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REVIEW

Retrocorneal membranes after penetrating keratoplasty

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Abstract

Purpose. To present a rare complication after penetrating keratoplasty.
Methods. The review presents the main types of retrocorneal membranes. The incidence, pathophysiology, diagnosis and treatment are shown for all of them.
Conclusions. The evaluation and management of a membrane behind the posterior surface of the cornea is a special challenge for ophthalmologists. The clearer understanding of the pathogenesis of the different types of retrocorneal membranes may allow a more specific and efficient treatment.
Keywords: retrocorneal membrane, epithelial downgrowth, fibrous ingrowth, retained host's Descemet's membrane.

Introduction

Penetrating keratoplasty is a surgery with indications in many kinds of corneal diseases: keratoconus, bullous keratopathy, corneal dystrophies, corneal infections et al.[**1**]. There are a lot of complications of this surgery: wound leak, endophthalmitis, primary graft failure, incidents related to sutures, persistent epithelial defects, high astigmatism, graft rejection, recurrence of disease [**1**].

The terminology for retrocorneal membranes is not very clear. Generally, the term includes all membranes located behind the cornea. The most devastating type of retrocorneal membranes appears during epithelialization of the anterior chamber; the etiology, evolution and treatment of this entity was a great concern for many generations of ophthalmologists. Not all membranes situated behind the posterior face of the cornea represent epithelial downgrowth. There is also a fibrous proliferation in the anterior chamber and some degenerative and inflammatory processes that can produce membranes on the posterior surface of the cornea. Some inadequate surgical procedures can also produce a different type of retrocorneal membrane [**2**].

A classification of retrocorneal membranes includes:

1. Epithelial downgrowth
2. Fibrous ingrowth
3. Inflamatory membranes
4. Retained host's Descemet's membrane
5. Descemet's detachment of the graft

1. Epithelial downgrowth

Epithelial downgrowth represents the epithelial invasion into the anterior chamber. The terminology for this entity has changed in

the last two decades. Classically, the terms epithelial ingrowth and epithelial downgrowth have been used to describe the epithelialization of the anterior chamber. In the era of LASIK, epithelial ingrowth has become a term used for epithelialization within the cornea, under the flap, and epithelial downgrowth for epithelialization that extends into the anterior chamber [**2**].

Epithelial downgrowth is an aggressive and sight-threatening complication, that appears after ocular trauma or different types of ocular surgeries.

Incidence

The clinical incidence of this entity is difficult to appreciate, because the diagnostic criteria are not very clear and the cases are relative rare. Cataract extraction is the most frequent cause of epithelial downgrowth [3,4]. In a 50-year review of proven cases of epithelial downgrowth, cataract was the cause for 59% of cases [4]. Older studies have reported incidence of 1,1%, but newer studies reported lower incidences of 0,06-0,2% [**2**]. Penetrating keratoplasty has a lower incidence of this complication than cataract surgery, but an incidence of 0,27 has been reported [**5**]. It seems to be the third cause of epithelial downgrowth [**4**].

Pathogenesis

Epithelial downgrowth occurs when epithelial cells from the conjunctiva or cornea migrate through a wound and proliferate in the anterior chamber. The epithelium grows as a sheet, over the cornea, iris, trabecular meshwork, lens or artificial lens and ciliary body. The source of epithelial cells is unclear; both surface conjuctival and corneal epithelium seem to be involved. Sections of enucleated specimen sometimes show continuity between the surface epithelium and the epithelial downgrowth into the anterior chamber through a fistulous tract. Goblet cells may be found, so the source of epithelial cells can be conjunctival epithelium [**2**]. However, in cases of epithelial downgrowth after penetrating keratoplasty, the goblet cells are absent, so the epithelial source must be the corneal epithelium [**6**].

An entry site into the globe is necessary, although insufficient for the development of epithelial downgrowth. There are some risk factors: multiple intraocular surgeries, incomplete or delayed wound healing, wound fistulas, iris or vitreous incarceration into the wound, implantation of epithelial cells with instruments [**7**].

The ingrowth of the epithelium produces profound inflammation and tissue damage. The loss of the blood-aqueous barrier in hypotonus, inflamed eyes may provide growth factors necessary for epithelium to proliferate [**2**].

Diagnosis

The onset of the disease is variable, from a few days to many years after the surgery [**4**]. They have nonspecific symptoms such as pain, photophobia and blurred vision.

Epithelial downgrowth appears as a translucent cystic or membranous growth with a scalloped border involving the posterior corneal surface or anterior iris in the area of the surgical incision. The membrane extends from the wound and rarely more than halfway across the cornea. Other potential findings that suggest epithelial downgrowth include distortion of the pupil and microcystic corneal edema overlying the affected area of the cornea.

Many eyes with epithelial downgrowth develop glaucoma. Initially the intraocular pressure may be low due to the filtering fistula. The mechanism of glaucoma is complex: shallow anterior chamber and inflammation predispose to peripheral anterior synechiae formation. Pupillary block develops when the membrane covers the pupil. Secondary open-angle glaucoma is the most important component. The membrane can cover the angle and the trabecular meshwork is disorganized under the epithelium [**2**].

If the diagnosis is in doubt, a spot of argon laser photocoagulation is applied to the area overlying the iris. The argon laser settings recommended are: 0,1-0,2 s, 100-200 microns in spot size and power of 100-200 mW. If a membrane is present, the laser spot will cause the tissue to blanch and whiten, while laser applied to normal iris will result in a sharp, darkened burn, much less visible.

The specular microscope can also confirm the diagnosis by visualizing the edge of the epithelium by focusing posterior to the endothelium [b].

Finally, nonkeratinized squamous epithelium on the posterior face of the cornea or on the anterior surface of the iris is diagnostic for epithelial downgrowth [**2**].

Treatment

It is important to first grossly remove the invading epithelium. In general, this is typically done via a large en-bloc excision of any involved tissue along with a full-thickness corneoscleral graft. However, if only the posterior corneal surface, drainage angle or ciliary body is involved, the invading epithelium can be devitalized using cryotherapy. Endothelial loss typically accompanies cryotherapy and a corneal transplant may be needed at a later time. It is important to choose the surgical technique that produces the least damage on the noninvolved tissues.

In managing the glaucoma associated with epithelial downgrowth, glaucoma drainage devices have been the mainstay of treatment. Because outflow is profoundly reduced, medical treatment alone typically does not sufficiently lower eye pressure. Even with the use of anti-metabolite agents, trabeculectomy usually fails due to the invasion of sheets of epithelial cells [9]. However, glaucoma drainage devices have better success in maintaining IOP control and some advocate leaving the intraocular portion longer or inserting the tube through the pars plana to minimize the invasion of the epithelial cells. Cycloablative procedures can also be used to lower the IOP. Endoscopic photocoagulation was effective in lowering intraocular pressure with less complications than cryotherapy.

2. Fibrous ingrowth

Fibrous ingrowth is a fibrous proliferation and invasion of the tissues surrounding the surgical site into anterior chamber [**2**].

Incidence

Estimates of the incidence of fibrous ingrowth vary widely, because the diagnosis is difficult to make and is frequently confused with epithelial downgrowth. The disease is less aggressive and less likely to result in enucleation, that allows for a clear diagnosis [**3**]. Penetrating keratoplasty is the most important source of fibrous ingrowth [**2**]. The disease was described after cataract surgery, glaucoma surgery; practically, almost any penetrating ocular event may promote fibrous proliferation [**2**].

Pathogenesis

Risk factors of fibrous ingrowth appear the same as those for epithelial downgrowth. The mechanism favoring the formation of fibrous ingrowth or epithelial ingrowth remains poorly understood. The source of fibroblasts is clearly distinct from the source of epithelial ingrowth. Subepithelial connective tissue and corneal stromal fibroblasts participate in normal traumatic and surgical wound healing and an exuberant response leading to fibrous ingrowth can be imagined [**2**]. Recurrent hemorrhage from a vascularized and inflamed wound margin may provide a fibrin scaffold for fibrous proliferation into anterior chamber. Also, the scar tissue in the corneal wound is an apparent source of membrane component [**10**].

Diagnosis

The diagnosis of fibrous ingrowth implies high clinical suspicion. The risk factors are the same to those for epithelial ingrowth. Symptoms are nonspecific and patients are usually not uncomfortable. The fibrous ingrowth appears as a translucent membrane on the posterior surface of the cornea, around the incision or wound. Unlike the epithelial downgrowth, this membrane may be vascular [**2**]. The cornea corresponding to the membrane is edematous. Intraocular inflammation is often present in the anterior chamber. The prognosis of this disease is variable; the invasion of the membrane is frequently limited, with less impairment of visual function compared to epithelial downgrowth. Glaucoma is frequent, but also less aggressive than with epithelial downgrowth [**2**].

No ancillary diagnostic tests have been useful to confirm the diagnosis of fibrous membrane [**11**].

Treatment

Medical treatment of inflammation, glaucoma and corneal edema is sufficient in many cases and fibrous proliferation matures into a quiet scar, that does not extend. Sometimes, uncontrolled proliferation may occur. Surgery is a very good option. Unlike epithelial downgrowth, removal of all proliferation is not necessary, because the remnants generally do not relapse.

Viscodissection of the fibrous membrane out of the visual axis is a minimal invasive and successful surgery [12].

3. Inflammatory membranes

An postoperative inflammation may produce a fine, linear opacity behind the cornea. Generally, these membranes are on the surface of the iris and in the pupillary area, but sometimes they can cover the angle. After penetrating keratoplasty, they may have contact with the host-graft junction. Often, the presence of a layer of viscoelastic substance in an inflamed eye may mimic a membrane binding the host-graft junction with the pupillary border.

The diagnosis is clinic. The onset is early postoperative and unlike the previous types of membranes, inflammatory membranes respond well to anti-inflammatory treatment.

4. Retained host's Descemet's membrane

Retained Descemet's membrane is a rare complication of penetrating keratoplasty. This complication appears after incomplete removal of the host cornea; after partial trephination an opening into the anterior chamber is made and then a curved corneal scissors is used to complete the corneal removal. Especially in an edematous cornea, it could occur that the lower blade is placed intrastromaly, anterior to Descemet's membrane, so that, when the button is lifted from the eye, a portion of Descemet's membrane is left behind.

Pathogenesis

The mechanisms which lead to Descemet's membrane retention are:

- incomplete trephination of the cornea and completing the cut with scissors
- longstanding corneal edema that causes loosening of the attachment of the Descemet's membrane
- marked hypotonia of the eye with decrease of the pressure during the cut
- marked fibrosis of the scars in case of retransplantation.

Diagnosis

The diagnosis is clinic. It appears as a wavy membrane that creates a supranumerary anterior chamber behind the graft on the first postoperative control with slit lamp examination. Initially, the membrane is quite transparent, then it is possible to become opaque. The time needed for the opacification of the retained Descemet's membrane is due to the thickness of the residual stroma retained along with the Descemet's membrane [**13**]. The cornea is clear; it is possible to become opaque later in the evolution of this type of membrane. The retained Descemet's membrane can compromise the endothelium of the graft by contact injury or by limiting diffusion of aqueous humour nutrients.

Ultrasound biomicroscopy and optical coherence tomography of the anterior segment can be very useful for the diagnosis. Both of these investigations can reveal the membrane, the space between the membrane and cornea or iris and the root of the membrane near the host-graft junction.

Treatment:

The best way to avoid this complication is to inspect the wound carefully and to try to pick up the iris with a fine tipped forceps; if it is possible to grasp the iris, there is no problem; if it is not possible, it is necessary to check again if you cut the Descemet's membrane. It is important to know that the loss of aqueous humour during trephination indicates that the Descemet's membrane is perforated in one or more places, but it is possible that it not completely cut.

Surgical treatment is recommended, if the potential best corrected visual acuity is limited, in three circumstances:

-the membrane begins to opacify

-the graft viability is compromised by contact with the retained tissue

-there is reduced diffusion and sequestration of aqueous between the Descemet's membrane and cornea resulting in an increased rate of endothelial cell loss [**13,14**].

There are more methods:

-surgical excision – it is easier to use a 23 or 25 Ga forceps and scissors for vitreoretinal surgery, so that the incision is less than 2 mm with minimal risk for astigmatism, infection or contact with the endothelium of the graft

- Yag-Nd laser opening of the membrane, allowing a normal circulation of the aqueous in the globe and a clear visual axis without an open surgery [**14**].

The results are very good. Unlike other types of retrocorneal membranes there are no chances for recurrences.

5. Descemet's detachment of the graft

Detachment of Descemet's membrane of the graft can be a major postoperative complication; it results in persistent epithelial edema, decreased visual acuity and if it is not treated can lead to early graft failure. This complication is more frequent after cataract surgery; the wound manipulation is more aggressive in cataract surgery; the phaco probe can detach the Descemet's membrane when entering the globe through a tight incision; after penetrating keratoplasty it is possible to detach the Descemet's membrane when the donor tissue is edematous and the adherence between Descemet's membrane and stroma becomes looser.

Clinic

The detached Descemet's membrane appears like a fine opacity behind the graft; unlike the previous type of retrocorneal membrane – retained host's Descemet's membrane, the cornea is edematous, because there is no endothelium and of course no endothelial pump to dehydrate the cornea. There is also a supranumerary anterior chamber, but generally the space between cornea and membrane is quite flat.

Treatment

The Descemet's membrane can be reattached; it is necessary to inject air into the anterior chamber, so that it pushes the membrane onto the cornea; it is necessary that the anterior chamber is filled completely with air and the globe pressurized; it is safer if the patient stays an hour in the operating room and the pressure of the eye is checked in this period; if the pressure decreases, the air is reintroduced through a paracentesis.

Conclusions

The evaluation and management of a membrane behind the posterior surface of the cornea are a special challenge for ophthalmologists. Some of them are very aggressive and difficult to treat – epithelial downgrowth, other can be solved only with medical treatment – inflammatory membranes. Accurate history, including details about previous surgery and postoperative course are very important. Follow-up must detect any worsening of the evolution, but can produce also some agreeable surprises – no worsening evolution of a fibrous membrane. The clearer understanding of the pathogenesis of the different types of retrocorneal membranes may allow a more specific and efficient treatment.

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