Intravitreous Tissue Plasminogen Activator With Pneumatic Displacement in Submacular Hemorrhage

Submacular hemorrhage–induced retinal damage appears to vary directly with the duration of hemorrhage. Hence, many investigators have advocated early evacuation of subretinal hemorrhage to minimize these damaging effects. In 1996, Heriot presented the benefits of the minimally invasive procedure of enzymatically liquefying the submacular blood with tissue plasminogen activator (tPA) and displacing it with gas. Many studies have since shown good results with this procedure, but the exact time of the intervention is still debatable. Although there is no consensus, submacular bleeding for more than 28 days is generally believed to give poor results. We report a case of submacular bleeding for 60 days that showed dramatic clearing within a day with tPA and gas.

Report of a Case. A 55-year-old, nondiabetic, nonhypertensive woman of Asian Indian origin had sudden decreased vision in her left eye for 2 months. Her visual acuity was 20/20 OD and 20/200 OS. The left eye revealed a reddish brown mound of subretinal blood over the posterior pole, about 5 to 6 disc diameters in size. Some of the subretinal hemorrhage was altered and yellow, indicating a long duration (Figure 1A). Indocyanine green angiography revealed a hypofluorescent area corresponding to the area of subretinal blood, and no hot spot was found (Figure 1B). Provisional diagnosis of idiopathic polypoidal choroidal vasculopathy causing submacular bleeding was made. The left eye was treated with intravitreous tPA with perfluoropropane gas. Topical anesthesia was achieved with topical proparacaine hydrochloride, 0.5%, ophthalmic eyedrops. Irrigation of the conjunctival cul de sac with povidone-iodine, 5%, was performed. Commercial tPA, diluted with balanced salt solution to a concentration of 100 µg/0.1 mL, and 0.3 mL of pure perfluoropropane gas were then injected via a 30-gauge needle introduced through the pars plana into the vitreous cavity. A paracentesis was then performed to reduce the intraocular pressure. After ensuring optic nerve head perfusion, the eye was covered with a sterile eye pad and the patient was allowed to go home. The patient was advised to maintain a supine position for the first 6 hours to facilitate tPA diffusion through the retina and then remain prone for at least 8 hours a day for 5 days. The next day, the left eye showed complete resolution of the un-

Figure 1. A 55-year-old woman had decreased vision in her left eye for 2 months. A, Fundus photograph showed a reddish brown submacular hemorrhage with an area of altered, yellow hemorrhage. B, Indocyanine green angiography revealed a hypofluorescent area with no hot spots. The probable cause was idiopathic polypoidal choroidal vasculopathy.
altered hemorrhage (Figure 2). Repeated indocyanine green angiography did not show any hot spots. Final best-corrected visual acuity was 20/30 after 2 months.

**Comment.** The size of the submacular hemorrhage has not been shown to affect the outcome of this procedure. Hassan et al showed good results even in large, thick submacular hemorrhages. There are conflicting reports with regard to the duration of submacular hemorrhage. In a series by Hattenbach et al, no eyes with a submacular hemorrhage duration longer than 21 days showed any improvement. However, in a series of 104 eyes, Chen et al did not find significant correlation with the duration of hemorrhage but most of the eyes were treated within 4 weeks. Despite the conflict, our case illustrates that it is worth while to attempt the use of tPA with gas even in longer-lasting hemorrhages where observation alone will likely lead to gross reduction of vision.

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**Ten-Year Evolution of Retinopathy Lesions in an Older Nondiabetic Population**

Retinopathy lesions are common in generally healthy adults without diabetes (6%-13%)1-4 and/or hypertension. In the Beaver Dam Eye Study, the 15-year incidence of retinopathy was 14.2% among nondiabetic participants aged 43 to 86 years at baseline; in the Hoorn Study, the 9-year incidence was 7.3% in persons with normal glucose levels aged 50 to 74 years at baseline.6 We report the 10-year incidence, regression, associated risk factors, and prognosis of retinopathy lesions among Blue Mountains Eye Study participants.

**Methods.** Of 3654 baseline participants aged 49 years and older at the 5-year follow-up, 543 (14.9%) had died, 383 (10.5%) had moved, and 393 (10.8%) refused to participate, leaving 2335 (75.1% of survivors) who attended 5-year visits. At the 10-year follow-up, 1103 (30.2%) had died, 375 (10.3%) had moved, and 224 (6.1%) refused to participate, leaving 1592 (53.4% of the original cohort, 76.6% of survivors) who attended 10-year visits. All examinations were approved by the Human Research Ethics Committees of the Western Sydney Area Health Service and the University of Sydney. Signed informed consent was obtained from participants at each visit.

Photographs were obtained for at least 1 eye in 98.1% of the baseline participants, 98.8% of the 5-year follow-up participants, and 86.5% of the 10-year follow-up participants. Masked assessment of retinopathy lesions used the modified Early Treatment Diabetic Retinopathy Study classification of diabetic retinopathy. Retinopathy was diagnosed if the following lesions were detected: microaneurysms, blot- or flame-shaped hemorrhages outside the optic disc area including 0.5 disc diameter away from the disc margin, hard exudates, or cotton-wool spots. Mild retinopathy was defined as a single microaneurysm or hemorrhage in 1 or both eyes, and moderate retinopathy was defined as at least 2 microaneurysms/hemorrhages or hard exudates/cotton-wool spots in either eye.

Incidence of retinopathy was defined as lesions detected at follow-up in persons without lesions in either eye at baseline. Progression of retinopathy was defined as an increase in the number of lesions in subjects with retinopathy at baseline. Disappearance of retinopathy was assessed in subjects with retinopathy lesions at baseline and defined as the lesion(s) having completely disappeared at follow-up. Person-specific cumulative incidence was calculated using Kaplan-Meier methods. Discrete logistic regression models were used to assess risk factors associated with retinopathy incidence or persistence, adjusting for age and sex. Assessed risk factors are shown in the Table.

**Results.** In 1678 participants without diabetes who attended at least 1 follow-up visit, the cumulative 10-year incidence of retinopathy was 19.4% (95% CI, 17.4%-21.6%). Apart from age, no significant associations were found for incident mild retinopathy. Persons with hypertension or obesity were more likely to develop moderate retinopathy (Table).