Tissue Plasminogen Activator to Treat Impending Pupillary Block Glaucoma in Patients With Acute Fibrinous HLA-B27 Positive Iridocyclitis

CRAIG A. SKOLNICK, MD, RICHARD G. FISCELLA, RPH, MPH, HOWARD H. TESSLER, MD, AND DEBRA A. GOLDSTEIN, MD, FRCS(C)

• PURPOSE: To report the use of intracameral tissue plasminogen activator to dissolve fibrinous membranes and break posterior synechiae in patients with acute HLA-B27–positive iridocyclitis with impending pupillary block.

• METHODS: Two patients with severe acute fibrinous iridocyclitis and seclusio pupillae were identified. Because of the concern of impending pupillary block, intracameral tissue plasminogen activator (12.5 μg in 0.1 ml, Activase; Genentech, Inc, South San Francisco, California) was injected with a 25-gauge needle through the corneal limbus.

• RESULTS: Both patients showed complete dissolution of fibrin with disruption of posterior synechiae. There were no adverse events after injection. Neither patient required further invasive intervention, and both fully recovered with medical management.

• CONCLUSIONS: Intracameral tissue plasminogen activator is a safe and effective agent for patients with severe acute iridocyclitis and pupillary seclusion. Patients with clinical signs suggestive of impending pupillary block glaucoma may be considered for tissue plasminogen activator injection to avoid the possible need for emergency surgical iridectomy and synechiolysis. (Am J Ophthalmol 2000;129:363–366. © 2000 by Elsevier Science Inc. All rights reserved.)

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From the Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine (Drs Skolnick, Tessler, and Goldstein and Mr Fiscella) and College of Pharmacy (Mr Fiscella), Chicago, Illinois.

Reprint requests to Debra A. Goldstein, MD, FRCS(C), Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, 1905 W Taylor St, Chicago, IL 60612-7243; fax: (312) 996-7773; e-mail: debrgold@uic.edu

SEVERE FIBRINOUS ANTERIOR CHAMBER REACTION may lead to permanent ocular sequelae. Topical and/or systemic anti-inflammatory therapy may be insufficient to prevent or resolve fibrinous membrane formation in cases of severe acute iritis or iridocyclitis.

Tissue plasminogen activator is a clot-specific fibrinolytic agent that has been successfully used to treat postcataract and postvitrectomy fibrin membrane formation.[1,2] It has also been effective in aiding resolution of posttrabeculectomy blood and fibrin clot causing aqueous outflow obstruction,[3,4] as well as clearing hemorrhage associated with retinal artery macroaneurysm[5] and age-related macular degeneration,[6] hyphema,[7] and central retinal vein occlusion.[8,9] The purpose of this report is to describe an additional indication for the use of tissue plasminogen activator. Intracameral tissue plasminogen activator can lyse extensive fibrinous membranes and may prevent impending pupillary block associated with severe fibrinous endogenous iridocyclitis.

CASE REPORTS

• CASE 1: A 34-year-old white man was referred to the uveitis service at the University of Illinois with a 1-week history of progressive pain, photophobia, and redness in his left eye, which was poorly responsive to atropine sulfate 1% four times daily and prednisolone acetate 1% every 2 hours. Review of systems was negative for joint/back pain, rash, dysuria, oral or genital ulcers, and shortness of breath. Best-corrected visual acuity was RE: 20/20 and LE: 20/200 without afferent pupillary defect.

External examination showed a diffusely injected left conjuctiva with mild eyelid edema. Slit-lamp examination of the right eye was unremarkable, with an intraocular pressure of 18 mm Hg. Examination of the left eye showed a clear cornea without keratic precipitates. The anterior

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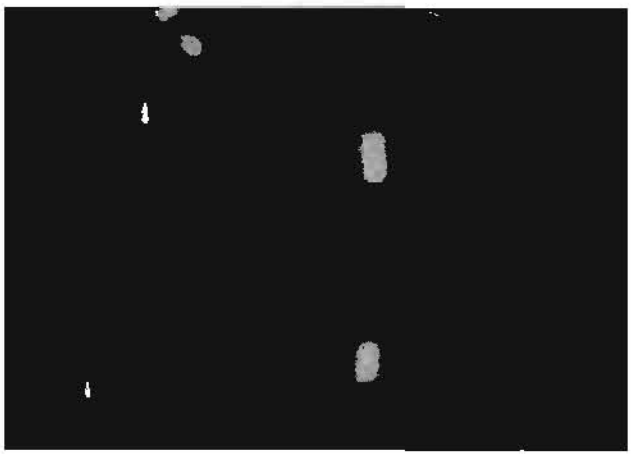

FIGURE 1. Patient 1 at initial examination. Note 360 degrees of posterior synechiae and fibrinous membrane covering the pupil.

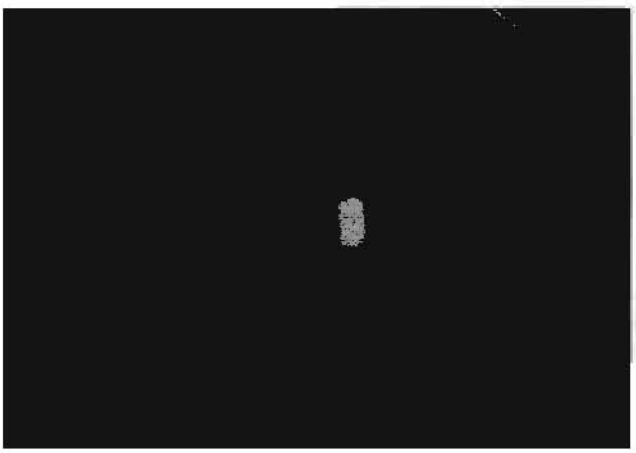

FIGURE 2. Patient 1, 30 minutes after injection of tissue plasminogen activator. Note that 180 degrees of posterior synechiae have broken.

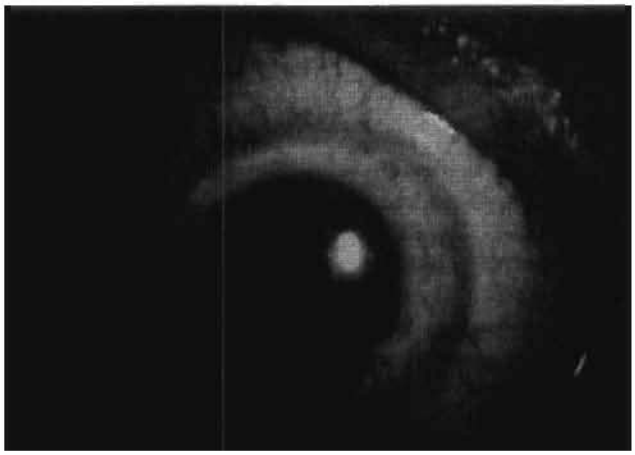

FIGURE 3. Patient 1, 2 days after injection of tissue plasminogen activator. Note resolution of fibrinous membrane and posterior synechiae.

chamber contained a dense plasmoid aqueous with a 1-mm hypopyon. There was a fibrin plaque bridging the pupil, with 360 degrees of posterior synechiae (Figure 1). There were prominent engorged iris vessels with moderate iris bombé, although intraocular pressure measured only 20 mm Hg, possibly secondary to aqueous hyposecretion because of ciliary body inflammation. The right fundus was normal. There was no view of the left fundus, and B-scan ultrasonography demonstrated no significant vitreitis.

Because of the severity of the fibrinous reaction, the 360 degrees of posterior synechiae, and the fear that decreasing ciliary body inflammation would lead to increased aqueous production with subsequent pupillary block glaucoma, the decision was made to inject 12.5 μg of tissue plasminogen activator intracamerally under topical anesthesia. The procedure was well tolerated, without subsequent change in intraocular pressure. Within 30 minutes, 180 degrees of posterior synechiae had broken (Figure 2). The patient was placed on a regimen of prednisone 100 mg orally per day and prednisolone acetate 1% every minute for 5 minutes at the top of every hour while awake, and atropine sulfate 1% four times daily was continued. The posterior synechiae were completely broken after 2 days (Figure 3), and visual acuity had improved to LE: 20/30 within 1 week. The oral corticosteroids were tapered over 2 weeks, while topical corticosteroids were slowly tapered until resolution of inflammation. Visual acuity returned to LE: 20/20. The evaluation disclosed borderline elevated angiotensin-converting enzyme and lysozyme levels, nonreactive fluorescent treponemal antibody absorption test, normal chest x-ray, and positive HLA-B27.

• CASE 2: A 40-year-old white man was examined because of 10 days of progressive redness, pain, photophobia, and decreased vision in his right eye, which was unresponsive to 4 days of prednisolone acetate 1% every hour and cyclopentolate 1% four times daily. Review of systems was unremarkable; specifically, the patient denied joint or back pains, dysuria, shortness of breath, genital or oral ulcers, and rash. Family history was significant in that the patient's father had Crohn disease and a maternal uncle had chronic iridocyclitis. Best-corrected visual acuity was RE: 20/70 and LE: 20/20. The right eye had diffuse injection with mild conjunctival chemosis. The right cornea had diffuse microcystic and midstromal edema without keratic precipitates. The anterior chamber contained a severe inflammatory reaction with a fibrinous membrane completely covering the pupil and lens. There were dilated iris vessels and almost 360 degrees of posterior synechiae. The left anterior segment was entirely normal. Intraocular pressure was RE: 28 mm Hg and LE: 15 mm Hg. The right fundus could not be visualized, but B-scan ultrasonography

showed no vitreitis and no retinal detachment. The left fundus was normal.

The patient was placed on a regimen of prednisolone acetate 1% every minute for 5 minutes at the top of every hour while awake, homatropine hydrobromide 5% four times daily, and prednisone, 100 mg orally per day. Intracameral tissue plasminogen activator was offered to the patient, but he refused. The pupil did not dilate after placement of a pledget of phenylephrine 10%, cyclopentolate 1%, and tropicamide 1%. The following day the patient had no improvement in symptoms and his visual acuity had decreased to RE: 20/400 secondary to worsening corneal edema. Intracameral tissue plasminogen activator (12.5 μg) was injected under topical anesthesia. Within 30 minutes the fibrinous pupillary membrane started to lyse and the synechiae to break. Within 1 week the visual acuity had improved to RE: 20/40 with nearly complete resolution of the posterior synechiae and normalization of intraocular pressure. Oral corticosteroids were tapered over 3 weeks, while topical corticosteroids were tapered over 10 weeks as inflammation subsided. Visual acuity returned to RE: 20/20. The evaluation showed normal angiotensin-converting enzyme and lysozyme levels, nonreactive fluorescent treponemal antibody absorption test, normal chest x-ray, and positive HLA-B27.

DISCUSSION

KNOWN SIDE EFFECTS OF INTRACAMERAL TISSUE PLASMINogen activator include rapid band keratopathy[10] and hyphema.[3] Endophthalmitis is also an uncommon but potentially devastating complication of any intraocular injection. A dose of 12.5 μg was chosen in these patients on the basis of previous reports of efficacy, and to avoid hyphema, which has been reported more frequently with a 25-μg injection.[3] Our pharmacy reconstitutes tissue plasminogen activator (Activase; Genentech, Inc, South San Francisco, California) with sterile water and dilutes it to 100 units per 0.1 ml with sterile normal saline (sterile water can also be used). Small aliquots are stored at −20 C and thawed to room temperature when required. They are further diluted (in a sterile hood) to the concentration requested (6.25 units to 25 units per 0.1 ml). Frozen stability and contamination have not been a concern.[11] Balanced salt solution is not a recommended diluent for dilution of tissue plasminogen activator because of concerns of precipitation.[12] The fibrinolytic effect of tissue plasminogen activator should occur fairly rapidly, typically within 30 to 60 minutes.

The decision to use tissue plasminogen activator in these two patients was prompted by concern that resolution of ciliary body inflammation and hyposecretion would result in pupillary block glaucoma, because both patients had seclusion of the pupil. Both patients had also failed to respond to topical corticosteroids and dilators. An alternative technique for breaking posterior synechiae is to soak cotton pledgets or applicators with a combination of phenylephrine 10%, cyclopentolate 2%, and tropicamide 1% and then to place the pledget in the conjunctival fornix or touch the anesthesized corneal limbus with the applicator. The risk of this procedure is elevation of blood pressure secondary to excessive phenylephrine absorption. The use of a pledget failed to dilate the pupil of Patient 2. A laser peripheral iridotomy was not believed to be an option initially because of the profoundly dilated iris vessels and severe inflammation. The alternative option would have been immediate surgical peripheral iridectomy if pupillary block angle closure developed. Neither of these was required, as the synechiae broke.

In most cases of severe fibrinous iridocyclitis, high-dose topical and systemic corticosteroids along with cycloplegics lyse fibrin and prevent permanent synechiae, rendering intracameral tissue plasminogen activator unnecessary. Judicious use of intracameral tissue plasminogen activator may prevent permanent synechiae and avoid the need for surgical interventions such as peripheral iridectomy and synechiolysis in those patients in whom corticosteroid and dilation therapy is initially insufficient. Because this report describes only two patients, and most cases of severe iridocyclitis resolve without the need for intracameral tissue plasminogen activator, the precise role this technique will play in the management of patients with uveitis has yet to be determined.

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