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CASE REPORT

Intracameral Recombinant Tissue Plasminogen Activator (rtPA) as the Primary Treatment for Secondary Pupillary Block

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ABSTRAK

Alteplase adalah sejenis pengaktif plasminogen tisu (tPA) yang telah melalui proses bioteknologi rekombinan. Ia berfungsi dengan memangkin pertukaran plasminogen kepada plasmin untuk proses fibrinolisis dan biasanya digunakan untuk mengubati penyakit saluran darah tersumbat seperti strok. Walaupun ia jarang digunakan dalam bidang oftalmologi, kami ingin melaporkan keberkesanan pengaktif plasminogen tisu rekombinan (rtPA) untuk merawat keadaan mata yang mempunyai saliran anak mata tersumbat (pupillary block) disebabkan penyakit endoftalmitis. Kami membentangkan kes endoftamitis akut yang terjadi berikutan komplikasi pembedahan katarak. Pesakit mempunyai radang pada segmen anterior mata (anterior chamber) menyebabkan seklusio pupil (seclusion pupillae), gelemair terkumpul di belakang iris menolak iris ke depan (iris bombe), dan menyebabkan sentuhan iris-kornea (iridocorneal touch) 360 darjah. Satu jam selepas suntikan 2.5 mikrogram alteplase dalam 0.1 ml ke dalam gelemair mata, iris bombe dilihat telah hilang sepenuhnya, segmen anterior mata dilihat lebih dalam dan anak mata (pupil) kelihatan sedikit besar berbanding sebelumnya. Segmen anterior mata yang lebih jelas membolehkan pembedahan membuang gelemaca 'pars plana vitrectomy' dan pengeluaran kanta intraokular boleh dilakukan lantas memberikan penglihatan yang baik selepas pembedahan. Penemuan kami mencadangkan suntikan rtPA, iaitu alteplase pada segmen anterior mata adalah efektif untuk rawatan 'pupillary block' sekunder yang disebabkan oleh radang yang serius seperti kes endoftalmitis. Oleh itu, penggunaan rtPA adalah berguna untuk menggantikan kebiasaan penggunaan laser pada sisi iris (laser peripheral iridotomy) untuk merawat 'pupillary

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block', kerana rawatan laser boleh memburukkan keadaan inflamasi pada segmen anterior mata.

Kata kunci: endoftalmitis, pengaktif plasminogen tisu, segmen anterior

ABSTRACT

Alteplase is a recombinant form of human tissue plasminogen activator (tPA) that converts plasminogen to plasmin essential for fibrinolysis. It is commonly used to treat embolic or thrombotic disorders such as ischemic stroke. Despite its rarity use in ophthalmology, we are reporting the effectiveness of recombinant tissue plasminogen activator (rtPA) in treating an eye with secondary pupillary block as a consequence of severe endophthalmitis. A patient presented with acute endophthalmitis after a complicated cataract extraction. Examination showed severe anterior chamber reaction leading to seclusion pupillae, iris bombe and presence of iridocorneal touch 360-degree. Following intracameral alteplase 2.5 microgram in 0.1 ml given, iris bombe was observed to resolve completely one-hour later. Anterior chamber was also significantly deeper and slightly larger pupil compared to before rtPA injection. Due to clearer view of anterior segment, pars planar vitrectomy and extraction of intraocular lens could be performed with significant visual improvement after surgery. Our findings suggest that usage of rtPA, which is alteplase, was effective in treating secondary pupillary block due to intense anterior segment inflammation in endophthalmitis cases. Thus it is useful in replacing the conventional use of laser peripheral iridotomy in treating pupillary block, as the latter potentially aggravates the pre-existing inflammatory condition.

Keywords: anterior chamber, endophthalmitis, tissue plasminogen activator

INTRODUCTION

Endophthalmitis is defined as severe eye inflammation involving anterior and posterior segments due to an infectious agent. It is a sight-threatening condition that can occur as a complication of ocular surgery or trauma, or following systemic infection. Common signs of endophthalmitis include reduced visual acuity, conjunctival injection, presence of cells and flare in anterior chamber and vitritis (Durand 2013). Early treatment following correct diagnosis is essential to optimise the visual outcome.

The systemic use of tissue plasminogen activator (tPA) has been approved since 1988 for thrombolysis in coronary artery disease. Since then, this drug has been extended to other indications, including the eye. Its safety and effectiveness for treatment of fibrin-related complications of ocular inflammation including endophthalmitis was reported in

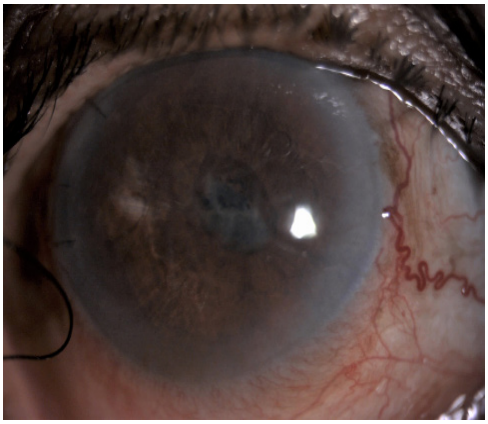

Figure 1: Prior to intracameral rtPA shows fibrin over the pupil and intraocular lens causing seclusion pupillae, iris bombe is not clearly seen in this photo but anterior chamber was very shallow with complete iridocorneal touch 360 degree

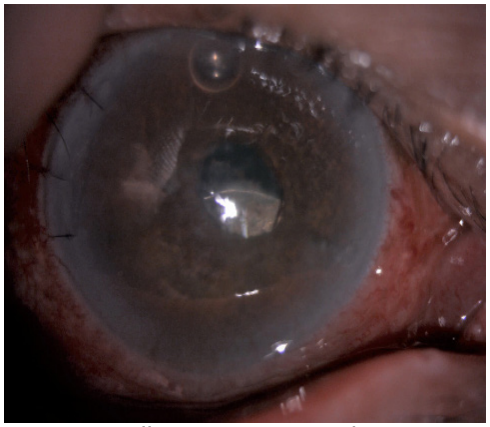

Figure 2: Following intracameral rtPA, fibrin reduced, anterior chamber deeper, iris bombe less and pupil slightly enlarged.

multiple studies (Damji et al. 2001; Wu & Wang 2009; Riaz et al. 2006). Severe anterior segment inflammation does not only cause poor visualisation of the posterior segment, synechiae that is formed can also leads to secondary pupillary block. Traditionally, laser iridotomy is the treatment of choice for pupillary block. This procedure however, may potentially aggravate the pre-existing inflammatory condition. Moreover, in severe fibrin reaction, anterior chamber details could not be distinguished thus hindering laser iridotomy procedure. We report the use of recombinant tissue plasminogen activator (rtPA) as a first line treatment for secondary pupillary block in a case of severe endophthalmitis. As a fibrinolytic agent, it accelerates the clearance of fibrin in endophthalmitis, thus preventing devastating complications of endophthalmitis such as loss of vision.

CASE REPORT

A 69-year-old man with background of diabetes mellitus underwent a complicated phacoemulsification surgery which was converted to extra capsular cataract extraction (ECCE) followed by implantation of intraocular lens (IOL) on his right eye in a private ophthalmology centre. Patient received topical Dexamethasone 0.1% and topical Moxifloxacin 0.5% post-operatively. At 2 weeks post-operatively, he developed acute endophthalmitis and was given intravitreal Vancomycin, Ceftazidime and Dexamethasone once. However, he defaulted subsequent follow-up and presented to us 2 weeks later with a complaint of right eye redness and pain. Examination revealed visual acuity of hand movement with severe inflammation in the anterior chamber with no fundus view. IOL was noted to be subluxated inferiorly. B-scan showed loculations in the vitreous but no retinal detachment. Intraocular

pressure (IOP) was 4 mmHg on the right eye.

Repeated intravitreal Ceftazidime (Duopharma, Malaysia) 2.25mg/0.1ml, Vancomycin (Mylan Lab, India) 1mg/0.1ml and Dexamethasone (Duopharma, Malaysia) 0.4mg/ 0.1ml were given. He was also started on oral Moxifloxacin (Bayer, Germany) 400 mg daily, in combination with 2 hourly dose of topical Moxifloxacin 0.5% (Alcon, Singapore), 6 hourly Dexamethasone 0.1% (Alcon, Belgium) and daily Atropine 1% (Alcon, Belgium). The cornea was very hazy with the presence of Descemet striations. He was prepared for pars plana vitrectomy. On the following day, worsening of the anterior chamber reaction was noted causing seclusio pupillae with shallow anterior chamber. Iris bombe and iridocorneal touch were present 360-degrees (Figure 1), while the IOP was still 12 mmHg. Following topical anesthesia, 25 micrograms of rtPA, Alteplase (Boringer, Germany) in 0.1 ml of saline was injected intracamerally through the inferonasal limbus using a 30-gauge needle. One hour following injection, the fibrin reduced, anterior chamber was deeper, iris bombe resolved completely and pupil was slightly larger (Figure 2). The patient was subsequently arranged for IOL explantation and vitrectomy. Surgery was uneventful, and the patient was left aphakic. Upon discharge, his vision improved to 6/36 assisted with +10D lens. Vitreous culture did not grow any organism.

DISCUSSION

Acute endophthalmitis is an ocular emergency which requires prompt diagnosis and treatment. The most important component of therapy is intravitreal antibiotic injection. However, even with correct timing of starting antibiotic therapy, intense inflammation may lead to severe fibrin reaction in anterior and posterior segment which may result in posterior synechiae, seclusio pupillae, peripheral anterior synechiae, iris bombe, and secondary angle-closure glaucoma (Durand 2013).

Alteplase is a recombinant form of tPA, which is a proteolytic enzyme in serine protease family found on endothelial cells. It is essential for fibrinolysis and acts as thrombolytic agent. Tissue plasminogen activator converts plasminogen to plasmin once it bounds to fibrin, which subsequently promotes fibrin degradation (Damji et al. 2001). Tissue plasminogen activator dissolves clots rapidly, within minutes to hours and it also has a short biological half-life. The use of alteplase for acute cases of ischemic stroke, myocardial infarction, massive pulmonary embolism, and occlusion of central venous access devices (CVADs) is permitted by Food and Drug Administration (FDA). Although it is not routinely used in ophthalmology, the high efficacy of intracameral rtPA has been reported for treatment of anterior chamber fibrin formation following cataract extraction, trabeculectomy, combined cataract and glaucoma surgery, penetrating keratoplasty, as well as vitrectomy (Damji et al. 2001; Georgiadis et al. 2003; Wedrich et al. 1997). Moreover, the effectiveness

of rtPA to treat severe fibrin reaction was also demonstrated in case of endophthalmitis (Wu & Wang 2009), and recalcitrant anterior uveitis (Patrick et al. 2018). Thus intracameral rtPA is probably underused in our fraternity.

In the present case, the clinical indication for rtPA was secondary pupillary block with iris bombe in a severely inflamed eye. A randomised prospective study by Heiligenhaus et al. (1998) revealed significant reduction of synechiae and successful synechiolysis after intracameral tPA injection in patients with intraocular fibrin formed following cataract surgery (Heiligenhaus et al. 1998). Intracameral rtPA was also noticed to be effective in decreasing the incidence of pupillary dysfunction due to the posterior synechiae formation and fibrin deposition at pupillary region, as shown in the study (Heiligenhaus et al. 1998). In another reports, fibrin membrane dependent pupillary block was shown successfully treated with intracameral tPA injection (Akcetin et al. 2015; Yoshino et al. 2012). These reports suggest the use of rtPA as the primary treatment for both fibrin reactions after cataract surgery and secondary pupillary block.

Meanwhile, Wu & Wang (2009) reported enlargement of pupillary size 24 hours after rtPA injection in endophthalmitis patients. In addition to previous studies, this study also demonstrated the effectiveness of using intracameral injection of rtPA in endophthalmitis, which eventually facilitates vitreous and fundus examination, including vitrectomy if needed. This will be a very valuable advantage for these type of patients as vitrectomy can be challenging not only if the cornea is hazy due to the severe anterior chamber reaction, low IOP and even worse if the pupil is small. Manipulation of pupil during surgery will eventually induce intense inflammation post operatively.

In terms of timing of rtPA injection following fibrin formation, various literatures reported successful fibrinolysis within hours of injection (Riaz et al. 2006; Damji et al. 2001; Erol et al. 2003). In a study by Dotan et al. (2014), they demonstrated the therapeutic effect of rtPA in refractory toxic anterior segment syndrome (TASS) patients. In their case, it is of different mechanism whereby the TASS is caused by breakdown of blood-aqueous barrier thus the initial hypothesis is that injection administration later (after 16 days of cataract surgery) would show better outcome than earlier intervention (within 10-15 days of cataract surgery) (Dotan et al. 2014). However, the study has proven that regardless the timing of injection following cataract surgery, fibrinolysis rate as well as visual acuity improvement have no statistically significant different. Successful fibrinolysis was shown in all subjects in the report. In our case, successful fibrinolysis was observed as early as one hour post rtPA injection. In case of fibrin membrane pupillary block, the rtPA injection should be given as soon as fibrin formation is noted because further delay could raise IOP and further optic nerve damage.

CONCLUSION

Intracameral rtPA, which is alteplase, is useful in replacing the conventional use of laser peripheral iridotomy in treating fibrin membrane pupillary block.

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