preoperative Considerations

Contraindications to lrCLAL include:
1. Any ocular surface requiring structural reconstruction.
2. Severe keratinization of the palpebral conjunctiva.
3. Inadequate lid closure.
4. Dry eye.
5. Severe inflammation.

In severe cases of bilateral disease, such as those following chemical injuries and Stevens–Johnson syndrome, severe cicatrization may be associated with lid abnormalities including keratinization, trichiasis, and entropion. Lid reconstructive and corrective procedures are best performed well in advance of epithelial transplantation. The goal of these procedures is to ensure adequate and atraumatic coverage of the ocular surface. Inadequate lid closure and severe keratinization of palpebral conjunctiva are incompatible with successful epithelial transplantation and are an absolute contraindication to lrCLAL. An ocular surface requiring reconstruction has been discussed above and is also a relative contraindication to lrCLAL.

Surface lubrication is crucial for survival of epithelium. Bilateral stem cell deficiency can be associated with severe dryness as a result of cicatrization of the main and accessory lacrimal ducts. The tear function index (TFI) is a method of evaluating status of lubrication, and methods to improve the TFI such as punctal occlusion are best carried out prior to surgery. Epithelial transplant procedures are contraindicated in instances in which there is absolute dryness with no tear function and where improvement is unlikely in the future.

Severe inflammation is a poor prognostic factor, and its presence is also a contraindication to lrCLAL. Treatment during the acute phase of an illness, for instance, soon after a chemical injury, is contraindicated. The goal in this instance would be to stabilize the eye and reduce inflammation. Other procedures, such as amniotic membrane transplantation with or without KLAL, are best utilized to promote epithelialization and downregulation of inflammation. Underlying causes of stem cell deficiency, such as ocular cicatricial pemphigoid, must also be adequately controlled prior to surgery. Inflammation, where present, can be controlled by topical and systemic steroids. Furthermore, it is best to have a period of 3 to 6 months free of inflammation prior to surgery.

Since many affected corneas are not transparent, some surgeons might consider performing a simultaneous visually rehabilitative procedure such as a penetrating keratoplasty. One report demonstrated a reduction in corneal opacification with improvement in visual outcome in 70% of eyes following lrCLAL alone, obviating the need for a penetrating or lamellar keratoplasty. In most cases, therefore, it is best to perform a lrCLAL alone and wait for at least 6 to 12 months before considering corneal graft. This allows the cornea to clear and also provides an opportunity for the ocular surface to improve, thereby optimizing graft survival, should it be required.

Surgical Techniques
Donor Selection

Since immune histocompatibility is one of the main reasons for embarking on this course of management, the best HLA-matched relative is the ideal donor. Human leukocyte antigen (HLA) typing is performed on all possible donors. If only parents are available, then HLA matching is not necessary, since the recipient will be a haplotype. Since expression of blood-group antigens has been demonstrated on epithelial cells, ABO matching is also advisable when there are several potential donors available.

Both eyes of the donor are evaluated to ensure there is no underlying ocular history that may preclude donation. A history of glaucoma, for example, would be a relative contraindication because of the possible need for a trabeculectomy in the future. Additionally, chronic use of topical medications and prior contact lens wear with Thimerosal-containing preservatives suggest potential stem cell depletion that could be exacerbated by removal of limbal conjunctiva. A prior surgical history would also be a relative contraindication because of the possibility of iatrogenic stem cell deficiency.

One should measure tear breakup time, Schirmer test, and employ rose bengal staining to ensure there is no underlying abnormality.

Following identification of the best-matched living relative, screening for the possibility of blood-borne diseases is necessary. The standard serologic tests required by the Eye Bank Association of America are advised; these include screening for human immunodeficiency virus 1 and 2 and hepatitis B and C.

Anesthesia

Topical retro- or peribulbar anaesthesia can be used for harvesting donor tissue. However, based on cultural and practical considerations, general anesthesia can be employed. The recipient’s eye can be similarly anesthetized using retro- or peribulbar anesthesia or, if necessary, general anesthesia.

Harvesting Tissue From the Relative

The nondominant eye of the donor is selected for the conjunctival limbal allograft, if it has not been used for tissue donation before. Since it is customary for surgeons to operate out of one operating room, removal of the donor tissue needs to be accomplished first. The procedure includes standard sterile preparation and draping of the eye. The sites for donation are marked on the donor eye (Figure 17.1A). Methods include a marking pen on the conjunctival surface or a 12-blade radial keratotomy marker with a gentian violet marking pad. The