

Management of corneal perforations in dry eye disease: Preferred practice pattern guidelines

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Corneal perforations in eyes with dry eye disease (DED) are difficult to manage due to the interplay of several factors such as the unstable tear film, surface inflammation, and the underlying systemic disease affecting the wound healing process, and the eventual outcome. A careful preoperative examination is required to identify the underlying pathology, and status of ocular surface and adnexa, rule out microbial keratitis, and order appropriate systemic workup in addition to assessing the perforation itself. Several surgical options are available, which include tissue adhesives, multilayered amniotic membrane grafting (AMT), tenon patch graft (TPG), corneal patch graft (CPG), and penetrating keratoplasty (PK). The choice of procedure depends upon the size, location, and configuration of the perforation. In eyes with smaller perforations, tissue adhesives are effective treatment modalities, whereas AMT, TPG, and CPG are viable options in moderate-sized perforations. AMT and TPG are also preferable in cases where the placement of a bandage contact lens may be a challenge. Large perforations require a PK, with additional procedures such as tarsorrhaphy to protect the eyes from the associated epithelial healing issues. Conjunctival flaps are considered in eyes with poor visual potential. The management of the acute condition is carried out in conjunction with measures to improve the tear volume bearing in mind the chances of delayed epithelialization and re-perforation in these cases. Administration of topical and systemic immunosuppression, when indicated, helps improve the outcome. This review aims to facilitate clinicians in instituting a synchronized multifaceted therapy for the successful management of corneal perforations in the setting of DED.

Key words: Aqueous deficient, corneal perforation, dry eye disease

Dry eye disease (DED) is one of the most common causes of non-infectious and non-traumatic corneal perforations.^[1,2] Perforations are more frequently seen in the aqueous deficient variant of DED (ADDE).^[2] The ocular surface in DED is compromised and the presence of inflammation makes these eyes susceptible to repeated breaches in the ocular integrity.^[3,4] The restoration of the globe integrity requires immediate intervention to prevent the occurrence of associated complications. Several surgical modalities are available for the same, and the choice of one procedure over the other is determined by the size, configuration, and location of the perforation, the status of the surrounding ocular structures, and the underlying disease process. Management of this entity in the setting of ADDE is particularly challenging because the primary pathology can independently affect the progression of the corneal lesion and the outcome of the

surgical intervention.^[5,6] Thus, corneal perforations in ADDE require a multipronged approach with the management of the ocular surface, the corneal defect, and the underlying ocular or systemic disease. This review aims to highlight the specific considerations in the management of corneal perforation in the setting of ADDE and improve the outcomes.

Risk Factors and Preventive Measures

Several factors can precipitate corneal melting and subsequent perforation in eyes with ADDE. Natural tear film, in addition to maintaining a smooth refractive ocular surface, has several epitheliotropic factors that maintain the ocular surface barrier, provide essential nutritional factors, and also act as a lubricant. The unstable tear film in ADDE lacks these epitheliotropic factors, resulting in a repeated breakdown of the corneal epithelium, chronic inflammation, infection, and stem cell failure.^[5] The areas of breakdown coalesce to form an epithelial defect in the presence of inadequate healing mechanisms. Not uncommonly, these epithelial defects might remain persistent

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resulting in the lysis of the underlying stroma progressing to corneal perforation.^[4] Several factors can hasten this process and a careful ocular examination is required to identify them. Adnexal issues such as trichiatic lashes, malpositioned lids, and lagophthalmos can weaken the corneal epithelial barrier, and need to be addressed. Staining of the ocular surface with judicious documentation helps detect early changes indicative of a progressive disease. An increase in the number of superficial punctate keratitis (SPKs) or the appearance of a confluent area of SPKs should prompt an increase in the frequency of topical lubrication. Other methods that help preserve tear film include the use of punctal plugs, punctal cautery, or tarsorrhaphy. The latter is particularly important in eyes with a concurrent neurotrophic or neuroparalytic component.^[7] The location of the SPKs can help ascertain the presence of any local pathology that requires correction. The presence of interpalpebral SPKs is suggestive of an evaporative disease process, whereas a focal area of SPKs may indicate misdirected lashes and lid margin keratinization. Inflammation of the ocular surface is a common feature with an underlying immune-mediated disease such as rheumatoid arthritis (RA), Sjogren's syndrome (SS), mucus membrane pemphigoid (MMP), ocular graft-versus-host-disease (GVHD), or Steven-Johnson syndrome (SJS), or secondary to the changes induced in the ocular milieu by the ADDE.^[6-9] This inflammatory cascade can independently accelerate the thinning of the corneal stroma. Adequate management of the underlying pathology with topical or systemic immunosuppressants is therefore additionally needed to retard the stromal melt.^[5] It is not uncommon for surgical procedures such as corneal refractive surgeries^[10] and cataract surgeries^[11] to worsen an already existing DED.

Approach to a Case of Corneal Perforation in ADDE

History

Patients with corneal perforations typically present with complaints of a sudden drop in vision along with redness or pain. A known dry eye patient complaining of sudden watering should also alert us about the possibility of this complication. A thorough history should be obtained regarding immune-mediated disorders such as RA, SS, MMP, ocular GVHD, or SJS, including the details of the immunosuppressive therapy instituted. If the cases have not been previously diagnosed with the same, then symptoms such as joint pains, dryness of mouth, and skin blisters can be suggestive of these diseases. Rarely, if carefully elicited, a history of nocturnal lagophthalmos may be positive in some patients. A history of local irradiation causing dry eye is another established etiological factor. Other disorders are likely to cause corneal melt including keratomalacia and rarely, ocular GVHD.^[12]

Ocular examination

The diagnosis of ADDE in a patient presenting with a corneal perforation may be challenging as a detailed ocular workup is usually precluded by the presence of the open globe. In such cases, examination of the fellow eye, especially with fluorescein staining and Schirmer's test, can help establish the diagnosis. The presence of symblephara or forniceal shortening is indicative of an underlying cicatricial disorder such as SJS or MMP. Patients with RA-associated dry eyes are likely to develop

peripheral ulcerative keratitis (PUK). Such patients might have peripheral corneal perforations in contrast to patients with SS or RA without PUK, who are more likely to develop corneal perforations that are more central in location.^[13,14] Careful examination of the limbus is essential to rule out concurrent limbal stem cell deficiency (LSCD) that might affect the course of the disease, management protocols, and the outcome of treatments. The perforation itself can be a micro-perforation or a macro-perforation with iris incarceration. The former is easily missed on slit-lamp evaluation and may require Seidel's test to elicit the presence of a leak.

Most perforations in ADDE are a result of sterile stromal melts. Nevertheless, a secondary infection is not uncommon and must be ruled out. A meticulous examination is imperative to determine the presence of microbial keratitis. Sterile perforations in ADDE usually have minimal cellularity. The presence of dense cellularity or a focus of infiltrate requires a complete microbiological workup to rule out a secondary infection. In such cases, the cornea adjacent to the perforation may be collagenolytic and the tectonically unstable area is often much larger than the size of the perforation. Thus, careful examination is essential to avoid underestimating the region of the cornea that needs to be managed. Another challenging scenario that is often encountered in eyes with ADDE is perforations with punched-out defects. Unlike routine perforations where the walls of the defect are sloping or collagenolytic, here an abrupt transition occurs from the area of perforation to the surrounding uninvolved stroma, which is of a normal thickness. As a result, these cases require techniques that provide volume replacement rather than those that merely bridge the surface of the defect. A detailed examination will help pick up these factors, which will determine the choice of surgery performed.

Preoperative workup

This includes both ocular and systemic workups. Corneal scrapings are smeared on slides and culture media for microbiological examination in cases with clinical suspicion of microbial keratitis. An anterior segment optical coherence tomography (OCT) might be of help in assessing the configuration of the perforation (concave or punched out). A gentle b-scan ultrasonography is carried out in cases with relative tectonic stability to rule out any posterior segment involvement. Patients should be subjected to a complete autoimmune panel to rule out any connective tissue disorder unless a diagnosis has already been established. This includes a complete blood count, c-reactive protein levels, erythrocyte sedimentation rates, rheumatoid factor, and antinuclear antibody profile. Since the patients may require systemic immunosuppression, baseline renal and liver function tests along with a Mantoux test and chest X-ray to rule out tuberculosis can also be completed in the same sitting. A physician consult can also be obtained to rule out any systemic involvement after the acute condition has stabilized.

Preoperative considerations

Counseling of the patient regarding the purpose of the surgery, the expected visual recovery, and the need for multiple interventions helps ensure compliance in the postoperative period. Based on the size of the perforation and the resources available, the surgery can be carried out under local or general anesthesia. Very small perforations can be managed under

topical anesthesia. During a peribulbar block, administration of local anesthesia should be done gradually to avoid any sudden increase in the intraorbital pressure. The use of adrenaline, hyaluronidase, and bicarbonate increases the permeability of the anesthetic agent and can decrease the overall dose administered.^[15-17] Addition of a facial nerve block can reduce the external pressure on the ocular contents induced by the movements of the lids. Similarly, a non-compressing lid speculum is preferred to obtain adequate exposure to the surgical field.

Surgical Modalities

Tissue adhesives

Principle

These can be synthetic (n-butyl-2-cyanoacrylate, isoamyl 2-cyanoacrylate, polyethylene glycol derivatives) or biological (fibrin glue). The former group is more commonly employed than the latter.^[5,18,19] Cyanoacrylate adhesives are ester derivatives of cyanoacrylic acid monomers, which polymerize in the presence of the anions within organic tissue to form a stable barrier across the area of defect.^[18] Optimal polymerization of the butyl derivatives of cyanoacrylate requires dry conditions.^[19] Apart from plugging the perforation, cyanoacrylate glue acts as a bacteriostatic agent against gram-positive as well as gram-negative organisms,^[20,21] and has also been shown to arrest stromal lysis in both infective and non-infective cases.^[22] Fibrin glue works by replicating the final steps of the human coagulation process and involves the thrombin-mediated conversion of fibrinogen to fibrin.^[23] In a manner similar to that of synthetic glues, the fibrin monomers are crosslinked to polymers by factor XIII, and this complex then adheres to the stromal collagen fibers.^[23-25]

Technique

The procedure can be carried out at the slit-lamp for eyes with micro-perforation with no frank egress of aqueous from the wound. The bed is dried with a surgical sponge and the cyanoacrylate glue is applied. A bandage contact lens (BCL) is placed over the adhesive. In cases with larger perforations, the surgery is performed under an operating microscope and the anterior chamber is formed with air or viscoelastic to prevent aqueous from leaking out of the wound. In the presence of iris incarceration, the iris is gently separated from the site of perforation before the application of the glue to ensure that the glue does not touch the intraocular contents. The surrounding epithelium along with any necrotic material is debrided to facilitate better adhesion of the glue. A thin layer is applied with the back of the surgical sponge or directly dropped onto the surface with a 26-gauge needle. Excess glue can be trimmed off. The anterior chamber is then formed with saline or air and a BCL is placed. Other techniques using discs made from sterile drapes to apply the glue have been described. The use of the discs aids in obtaining a smoother surface.^[26] In cases of iris incarceration, a double drape technique is described to prevent the glue from coming in contact with the iris and other intraocular structures.^[27] Another alternative to this is to create a mesh with 10-0 nylon sutures and allow tissue adhesives to polymerize within the mesh.^[28] However, passing multiple bites of sutures to create the mesh may be challenging if the cornea around the area of perforation is not tectonically stable.

The technique of fibrin glue application is similar. The glue is available as separate vials of fibrinogen and

thrombin, which are applied individually to the site of the perforation.^[23] A combined applicator is also available, which allows simultaneous administration of both components.^[23]

Tenon's patch graft (TPG)

Principle

Tenon's layer allows the epithelium to migrate over its surface.^[29] As the wound heals, the tissue gets integrated within the scar that forms in the area of the perforation.^[29,30] Thus, the volume deficit is also addressed to a certain extent. Fibroblasts within Tenon's layer can also help hasten wound healing.^[31]

Technique

Tenon's layer is harvested after separating it from the overlying conjunctiva. After debriding the surrounding epithelium, the layer is then tucked into the area of the defect with the help of fibrin glue. Sutures can also be placed over the area of the defect to provide additional support. The anterior chamber is then formed with air or saline and care is taken to avoid dislodging the graft. Similarly, a single layer of amniotic membrane (AM) can also be used as a patch graft to ensure a watertight seal as Tenon's layer itself is not impermeable to aqueous.^[29] Other modifications of the technique include tucking Tenon's layer within a stromal pocket or securing it to the bed with tissue adhesives.^[29]

Amniotic membrane transplantation (AMT)

Principle

The AM has a two-fold function as it acts as a scaffold for the migration of epithelial cells and also addresses the volume deficit that is often present in these cases. Factors such as epithelial growth factor, tissue inhibitors of metalloproteases, and transforming growth factor- β , which are present in the AM promote epithelialization.^[32] The AM also possesses anti-angiogenic properties and helps reduce the underlying inflammation by inhibiting active inflammatory cells.^[32] Additionally, studies have shown AM to have antimicrobial and wound-healing properties.^[33,34]

Technique

The AM can be fresh, cryopreserved, or dehydrated with fresh AMs having the greatest concentration of active biological agents.^[24,32] A multilayered amniotic membrane is usually required in cases with corneal perforation. The AM can be folded upon itself until the defect is filled or multiple smaller pieces can be fashioned to fit within the perforation. Fibrin glue is used between the layers and the entire complex can be further secured with a single layer of AM placed as a patch beyond the area of the defect. Monofilament nylon (10-0) can also be used to anchor the AM to the stromal bed. These sutures are passed through the uninvolved cornea to avoid any cheese wiring. The anterior chamber is formed with saline to ensure a watertight globe at the end of the procedure following which a BCL is usually placed.

Tectonic keratoplasty

Principle

The corneal donor tissue seals the perforation and provides complete volume replacement restoring the tectonic integrity of the globe. Penetrating as well as lamellar patch grafts and keratoplasties have been described.^[19]

Technique

Preoperative mannitol is recommended to reduce the volume of the vitreous, which in turn will decrease the vitreous

upthrust during intraoperative maneuvers. In cases of patch grafts, the size of the defect is measured, and a corneal graft of the corresponding size is trephined from a donor corneal button. Sometimes, the perforation might be too large to be covered using a patch graft. In such cases, a penetrating keratoplasty (PKP) is required. In addition to removing the necrotic tissue and restoring tectonic integrity, PKP also helps in reducing the microbial load in infected cases.^[35]

Trephination of the host cornea can be a challenge when a corneal perforation is present. This is usually carried out by marking the area to be trephined and a manual trephination is performed. The remaining steps are similar to that of a routine keratoplasty.^[36] A lamellar graft can also be attempted to avoid an open-sky procedure. Here a manual dissection of the stromal layers is carried out and a layer-by-layer dissection from the periphery to the center has been described for the same.^[37] If the perforation is larger, then the anterior chamber is injected with fibrin glue, which seals the perforation and this is followed by the manual stromal dissection.^[38] Postoperatively, the glue gets absorbed from the anterior chamber. A peripheral corneal perforation not amenable to PKP can be managed with shaped, non-circular grafts such as crescentic keratoplasties.^[39] The graft is secured with interrupted 10–0 nylon sutures. In cases of corneal patch grafts (CPG), sources of donor tissue can include the anterior stromal cap obtained after preparing the lenticule for Descemet stripping automated endothelial keratoplasty and small incision lenticule extraction lenticules.^[40–42] Grafts in these cases have epithelialization issues and thus they can be combined with an AMT to help improve the ocular surface. Additionally, a generous tarsorrhaphy is also advocated in these cases.

Conjunctival flap

Conjunctival flaps are reserved for cases with perforations where tissue adhesives, TPG, and AMT are not feasible, and a corneal tissue is either not available or a poor outcome of the transplant is anticipated as in cases with MMP. These flaps can completely cover the cornea or be in the form of a partial flap that covers only the affected area.^[43,44] Superior forniceal conjunctival advancement pedicles such as Gundersen flap or Cies's racquet conjunctival flap are described.^[45] The conjunctiva is dissected from Tenon's layer and secured to the corneal bed with sutures. In eyes with significant volume loss, conjunctival flaps can be combined with an amniotic membrane as well.^[46] The flap acts as a biological bandage over the affected area and also provides an influx of mediators from the blood vessels, which aid in faster healing.^[46] This procedure has good efficacy of up to 95%; however, the visual and cosmetic outcomes are suboptimal.^[47,48] Thus, it is preferred in eyes, which do not have a good visual prognosis.

Scleral patch grafts

Scleral patch grafts with tissue adhesives have also been described as an alternative to CPG in cases with moderate-sized perforations in immune-mediated diseases. The advantage of scleral patch graft is the ease of availability, higher tensile strength, and no risk of rejection.^[49] A lamellar scleral patch fashioned to match the size of the corneal perforation is placed on the site, and a tissue adhesive is applied to secure the patch in place and cover it with a BCL. This technique has shown promising results in non-infectious cases.^[50,51]

Choice of procedure

Various surgical modalities are available for the management of corneal perforations, and the choice of procedure is based on the severity of the defect, the status of the surrounding cornea, and the underlying disease [Fig. 1]. A stepwise approach has been presented below, which details the different surgical techniques opted in perforations of varying sizes [Fig. 2].

Small perforations (<3 mm)

These perforations are typically managed with tissue adhesives. The outcomes of cyanoacrylate glue vary in the literature with anatomical success ranging from 20–90%.^[52–54] Larger defects and frank perforations have been associated with a higher failure rate.^[52,53] The success of treatment also depends on the etiology and location of corneal perforation. Tissue adhesives have a lower success rate in peripheral corneal perforations and those with herpetic etiology.^[55] Several of these cases eventually require a keratoplasty to manage the corneal perforation.^[1] Case selection thus plays a very important role in ensuring optimal outcomes following this procedure. Fibrin glue can be used in sealing perforations of up to 2 mm.^[56] Sharma *et al.*^[57] compared fibrin glue to cyanoacrylate glue and found a faster response with the former with lesser toxicity-related issues. The use of cyanoacrylate glue requires a BCL as the polymerized compound has an abrasive nature. Thus, this glue is avoided in eyes where difficulty in the placement of a BCL is anticipated. This is typically seen in cases with cicatrizing conjunctivitis where there is forniceal shortening or symblephara, which can cause recurrent displacement of the BCL. In such cases, a TPG can be used to plug the site of perforation. Multilayered AMs are usually not required for very small perforations.

Moderate perforations (4–6 mm)

Here the management depends upon the configuration of the perforation. If the defect has sloping edges, a tissue adhesive can still be employed. However, if a volume deficit is present or if the defect has punched out margins, then a TPG or multilayered AM is the preferred technique. Good clinical efficacy of TPG has been reported in cases of moderate-sized corneal perforations.^[58,59] The integrated tissue results in a corneal scar with good tensile strength.^[30] Similarly, multilayered AMT has good outcomes in the management of perforated corneal ulcers, with epithelization occurring 2–3 weeks after the procedure.^[60,61] Better success rates have been observed when the AM is secured with fibrin glue as opposed to sutures.^[61] The resultant scar formation may require a keratoplasty for visual rehabilitation. The use of AM in cases with ADDE has the added advantage of improving the ocular surface milieu and has been shown to better the inflammatory scores in these patients.^[62] More than one AMT sitting may be required to achieve tectonic stability.^[63] CPG are preferred in cases with peripheral perforations that are not amenable to a TPG or AMT. Patch grafts are also preferred over TPG and AMT in cases with superadded infection, which cannot be managed by tissue adhesives. However, the outcomes are better in cases with sterile perforations when compared to those with microbial keratitis.^[40] Rarely in cases with poor visual potential, a conjunctival flap can be performed.^[64]

Large perforations (>6 mm)

Large perforations and moderate perforations, where the surrounding cornea is not tectonically stable, require

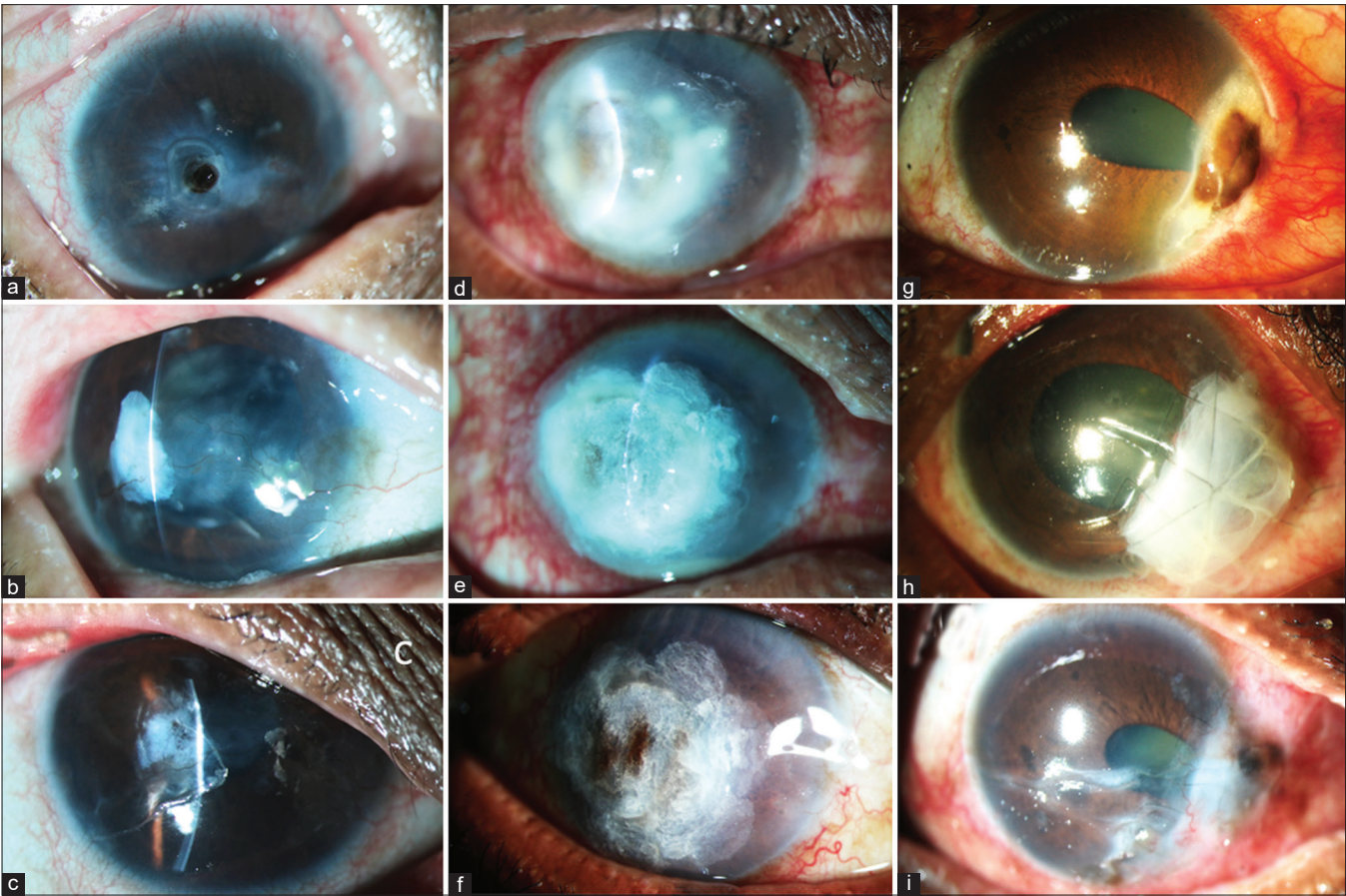


Figure 1: (a) Central perforation in a case of rheumatoid arthritis with surrounding punched-out margins. (b) The patient underwent Tenon's patch graft and had a well-formed globe at the end of 3 months. (c) Tenon's layer was integrated within the scar as seen in the ninth-month visit. (d) Paracentral perforation with a shallow anterior chamber and significant surrounding infiltration. (e) Tissue adhesive with the reformation of the anterior chamber was carried out. (f) Resolution of the infiltrate beneath the glue with a tectonically stable globe was noted. (g) Peripheral perforation with iris prolapse. (h) multi-layered amniotic membrane graft secured with 10–0 monofilament nylon sutures was performed, which restored the tectonic support of the globe. (i) The eye remained stable with a scar formation, 7 months following the procedure

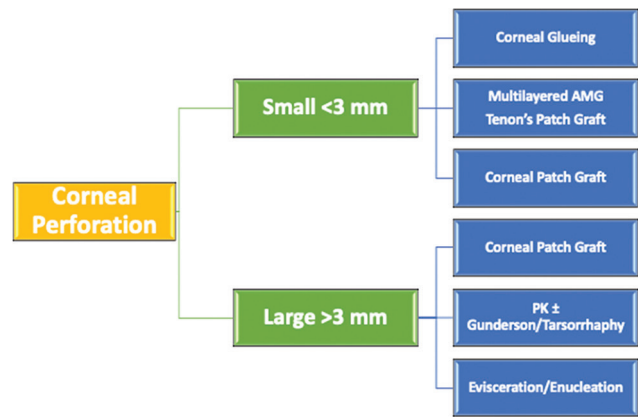


Figure 2: Algorithmic approach to a patient of corneal perforation in dry eye disease. AMG-multilayered amniotic membrane transplantation, PK-penetrating keratoplasty

full-thickness corneal transplantation. These grafts may be combined with AMT and tarsorrhaphy to help preserve the donor corneal epithelium. Several studies have reported that although good anatomical outcomes are present after

penetrating keratoplasties in primary and secondary Sjogren's syndrome, the functional outcomes are not the same.^[6,65] Similarly, the outcomes in eyes with cicatrizing conjunctivitis due to SJS or MMP are poor, with limited visual recovery.^[66] The immune dysregulation in these patients leads to a high risk of graft rejection, and the 5-year graft survival rates in these eyes are significantly lower than those of grafts done in eyes without autoimmune disorders.^[67,68] The concurrent presence of LSCD in these eyes is an additional risk factor that hampers recovery of visual function. Furthermore, these eyes are prone to recurrent attacks, and performing repeat grafts in eyes with ADDE is not desirable.

Postoperative Considerations

In addition to the general postoperative considerations in the above-mentioned techniques,^[19] other concerns in cases of perforations in ADDE include delayed epithelialization and chances of re-perforation.

Delayed epithelialization is consequent to the altered tear film, coexisting LSCD, and unhealthy ocular surface affecting the epithelial healing. Copious use of lubricants, preferably preservative-free is advisable. However, despite ensuring

adequate tear supplementation, the perforation is expected to take a longer duration to heal completely as compared to normal eyes. It is important to not be in a haste and forcibly remove the tissue adhesive, but to allow it to dislodge by itself. Premature removal of the glue is likely to result in a re-perforation. History of the use of topical anesthetics^[69] or topical non-steroidal anti-inflammatory drugs (NSAIDs)^[70] should be asked. These drugs are likely to cause corneal melts and patients must be advised to discontinue their use. It is also important to note that stromal vascularization is expected and must not be considered as an indication for early removal of the glue.

Similarly, in cases of TPG and tectonic keratoplasties (PK or CPG), delayed epithelial healing and persistent epithelial defects are expected and BCL might be needed for a longer time. When preservative-free lubricants are not sufficient, autologous serum eye drops are an alternative to aid in the healing process.^[71] It is worthwhile to keep a low threshold to perform AMT in these cases to improve graft survival. The importance of tarsorrhaphy cannot be undermined and when not performed concurrent with the PK, it must be considered during the postoperative course.

Re-perforation is another common complication in these cases. This could be a result of delayed epithelial healing or an ongoing immune-mediated stromal lysis because of the underlying systemic disease. Another important cause of re-perforation is a secondary microbial infection.

In addition to the above-listed measures to ensure adequate epithelial healing, it is important to arrest stromal melt and adequately treat any co-existing infection. Stromal melt resulting from an immune-mediated systemic disease such as RA, MMP, SJS, SS, or ocular GVHD is controlled using topical and systemic immunosuppressive therapy.^[72] Additionally, oral doxycycline can be considered owing to its anti-collagenolytic properties.^[73] Neurotrophic keratopathy in patients suffering from herpes zoster ophthalmicus or diabetes mellitus is another cause of stromal melt, particularly following epitheliopathies or secondary infections.^[7] Prompt AMT or tarsorrhaphy helps avoid complications in these cases. Lastly, microbial infection complicating the perforation is an important cause of re-perforation. Avoiding a secondary infection, therefore, becomes important. The sudden onset of unbearable pain or appearance of hypopyon is highly indicative of secondary infection. It is important to have a high index of suspicion, particularly in cases of tissue adhesives, TPG, or AMT, where visualization of underlying stroma is obscured. Careful evaluation of the surrounding cornea for stromal infiltration, endothelial exudates, anterior chamber inflammation, and hypopyon helps detect infection and initiate management.

Visual Rehabilitation

Once the perforation is sealed and the scar is formed with adequate stabilization of the ocular surface, visual rehabilitation is considered. Modalities used for visual rehabilitation depend on the size and location of the scar. In most cases with peripheral scars, not involving the visual axis, spectacles help restore functional vision. In cases where spectacles are not helpful, and in cases with central scars, contact lenses could be tried. Scleral contact lenses are an invaluable tool in the armamentarium of any ophthalmologist handling patients with

ADDE. These lenses provide a fluid reservoir that addresses the dry eye component by improving tear osmolality and surface staining.^[74,75] These changes better the symptomatology profile and overall quality of life in these cases.^[75,76] They also improve visual acuity by reducing astigmatism induced by corneal scarring and surface irregularities.^[76] In cases where visual improvement with contact lenses is not significant, optical iridectomy should be considered in a sector where the cornea, as well as the lens, is clear.^[77,78] When visual improvement remains unsatisfactory, the patient should be evaluated for a possible cataract. Cataract formation is common in these cases due to ongoing inflammation following surgery, or due to the chronic steroid treatment in cases with systemic diseases. Cataract surgeries in such cases must be considered at an early stage to restore vision. In cases where all the above measures fail, keratoprostheses are considered. Boston keratoprosthesis type 2,^[79] Pintucci keratoprosthesis,^[80] osteo-odonto keratoprosthesis,^[81] and LVP Kpro^[82] are some of the examples that can be used in such cases. It is crucial to understand that these eyes are not suitable for keratoplasties, and performing a PK in such scenarios might lead to an 8 × 8 mm necrotic cornea following a graft, which is more difficult to manage than a 3 × 3 mm perforation that the patient originally presented with. However, in desperate situations, a PK with Gundersen flap can be attempted [Fig. 3].

Recent Advances and Future Directions

Although the surgical techniques detailed above can provide an anatomically stable globe, the functional and visual outcomes of these procedures are still suboptimal. They necessitate the presence of an eye bank infrastructure and because these cases are typically an emergency, these resources may not be available. Thus, there is ongoing research that strives to address these issues and at present two avenues are being explored for the same. The first is the development of an inexpensive and biocompatible tissue adhesive, which not only seals the corneal perforation but is also optically clear. One such low-cost, naturally derived biopolymer is gelatin methacryloyl (GelMA).^[83-85] This adhesive has similar stability as cyanoacrylate glue with good transmittance rates. Unlike cyanoacrylate glue, this sealant does not induce significant tissue inflammation and allows good wound healing to occur.^[83] The other option that can be considered in these cases is a bioengineered cornea. Several attempts are being made to structure one that closely mimics the human tissue. These constructs contain synthetic material with limbal and mesenchymal stem cells that can replenish and maintain the normal corneal anatomy.^[86-87] This will be particularly useful in larger perforations, which are not amenable to tissue adhesives or AMT and require the availability of a cornea donor tissue. Both the adhesives and artificial cornea are being experimented upon in animal models and the extension of the same in human trials is awaited.^[88,89] The use and durability of these novel agents in the context of ocular and systemic inflammation, that is, usually present in patients with ADDE will have to be explored in future studies.

Conclusion

Corneal perforations in eyes with ADDE require a multifaceted approach, which not only restores the tectonic support of the globe but also addresses the tear film instability, surface inflammation, and the underlying pathology. Preoperative

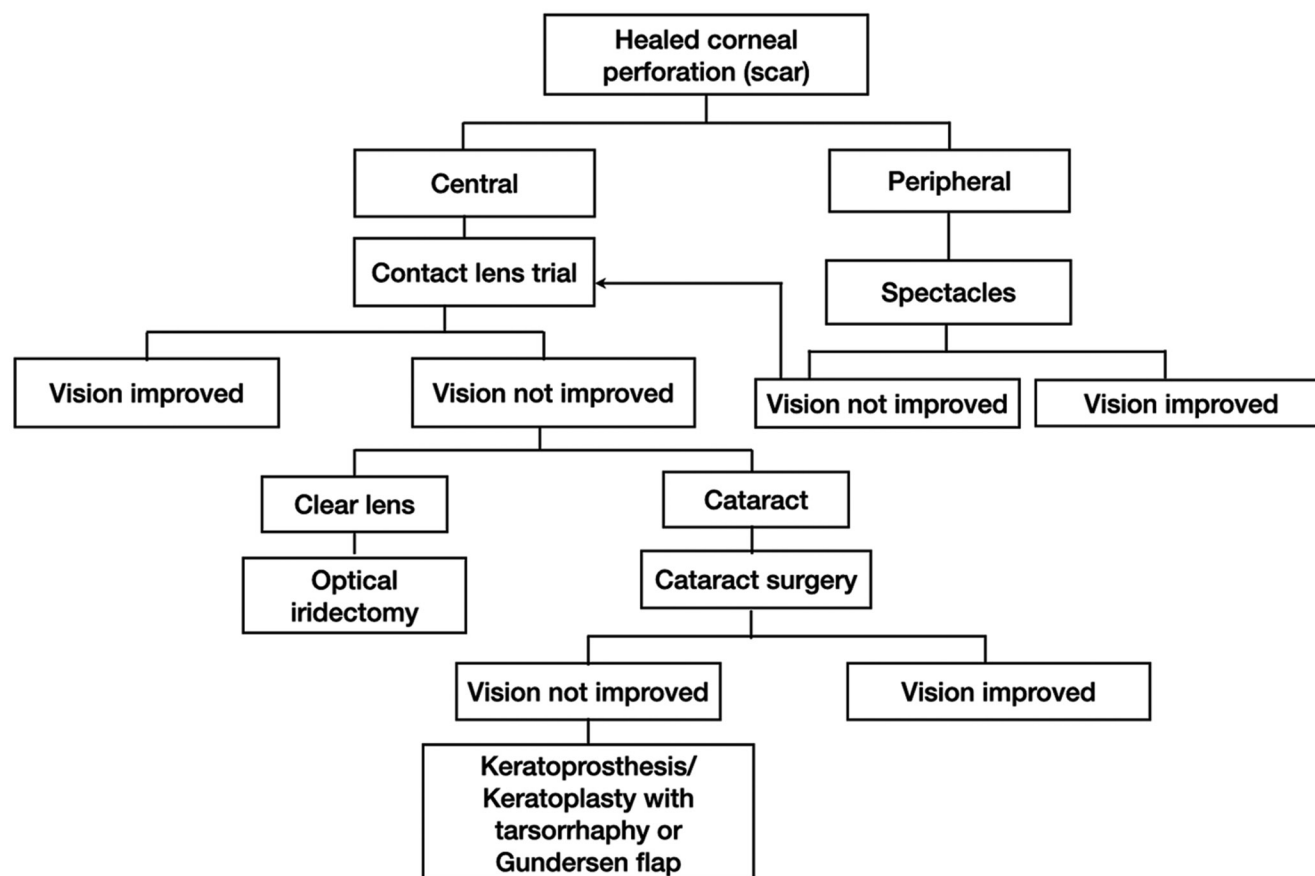


Figure 3: Approach for visual rehabilitation in a patient with healed corneal perforation in dry eye disease

counseling making the patient aware of the slow healing process, possible need for multiple surgeries, and need for topical and systemic immunosuppressive therapy helps improve patient compliance post-operatively. A careful ocular examination is required to pick up subtle findings, which will affect the outcome of the procedures and the subsequent postoperative course. Several surgical modalities are available for the management of these perforations and the choice of one technique over the other is determined by the size and location of the defect. It is important to bear in mind that these eyes are prone to delayed epithelial healing and recurrence of perforation. Topical and systemic management for adequate epithelial healing and arresting stromal melt is essential to avoid these complications. Visual rehabilitation needs spectacles or scleral contact lenses and cataract surgery can be considered in cases that have dissatisfactory vision with these modalities. Keratoplasties are best avoided, and lack of visual improvement following lens replacement surgery should be managed using keratoprosthesis. Overall, a careful examination and a low threshold for managing possible complications help improve postoperative recovery.

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Conflicts of interest

There are no conflicts of interest.

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