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SHORT COMMUNICATION

Rapid development of band keratopathy of corneal graft associated with treatment with intracameral recombinant tissue plasminogen activator for postoperative fibrin reaction

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PURPOSE. *To report a corneal transplant complication associated with intracameral recombinant tissue plasminogen activator (rTPA) treatment of postoperative fibrin reaction.*
METHODS. *In a 71-year-old patient, a triple procedure was performed for perforated rheumatic ulcer and secondary cataract.*
RESULTS. *A dense band keratopathy developed rapidly within 36 hours after the use of intracameral injection of rTPA for the treatment of a dense fibrin clot.*
CONCLUSIONS. *This is the first report of rapid development of massive band keratopathy in a corneal graft after triple procedure and treatment with intracameral rTPA. Intracameral rTPA should be used with caution in patients with attenuated endothelium. (Eur J Ophthalmol 2007; 17: 433-6)*

KEY WORDS. *Band keratopathy, Corneal graft, rTPA, Recombinant tissue plasminogen activator, Postoperative fibrin reaction*

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INTRODUCTION

Intracameral recombinant tissue plasminogen activator (rTPA) is successfully used for the treatment of severe and prolonged postoperative fibrin reaction. The procedure is considered to be safe and hardly shows side effects such as hemorrhage (1-4). rTPA can be used with good results for excessive fibrin response after penetrating keratoplasty (3). We report a case of pronounced band keratopathy of corneal graft shortly after treatment with rTPA.

Case report

A 71-year-old man presented with a perforated corneal ulcer of the left eye. He complained of decreased vision for 3 days and moderate pain in the left eye. The patient had a longstanding history of rheumatoid arthritis (PcP) and his past ocular history was remarkable for a chronic rheumatoid corneal ulcer with marked corneal thinning, which reportedly has been treated by the patient's ophthalmologist for many years.

According to the patient's ophthalmologist, the situation had been stable for years until the ulcer recurred a few days previously and rapidly worsened. The patient was not HLA B27 positive and there were no episodes of iridocyclitis in the past. There were no signs of band keratopathy bilaterally when the patient presented to our eye emergency room. Slit lamp examination showed a perforated central corneal ulcer (Fig. 1A). The anterior chamber was very flat with less than 1 mm maximum depth. There was a mild cellular reaction in the anterior chamber, but no fibrin and no incarceration of the iris. Funduscopy was not possible due to opacity of the lens. Ultrasound examination did not reveal infiltration of the vitreous or retinal pathology. There were no signs of a bacterial or fungal

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corneal infection in the left eye. Examination of the right eye did not reveal any abnormalities apart from a mild corticonuclear cataract. The left eye was treated with a bandage contact lens and topical (ofloxacin eyedrops) and systemic antibiotic therapy for prophylaxis of infection. Two days after presentation an uncomplicated triple procedure (penetrating keratoplasty and cataract surgery with phacoemulsification and implantation of a foldable acrylic posterior chamber intraocular lens [AcrySof MA60BM 22.0 Dpt., Alcon, Fort Worth, TX, USA]) was performed. The graft was from a 72-year-old donor, contained 2900 endothelial cells, did not show calcifications, and contained no arcus. Histology of the removed button showed a sterile ulcer without calcification.

Best-corrected visual acuity improved from light perception preoperatively to 20/400 on the first and second postoperative day. Postoperatively the anterior chamber was deep, the graft was well adapted, and the endothelium appeared normal without signs of endotheliitis. There were mild Descemet folds and a moderate fibrin reaction in the left eye. The patient was given topical steroids (prednisolone acetate), antibiotics (ofloxacin), artificial tears (containing no preservatives and no phosphate), and atropine eyedrops. The amount of fibrin increased over the following days, although an intensive therapeutic regimen with topical (prednisolone acetate eyedrops), subconjunctival, and systemic steroids (dexamethasone) was applied. As endophthalmitis could not be excluded the patient received intravenous and topical antibiotics (ofloxacin eyedrops) although there was only a mild cellular reaction in the anterior chamber and daily ultrasound examinations of the globe were not suspicious of endophthalmitis.

The corneal graft remained clear, and the sutures were well adapted, the intraocular lens was stable in the capsular bag throughout the entire postoperative course. The graft was completely re-epithelialized on the fifth postoperative day. As the fibrinous membrane became increasingly dense we decided to perform an injection of rTPA in the anterior chamber on day 9 after keratoplasty (Actilyse, Boehringer Ingelheim, Germany). The phosphate buffer containing the TPA was 1:10 diluted with physiologic saline prior to injection. The rTPA was injected through a temporal paracentesis at the 3 o'clock position at the limbus without complications (0.2 mL containing 20 µg rTPA).

Eighteen hours after the procedure almost complete resolution of the fibrin was noted and visual acuity rose from hand movements preoperatively to 20/200 in the left eye. No epithelial defect was seen at the time of formation of the calcific deposits as a possible predisposing factor. However, 36 hours after the injection marked band keratopathy was visible that increased only slightly over the next weeks (Fig. 1B). Visual acuity decreased to hand movements within 1 week. Corneal abrasion using a hockey knife, polishing of Bowman layer, and ETDA chelation was performed 6 weeks after the rTPA injection in order to remove the calcific deposits. Histologic examination (van Kossa stain) of the removed material was consistent with band keratopathy. The granules were presumably only localized to Bowman's layer as only a superficial keratectomy was done and no stromal tissue was found on histology. After keratectomy the corneal surface appeared rather smooth with a mild amount of remaining calcium deposits (Fig. 1C).

Twelve months after the procedure the graft showed a stromal haze and a mild amount of recurrent band keratopathy peripherally. Visual acuity was stable at counting fingers at 3 feet. The patient opted not to undergo additional surgery at this time as he sustained a hip fracture a few weeks after the last follow-up visit which required urgent treatment.

DISCUSSION

This is the first report of rapid onset of band keratopathy in a corneal graft following intracameral rTPA injection for postoperative fibrin reaction after a triple procedure.

In our case the strong postoperative fibrin reaction probably was due to the previously perforated ulcer, the underlying rheumatoid disease, and the complicated triple procedure necessitating the use of steroids and even intraocular rTPA.

Rapid onset of band keratopathy after rTPA use has been reported in rare cases after cataract surgery necessitating superficial keratectomy in some cases (5-6).

Our patient did not show any signs of band keratopathy before the rTPA injection was performed. There was no indication for ocular surface dryness. The rapid development and progression of band keratopathy was striking.

In previous reports transient endothelial dysfunction or defects have been considered to be important risk factors responsible for the development of rapid band keratopathy after the use of rTPA (5, 7). In our patient the endothelium was presumably compromised due to the triple pro-

cedure and because it was a corneal graft. In rabbit experiments it could be shown plausibly that both phosphate of the rTPA buffer and calcium from the fibrin clot and aqueous can diffuse into the corneal stroma through the endothelial defects (7). Once the transitory corneal edema is removed by the endothelial pump calcium phosphate is precipitated—preferably in Bowman's membrane and the anterior stroma because of the higher pH in the superficial layers (7). Concurrent with this endothelial hypothesis the calcium deposits were found mainly in the graft but not in the host cornea in our case. Similar observations have been made after the use of intracameral Viscoat, which contains phosphate (8). We did not use viscoelastics during rTPA injection.

However, Healon OVD (AMO, Santa Ana, CA, USA), which also contains phosphate, was used when the triple procedure was performed. As most of this viscoelastic was removed at the end of surgery and the rTPA was applied 9 days after this procedure, we believe that this was not a major contributing factor. Two and 3 days prior to the rTPA injection the patient received two subconjunctival injections of steroid formulation that contained phosphate (dexamethasone phosphate). Although it seems unlikely that remnants of this medication may have increased the phosphate concentration in the cornea at the time of rTPA injection we cannot exclude that this also contributed to the development of band keratopathy.

The eyedrops we used did not contain phosphate, but the phosphate in the buffer of the rTPA solution (although diluted) may have played a role in the rapid formation of the band keratopathy (6).

Pre- and postoperatively the patient received fluoroquinolone antibiotic drops (ofloxacin). While reversible corneal precipitates have been reported with several cases of topical ciprofloxacin and norfloxacin (9, 10), corneal deposits due to ofloxacin seem to be exceptionally rare (11). Moreover, deposits due to fluoroquinolone eyedrops would rather have a crystalline or granular pattern. Furthermore, before the rTPA injection was performed the patient was on ofloxacin eyedrops for almost 2 weeks without any signs of corneal drug deposits.

Our patient underwent triple procedure because of a perforated corneal ulcer, which by itself is associated with a higher complication rate. But apart from the massive fibrin reaction the postoperative course was completely uneventful with a clear and well adapted corneal graft for almost 2 weeks. No sign of graft rejection could be detected at any time. So it seems likely that the rTPA injection in

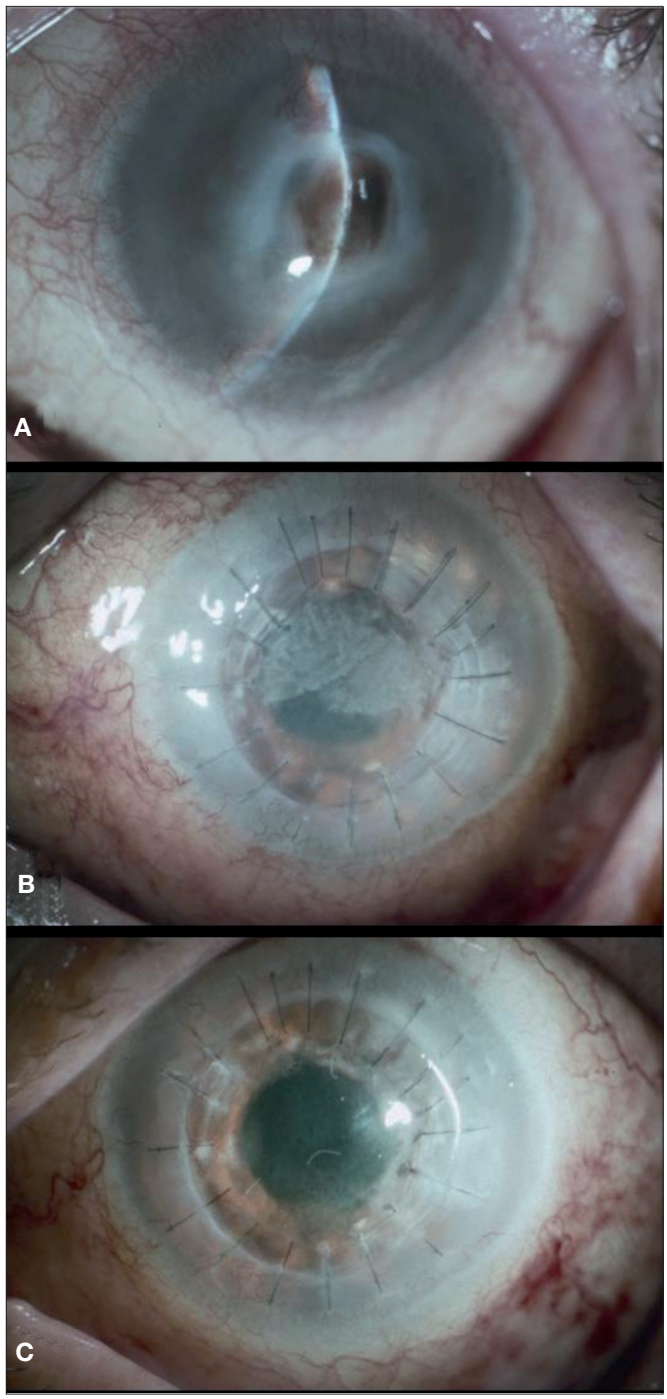

Fig. 1 - (A) *Corneal ulcer in the left eye with central perforation at time of first presentation. A bandage contact lens is in place. There is no iris incarceration.* **(B)** *Corneal graft showing band keratopathy 48 hours after intracameral injection of recombinant tissue plasminogen activator.* **(C)** *Corneal graft 2 days after corneal abrasion, polishing of Bowman layer, and ETDA chelation.*

the anterior chamber was the causative factor for the fast developing band keratopathy.

Our patient had rheumatoid arthritis as an underlying disease. Possibly the patient's rheumatoid arthritis has contributed to marked postoperative inflammation and the rapid development of the keratopathy. Inflammation can affect the pH in the aqueous and on the corneal surface. This in itself may be a contributing factor. The poor visual outcome in our patient was mainly due to the stromal haze and later to endothelial failure.

After corneal grafting and postoperative fibrin reaction the use of intracameral rTPA must be done cautiously, depending on the endothelial status of the graft. In addition, rTPA should be diluted even further (or be phosphate free) prior to its use to reduce the amount of phosphate in the buffer. It also may be wise to avoid the use of eyedrops or subconjunctivally applied medications that contain phosphate.

If, however, a band keratopathy has been induced, it should be removed using EDTA if possible without combined superficial keratectomy to avoid postoperative corneal scarring and surface irregularities.

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