Intravitreal bevacizumab (Avastin) for post laser anterior segment ischemia in aggressive posterior retinopathy of prematurity

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Aggressive posterior retinopathy of prematurity (formerly known as fulminate/type II/rush disease) occurs in zone 1 or posterior zone 2. Treatment involves extensive near confluent laser ablation of a large area of avascular retina. Anterior segment ischemia is a rare complication that can occur due to injury to the long posterior ciliary arteries in the horizontal meridians during aggressive posterior laser treatment. The outcome of this rare complication is very poor. This case describes a favorable outcome of intravitreal injection of bevacizumab (Avastin) in a case of anterior segment ischemia.

Key words: Bevacizumab, intravitreal, lamellar cataract, retinopathy of prematurity.

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Anterior segment ischemia is a rare complication of laser ablation for threshold retinopathy of prematurity (ROP). This invariably results in phthisis.[1,2] Recently, there has been successful treatment of iris, retinal and choroidal neovascularization with bevacizumab[3,4] (Avastin, Genentech, San Francisco), a potent inhibitor of vascular endothelial growth factor (VEGF). Herein we report the first case of intravitreal bevacizumab for anterior segment ischemia following retinal ablation for aggressive posterior retinopathy of prematurity (AP-ROP).

Case Report

A male twin born at 31 weeks of gestation with birth weight of 1170 g had bilateral AP-ROP on his first screening examination at 2.5 weeks of age. The other twin also had similar ocular findings but unfortunately the baby expired because of unknown cause. The twin was born with *invitro* fertilization technique after prolonged infertility. Both eyes of the surviving twin received 3,000 spots of near-confluent infrared laser to the avascular retina. One-week postlaser the left eye developed neovascularization of iris (NVI) and mild vitreous haze. We started topical steroids and cyclopegic drops. Ten days postlaser the left eye NVI had increased, posterior synechiae had developed and dense anterior fibrovascular proliferation (FVP) was seen waxy yellow in colour just behind the lens along with hypotony [Figs. 1a and 1b]. The right eye also started developing early NVI. The vitreous was hazy in both eyes (left eye more than right eye) but retinopathy was regressing [Fig. 2]. Vitreous surgery was offered for the worse eye (left) but declined by the parents due to the poor prognosis. Considering the severity of the disease affecting both eyes and based on promising results with other proliferative retinopathies,[5-7] an off label use of intravitreal injection of bevacizumab was offered for left eye for which the parents agreed. Under topical anesthesia and aseptic conditions, 0.03 ml (0.75 mg) of bevacizumab was injected intravitreally via a 30-guage needle placed 1mm behind the limbus. At one week follow-up all the NVI had regressed. Weekly examination showed gradual regression of anterior FVP. By Week 10, there was reversal of hypotony, anterior FVP and all NVI [Fig. 3], with a clear view of the fundus showing growth of regression vessels in the lasered retinal periphery [Fig. 4]. There was secondary iris atrophy and mild cataract. No ocular or systemic complications were noted. The right eye became better with hourly and twice a day application of topical steroid and cycloplegic drops respectively. At ten-month follow-up fundus of both eyes showed clear media with well-regressed ROP. Both eyes, however, were seen to develop a lamellar cataract. As the media was clear and retinoscopy was equal in both eyes, the lamellar cataract was just observed.

Discussion

Anterior segment ischemia may result from thermal injury to the long posterior ciliary arteries in the horizontal meridian. It is the most devastating complication of ablative laser for threshold ROP, a procedure with an otherwise high benefit to risk ratio. Treatment with topical steroids and cycloplegics is insufficient. Vitrectomy with lensectomy and silicone oil injection may be helpful but has a high rate of re-proliferation. Bevacizumab is a full-length antibody, which binds all VEGF isoforms and is approved for intravenous treatment of colorectal cancer. Our patient responded favorably to a single injection of intravitreal bevacizumab and by ten weeks all features of ischemia disappeared.

Intravitreal bevacizumab seemed in this case to strikingly halt the progression of anterior neovascularization, cyclitic membrane formation and hypotony that typically evolves to phthisis. Although it is conceivable that the long posterior ciliary neurovascular injury in this case was not complete and may have improved spontaneously, the prompt resolution of anterior neovascularization postinjection suggests a therapeutic effect. Although we propose that intravitreal bevacizumab may have an important role in the salvation of eyes with dire complications of ROP such as anterior segment ischemia and neovascularization and our patient did not suffer any negative effect on the growth of normal retinal vessels even at ten-month follow up, we urge caution in the generalization of these findings. Formal controlled studies with long-term follow-up are warranted to determine the potential safety and benefit of VEGF inhibitors in ROP that fails conventional therapy.

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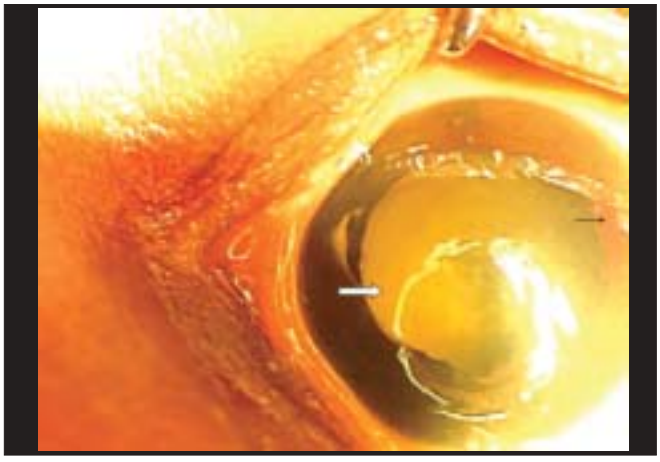

Figure 1a: Retcam photo of anterior segment of left eye showing neovascularization of iris (black arrow), posterior synechiae, ectropion uvea inferiorly and dense retro lental anterior fibrovascular proliferation (white arrow)

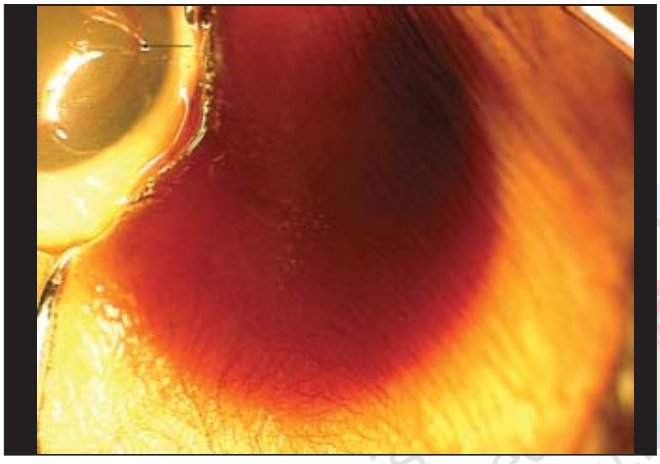

Figure 1b: Anterior segment photo of the same eye showing neovascularisation of iris (black arrow) more clearly

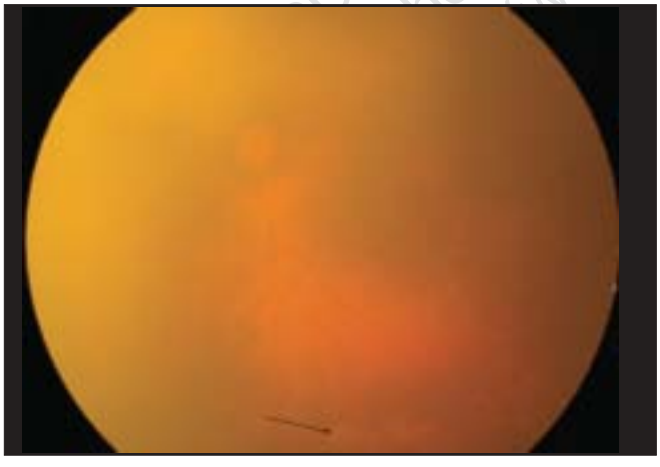

Figure 2: Retcam photo of fundus of left eye showing hazy media with regressing plus disease and peripheral laser scars (black arrow)

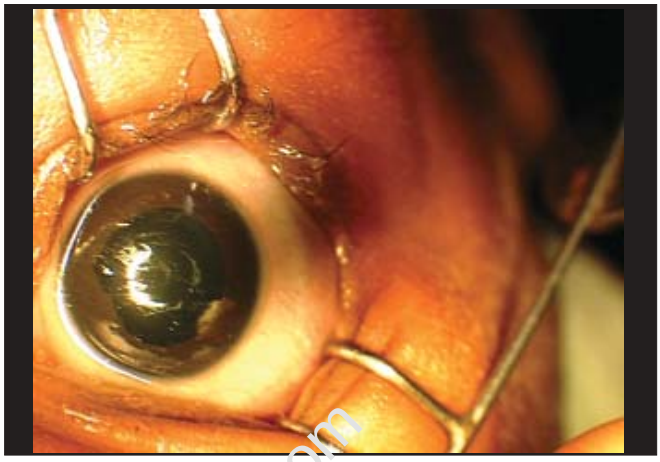

Figure 3: Retcam photo of same eye taken ten weeks postintravitreal injection of bevacizumab showing totally regressed neovascularization of iris and retrolental anterior fibrovascular proliferation

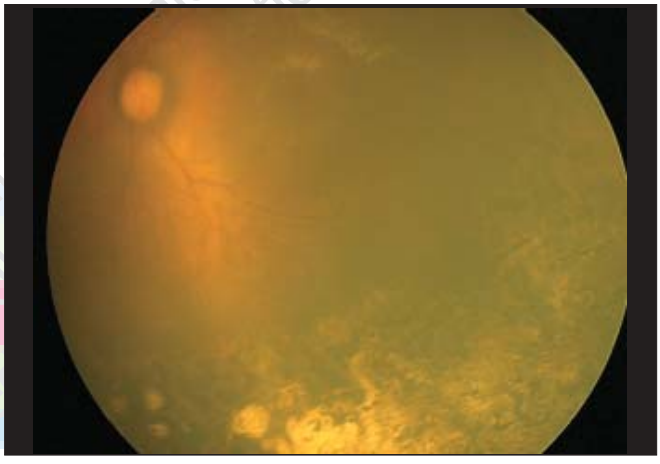

Figure 4: Retcam photo of same eye showing clear media with laser scars and growth of normal vessels into the lasered retinal periphery

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