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CASE REPORT

Intracamaral recombinant tissue plasminogen activator as a treatment for refractory fibrin reaction following penetrating keratoplasty: A case report

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Abstract

We report a case of severe fibrin reaction following penetrating keratoplasty (PKP) that was successfully treated with intracameral recombinant tissue plasminogen activator (r-TPA). A 62-year-old male with a history of herpetic keratitis and retinal detachment surgery presented with corneal scarring in the left eye. He underwent PKP combined with cataract extraction and intraocular lens (IOL) implantation. One month postoperatively, he developed an intense anterior chamber reaction with fibrin accumulation, endothelial plaque formation on the graft, and creamy-white iris infiltrates, raising suspicion of fungal keratitis. Therapeutic PKP was performed due to treatment-resistant ulcerative keratitis, and the patient subsequently received an intracameral injection of r-TPA (25 µg/0.05 cc) for persistent fibrinoid reaction. At the 24-hour follow-up, the fibrin had markedly resolved, and the graft appeared clear. While topical or subconjunctival steroids may be sufficient in mild to moderate cases, intracameral r-TPA may serve as a valuable adjunct in refractory cases, offering long-term morphological and functional improvement.

Keywords: r-TPA, keratitis, penetrating keratoplasty, case report

Fungal keratitis is a significant cause of corneal blindness worldwide, particularly in developing regions where agricultural trauma is common [1]. It represents a severe form of infectious keratitis caused by fungal invasion of the corneal tissue, most frequently by filamentous fungi such as Fusarium and Aspergillus, or yeasts such as Candida [2]. Clinically, it presents with corneal ulceration, stromal infiltration, endothelial plaques, hypopyon, or fungal balls in the anterior chamber [2,3].

Management of fungal keratitis is challenging due to delayed diagnosis, limited antifungal options, and poor ocular drug penetration. Topical antifungal agents often demonstrate suboptimal bioavailability, and treatment responses are frequently incomplete [2]. Even natamycin 5%, the most widely used agent for filamentous fungal infections, has poor stromal penetration in deep infections [4]. Consequently, surgical interventions such as therapeutic or tectonic penetrating keratoplasty (PKP) are often required to eradicate infection or restore ocular integrity [5,6].

Severe intraocular inflammation associated with fungal keratitis can result in dense fibrinous anterior chamber

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reactions. These membranes impair fundus visualization, complicate further surgical intervention, and may lead to sequelae such as posterior synechiae or angle-closure glaucoma [7]. While topical corticosteroids are widely used to suppress inflammation, their role in fungal keratitis is limited due to the risk of exacerbating microbial proliferation [3,7].

Recombinant tissue plasminogen activator (r-TPA) is a fibrin-specific fibrinolytic agent that catalyzes plasminogen-to-plasmin conversion, facilitating clot breakdown. Intracameral r-TPA has been reported as an effective adjunctive therapy for severe anterior chamber fibrin in various clinical contexts, including postoperative inflammation and endophthalmitis [8–10]. In eyes unresponsive to conventional anti-inflammatory therapies, r-TPA may promote anterior chamber clearing and support visual rehabilitation [10].

Case Report

A 62-year-old male presented with corneal opacity in the left eye. His history included penetrating keratoplasty (PKP) for herpetic keratitis and retinal detachment surgery due to high myopia two decades earlier. His medical history was otherwise unremarkable except for type 2 diabetes mellitus.

Best-corrected visual acuity (BCVA) was 20/20 in the right eye and hand motion in the left eye. Slit-lamp examination revealed a normal anterior segment in the right eye, while the left eye showed a +4 anterior chamber reaction, raising suspicion of graft rejection. Intraocular pressure (IOP) was 15 mmHg in the right eye and 14 mmHg in the left eye. The patient was bilaterally phakic. Fundus examination was normal in the right eye but obscured in the left eye; B-scan ultrasonography revealed no signs of intraocular inflammation or retinal detachment.

Topical dexamethasone was increased to hourly dosing, and a subconjunctival dexamethasone injection (0.4 mg/0.1 mL) was given. Three days later, the left eye developed intense flare and fibrin accumulation, endothelial plaque on the graft, and round creamy-white iris infiltrates. The conjunctiva was hyperemic with marked ciliary injection. BCVA declined to light perception. Fungal keratitis was suspected, and treatment with topical 0.3% fluconazole, amphotericin B, cefazolin, and gentamicin was initiated. Based on infectious disease consultation, intravenous and topical 1% voriconazole were added. Aqueous humor sampling, intrastromal, and intracameral voriconazole injections (50 µg/0.1 mL) were performed. Microbiological cultures showed no growth.

Highlights

- Severe fibrin reaction after penetrating keratoplasty can complicate fungal keratitis management and threaten graft survival
- Intracameral r-TPA provided rapid and effective fibrin resolution when conventional therapy failed
- r-TPA may serve as a valuable adjunct in refractory anterior chamber fibrin cases following therapeutic keratoplasty

After one week, IOP rose to 27 mmHg with ocular pain, leading to graft edema. Systemic acetazolamide was added. The anterior chamber fibrinoid reaction persisted with no regression of iris or graft infiltrates (Fig. 1A).

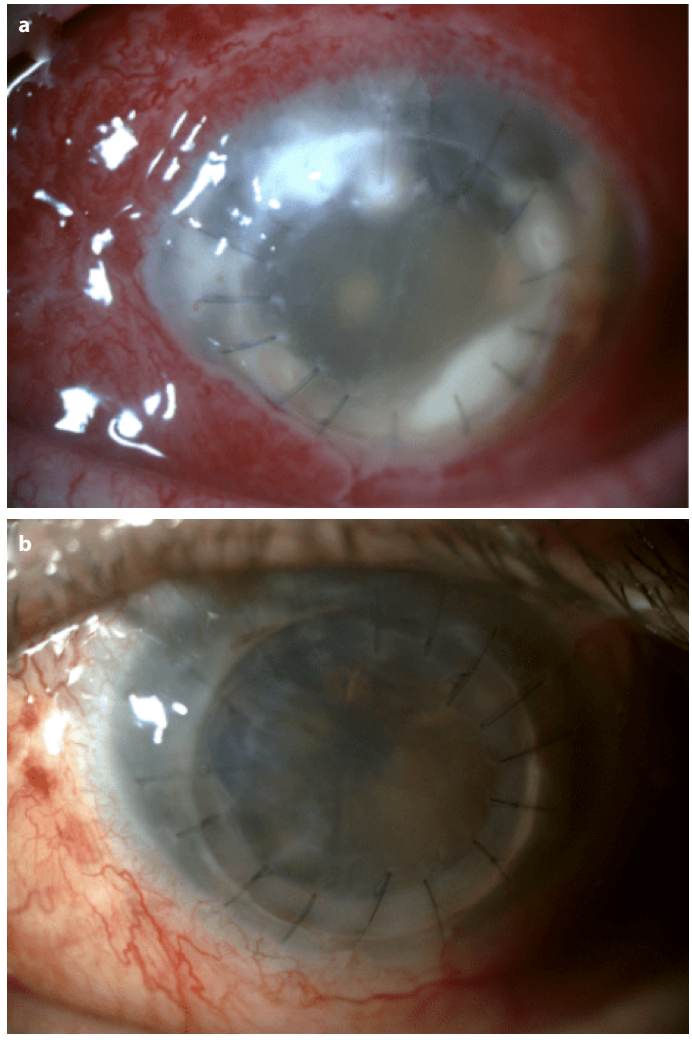

Fig. 1. Postoperative anterior segment findings. **(a)** Slit-lamp image showing intense anterior chamber fibrinoid reaction, endothelial plaque formation on the corneal graft, and round creamy-white infiltrates on the iris suggestive of fungal infection. The conjunctiva is markedly hyperemic with significant ciliary injection. **(b)** Following repeat penetrating keratoplasty and intensified antifungal therapy, the corneal graft appears clearer with residual posterior synechiae and persistent anterior chamber fibrinoid reaction.

The patient underwent repeat PKP (re-PKP) with anterior chamber lavage. Intraoperatively, a fibrinoid membrane and posterior synechiae were noted. Histopathology of the excised graft confirmed fungal hyphae and spores; Candida albicans was isolated from aqueous humor. Postoperatively, systemic therapy was adjusted to oral voriconazole. Topical antifungals were tapered only after complete clinical resolution and maintained for 12 weeks at a low dose.

By postoperative day 3, active infection had subsided. However, dense posterior synechiae developed, and the fibrinoid anterior chamber reaction persisted (Fig. 1B). IOP measured 25 mmHg. The patient was treated with intracameral r-TPA (25 µg/0.05 cc).

At 24 hours, fibrin had significantly resolved and the graft appeared clear (Fig. 2). IOP was 18 mmHg. No complications such as hypotony, corneal edema, or anterior segment toxicity were observed. Two weeks later, persistent posterior synechiae necessitated pupilloplasty. Postoperatively, the graft remained clear and BCVA improved to hand motion.

This represents one of the few reported cases in which intracameral r-TPA was successfully used for persistent anterior chamber fibrin following fungal keratitis treated with therapeutic PKP.

Discussion

Fungal keratitis is often complicated by severe intraocular inflammation, leading to fibrin deposition in the anterior chamber. This process arises from blood-aqueous barrier disruption and fibrinogen accumulation, particularly when corticosteroids are restricted to avoid exacerbating infection [1,4]. Persistent fibrin membranes can result in posterior synechiae, pupillary block, secondary glaucoma, and reduced intraocular drug penetration [5,9]. Despite maximal antifungal therapy, many patients ultimately require PKP [5,6]. In our case, fibrin formation persisted postoperatively, necessitating additional intervention.

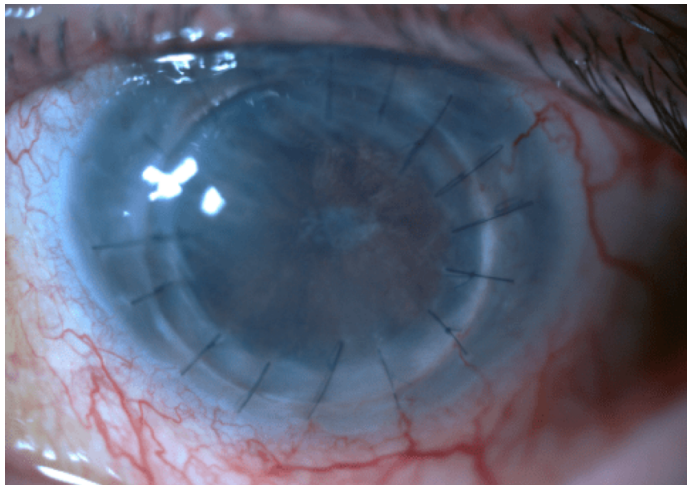

Fig. 2. Postoperative anterior segment findings after intracameral recombinant tissue plasminogen activator (r-TPA) injection. The corneal graft appears clearer with reduced fibrinoid reaction and improved visibility of the anterior chamber structures.

Recombinant tissue plasminogen activator (r-TPA) is a fibrin-specific serine protease that induces localized fibrinolysis via plasminogen activation. At low intracameral doses (5–25 µg), it rapidly dissolves fibrin without significant ocular toxicity [9,10]. In this case, r-TPA enabled complete fibrin resolution, restored pupillary visualization, and facilitated postoperative monitoring. This outcome aligns with prior reports describing rapid fibrinolysis after r-TPA in postoperative inflammation and endophthalmitis [9,10]. Although evidence remains limited in fungal keratitis, our case highlights its potential role in this setting.

Previous reports have described the use of r-TPA in microbial keratitis-related anterior chamber fibrin. Riaz et al. demonstrated clearance within two hours in postoperative endophthalmitis [10], and Sherman reported its intraoperative application during keratoplasty for infectious keratitis to prevent pupillary block [11]. Together with our findings, these observations suggest that r-TPA may be considered for selected fungal keratitis cases complicated by dense, refractory fibrin, provided infection control is achieved.

In conclusion, intracameral r-TPA may serve as an effective adjunct to surgical and antifungal management of fungal keratitis complicated by severe fibrin reaction. By addressing the inflammatory by-products of infection, r-TPA may reduce complications and improve visual outcomes. Although our results were favorable, clinicians should remain cautious of potential adverse effects such as transient hypotony, corneal edema, or endothelial toxicity, which have been reported in rare cases [9,10]. This case contributes practical insight into the potential role of fibrinolytic therapy in a surgically managed, steroid-limited context of infectious keratitis.

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