

Recombinant Tissue Plasminogen Activator (r-TPA) in Fibrin Dissolution due to Postoperative Endophthalmitis

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Abstract

Introduction: The aim of this paper was to describe the use of r-TPA for fibrin clot dissolution following endophthalmitis. **Clinical Picture:** A 74-year-old man presented with painful loss of vision following routine uncomplicated cataract surgery. **Treatment:** He underwent standard treatment for postoperative endophthalmitis but despite this, developed a dense fibrin clot. He underwent further intracameral injection of r-TPA. **Outcome:** Following the injection, he had complete clot dissolution within 2 hours without any complications. **Conclusion:** R-TPA may be used effectively in the treatment of fibrin clots secondary to endophthalmitis following cataract surgery.

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Key words: Cataract surgery, Fibrinolysis, Infection

Introduction

Cataract surgery is one of the most successful surgical procedures performed. However, postoperative endophthalmitis, defined as severe inflammation involving both the anterior and posterior segments of the eye secondary to an infectious agent, is an uncommon but devastating complication. Most large international studies quote an incidence rate of between 0.04% and 0.2%.¹⁻⁷ Patients typically present with reduced or blurred vision, ocular pain, conjunctival hyperaemia, lid swelling and a hypopyon.^{8,9}

Complications from postoperative endophthalmitis may be devastating despite appropriate therapy. Severe visual loss may be seen in 30% of patients,¹⁰ blindness in up to 18% of patients¹¹ and retinal detachment in 8% to 10%.¹²

We present a case of postoperative endophthalmitis following uncomplicated cataract surgery who recovered successfully following a novel treatment.

Case Report

A 74-year-old gentleman presented to the eye casualty department at the Western Eye Hospital, with sudden onset of ocular pain and reduced vision. Two days earlier, he had undergone an uncomplicated left eye cataract surgery, with

the use of subconjunctival antibiotics postoperatively. The surgery had taken 20 minutes. He was not diabetic, uveitic and showed no evidence of pseudoexfoliation. He had not undergone any ocular surgery prior to his recent cataract extraction. On examination, his visual acuity was perception of light, with severe anterior chamber inflammation, a 2-mm hypopyon and an absent red fundal reflex. A B scan ultrasound confirmed the presence of vitreous opacities but showed no evidence of retinal detachment. A diagnosis of postoperative endophthalmitis was made and he underwent an aqueous and vitreous tap under sterile conditions. The samples cultured alpha-haemolytic streptococci. Intravitreal amikacin and vancomycin was given at the time of the tap, and topical hourly preservative-free dexamethasone, 4 hourly chloramphenicol, and twice daily atropine were started. Twenty-four hours later, he was commenced on 60 mg oral prednisolone. Although the hypopyon resolved, he developed a dense fibrin plaque (Fig. 1A) 2 days after initial presentation. His visual acuity was 6/60. This was despite the intensive steroid regime he was on and the commencement of oral steroids. An intracameral injection (directly into the anterior chamber) of 25 µg of r-TPA was administered under sterile conditions. Within 2 hours, the dense fibrin plaque had dissolved (Fig. 1B). There was no change in his intraocular pressure. The number of doses of

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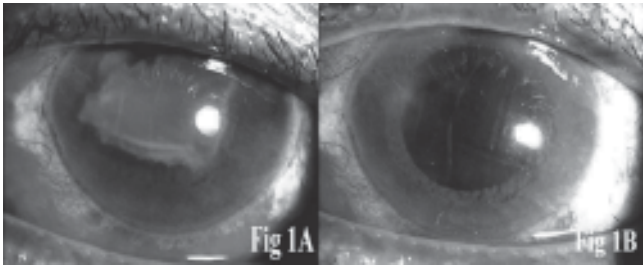


Fig. 1A. Dense fibrin formation following development of endophthalmitis post cataract extraction.

Fig. 1B. Resolution of membrane 2 hours after injection of r-TPA.

his topical steroids was reduced to 4 a day. His visual acuity improved to 6/18 unaided and 2 weeks after presentation, his vision had settled to 6/9 unaided.

Discussion

Endophthalmitis is a rare but serious complication of cataract surgery. Increased incidence has been associated with complicated surgery procedure (i.e., posterior lens capsule tear \pm vitreous loss), prolonged surgical time, the use of foldable versus injectable intraocular lenses¹³ and an infective ocular surface preoperatively.¹⁴ The use of topical povidone-iodine preoperatively¹⁵ and subconjunctival antibiotics postoperatively⁶ are the few interventions that have been shown to reduce the incidence of postoperative infection.

As a sequel to the intense inflammation there is an excess amount of influx of polymorphonuclear leukocyte, aqueous flare from protein influx and conversion of intracameral fibrinogen to fibrin. That provides all the constituents necessary for the development of a fibrin clot. The development of a severe membrane after uncomplicated cataract surgery is rare but may be seen in diabetics, patients with a history of anterior segment inflammation (uveitis), patients with pseudoexfoliation and patients with prolonged surgical operating times. The fibrin membrane in the anterior chamber may cause further complications e.g., pupillary adhesions, intraocular lens dislocation, and secondary glaucoma.¹⁶ Mild or moderate membranes may be treated by intensive steroids but in our patient, the development of the fibrin occurred despite prior intensive steroid treatment and even though the eye clinically looked less inflamed after 48 hours, a dense membrane was present.

R-TPA is a serine protease with thrombotic-fibrinolytic activity. It is an enzyme that binds to fibrin in a thrombus and catalyses the conversion of plasminogen to plasmin and promotes the lysis of newly formed clots. It has a short biological half-life, and rapidly dissolves clots within minutes to hours. It has been used extensively in the treatment of ischaemic strokes, acute myocardial infarction

and acute massive pulmonary embolus. It has been used intraocularly since the late 1980s mainly as an intracameral injection (into the anterior chamber), intravitreal injection or directly into the retinal vasculature.

Intracameral r-TPA has been used in ophthalmology to treat a variety of pathologies. In the anterior segment, it has been used to dissolve clots following traumatic hyphaema, used 5 to 6 days after hyphaema formation.¹⁷ It has also been used in the treatment of fibrinous membrane formation following adult cataract surgery. This occurs in 4% of routine cases after small incision cataract surgery (phacoemulsification).¹⁸ In the treatment of fibrin membranes following paediatric cataract surgery, r-TPA can be used safely and effectively.¹⁹ In children especially, the prompt resolution of the membrane is important since it may cause a reduction in visual acuity and hinder visual development (amblyopia). The disadvantage of its use in children is the necessity for administration under a second general anaesthetic.

In glaucoma, it has been used to revive previously functioning trabeculectomy blebs in the immediate postoperative period following cataract extraction or penetrating keratoplasty.²⁰ Intracameral r-TPA is also used to clear and prevent obstruction of glaucoma drainage devices by fibrin or blood clots. Intraocular blood or fibrin may obstruct the internal tube lumen, thereby compromising aqueous outflow and causing filtration failure. Doses of 5 to 20 μ g of r-TPA are used intracamerally, depending on the severity of fibrin or blood in the anterior chamber. Multiple r-TPA injections are often required. Patency and prevention of aqueous shunt tube occlusion have been reported in 89% of eyes.²¹

In the posterior segment, it has been used for the dissolution of haemorrhage either in the vitreous or submacular. However, its effect on the removal of vitreous haemorrhage has been variable. There is certainly a need for a large multicentre randomised control trial before its widespread use can be advocated. Submacular haemorrhage, particularly in patients with age-related macular degeneration, is associated with poor visual outcome. The use of intravitreal r-TPA injection and pneumatic displacement of blood from the foveal area may aid in dispersion.

As with systemic vascular disease, r-TPA has been used for retinal vascular occlusive disorders e.g., central retinal vein occlusion (CRVO) and retinal arterial thrombi. The cause of central retinal vein occlusion has been shown to be thrombus formation within the retinal vein. Intravenous thrombolytics e.g., r-TPA, have been used in an attempt to treat CRVO but systemic side effects have limited this use. Weiss and Bynoe²² have reported the direct injection of r-TPA into a retinal vein for CRVO resulting in a subjective

improvement in vision. However, the technique is technically challenging. The use of intravitreal r-TPA for the treatment of retinal vein occlusions is promising. The ability of r-TPA to penetrate the blood-retinal barrier to reach the thrombus is currently being investigated. The use of r-TPA in the setting of retinal artery occlusion has not been well explored. Experimentally, intravenous r-TPA has been successfully used to lyse retinal arterial thrombi in a rat model.²³

Complications following the use of intracameral r-TPA have been reported at doses as low as 10 µg and include anterior chamber haemorrhage (hyphae), raised IOP, corneal band keratopathy (calcium deposition) and corneal toxicity. The risk of anterior chamber haemorrhage is reduced significantly if the r-TPA is given after the third day following surgery. Hypotony (low pressure) and anterior chamber flattening occurred in 11% of cases following its use in glaucoma drainage devices.²¹

Intravitreal r-TPA toxicity can cause a pigmentary retinopathy. Retinal toxic reactions from intravitreal r-TPA injections of 50 µg/0.1 mL or more have been reported in an animal model.²³ There are case reports of patients having retinal toxicity after 2 successive injections of 50 µg r-TPA. The toxic reaction was attributed to the arginine-based vehicle of commercial r-TPA solution.

Our patient did well following his injection of r-TPA. The indication for its use is to prevent further complications from fibrin clot formation. However, early clinical intervention is of paramount importance in patients suspected of endophthalmitis. The intravitreal/aqueous tap and intravitreal antibiotics are mandatory to ensure successful treatment of this devastating complication. Early successful medical management of these conditions will significantly affect visual recovery. The use of r-TPA will be a useful adjunct to this initial management.

In conclusion, the use of r-TPA in the anterior segment may supplement the use of steroid-resistant fibrin membrane dissolution. Systemic side effects are minimal and local side effects must be monitored following administration. Due to its efficacy in clot dissolution, its use will prevent complications arising from fibrin formation in the eye. Further studies are needed with respect to its use in the posterior segment.

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