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Bevacizumab (Avastin) as an Adjunct to Vitrectomy in the Management of Severe Proliferative Diabetic Retinopathy: A Prospective Case Series

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Key Words
Bevacizumab · Vitrectomy · Proliferative diabetic retinopathy

Abstract
Purpose: To evaluate the role of preoperative intravitreal bevacizumab as an adjunct to vitrectomy in diabetic eye disease. ***Methods:*** Twenty eyes of 18 patients were recruited and underwent a single intravitreal injection of bevacizumab 1.25 mg 1 week prior to vitrectomy. Fundus fluorescein angiography (FFA) was done before and 1 week after injections. Best corrected visual acuity (BCVA) and ophthalmic evaluation were done before, 1 week after injections, 1 day, 1 week and monthly for 3 months after vitrectomy. ***Results:*** The mean age was 47.7 ± 10.39 years. The male:female ratio was 2:3. Mean preinjection BCVA (logMAR) was 1.460 ± 0.439. FFA showed a dramatic reduction in dye leakage 1 week after injection. Intraoperative bleedings were minimal in most cases (85%, n = 17). Postoperatively, 16 patients had no bleeding (80%), 4 had minimal bleeding (20%), and 1 had recurrent fibrovascular proliferation (5%). The mean BCVA on day 1, week 1, months 2 and 3 after surgery were 1.645 ± 0.422, 1.300 ± 0.413, 1.065 ± 0.538 and 1.065 ± 0.538 logMAR, respectively (p = 0.078, 0.123, 0.002 and 0.002, respectively). ***Conclusion:*** Bevacizumab administered prior to vitrectomy was well tolerated and was particularly useful during surgery.

Introduction

Traction retinal detachment (TRD) and combined traction and rhegmatogenous retinal detachment (T + RRD) are among the most challenging vitreoretinal surgical scenarios in patients with proliferative diabetic retinopathy (PDR). The surgical management of these cases is complex because these eyes have very thin ischemic retinas, often with massive neovascularization. Intra- and postoperative complications are frequent and include intraoperative bleeding, iatrogenic breaks, postoperative bleeding and redetachments. Of these, intraoperative bleeding that decreases visualization while removing fibrovascular tissue can hinder the completion of a surgical intervention.

Reports of the off-label use of intravitreal bevacizumab (Avastin, Genentech) for the reduction of neovascu-

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larization in PDR have demonstrated significant regression in the number of new vessels [1–3]. Reducing the vascularity of neovascular fibrovascular tissue can potentially reduce bleeding intraoperatively and thus facilitate the vitrectomy procedure. Recently, intravitreal bevacizumab has been suggested as a useful preoperative adjunct for cases with severe active PDR complicated with TRDs [4–18] and postoperatively for recurrent vitreous hemorrhage [19, 20]. The aim of this study was to evaluate the effectiveness of intravitreal injection of bevacizumab as a preoperative adjunct in order to reduce potential intra- and postoperative bleeding, facilitate surgery and improve visual outcomes for patients with severe PDR.

Patients and Methods

Approval for the study was obtained from the hospital's ethical committee. All patients received a thorough explanation of the study design and aims, and gave their written informed consent.

This is a prospective nonrandomized noncomparative clinically controlled study, where bevacizumab (Avastin) was injected intravitreally in 20 eyes suffering from PDR with TRD involving or threatening the macula, combined tractional/rhegmatogenous retinal detachment (T + RRD) and fibrovascular tissue (FVT) covering and distorting the macula. This was followed 1 week later by pars plana vitrectomy for the 20 eyes. The patients were selected from the outpatient ophthalmology clinic of Kasr El-Aini teaching hospital, Cairo University, in 2008.

The inclusion criteria for the patients were eyes with PDR complicated with either (1) TRD involving or threatening the macula, (2) T + RRD and/or (3) FVT covering and distorting the macula. In contrast, the exclusion criteria were eyes with PDR with any of the following: (1) previous vitrectomy, (2) eyes with dense media opacity precluding fundus fluorescein angiography (FFA) as dense cataract and dense vitreous hemorrhage, and (3) eyes with neovascular glaucoma.

Preoperatively all patients were evaluated before injection for best corrected visual acuity (BCVA), slitlamp examination, intraocular pressure (IOP), dilated fundus examination and FFA. Intravitreal injection of bevacizumab (1.25 mg/0.05 ml) was done 1 week before the vitrectomy. All patients were examined on the first day after injection to check for complications resulting from the intravitreal injection. All patients were then re-examined 1 week after the injection and just before the pars plana vitrectomy for BCVA, slitlamp, IOP and FFA. We clinically compared the patients' colored and FFA photographs before and after injections (before surgery) to assess the amount of regression of neovascularization.

Pars plana vitrectomies were performed under general anesthesia. Eyelids were sterilized with betadine 10% and betadine eyedrops 5% for the conjunctival cul-de-sac. Phacoemulsification with implantation of a posterior chamber intraocular lens was done for cases with an age of 50 years or older. Core vitrectomy was done, followed by fenestration of the posterior vitreous cortex with the vitreous cutter for 360° in ring-like fashion to truncate the conical so-called anteroposterior traction. The peripheral margin of the posterior vitreous cortex (vitreous skirt) was trimmed, leaving a minimal amount attached to the vitreous base. Conformal cutter delamination using a side approach was used to remove a significant portion of the FVT. Some of the FVT was judged to be too adherent to the retina for removal with the vitreous cutter and was removed using inside-out scissors delamination with curved scissors. The vascular attachment points were coagulated with the endodiathermy probe when needed. Segmentation is primarily used as access to expose the dissection plane (potential space) for delamination.

A bimanual delamination technique was used for eyes with combined T + RRD and/or when the fibrovascular tissue is covering and distorting the macula using an illuminated infusion cannula or a twin light. Perfluorocarbon liquid was injected. Vitrectomy for the vitreous base was performed for 360° with scleral indentation accomplished by the assistant for all eyes. Endolaser panretinal photocoagulation and endolaser application to retinal breaks were done. Perfluorocarbon liquid/silicone oil exchange was performed through the infusion cannula. Lastly, the sclerotomies were closed using a 7-0 Vicryl suture.

The severity of intraoperative hemorrhage was assessed by the amount of bleeding, the need to raise the infusion pressure and the use of endodiathermy to stop the bleeding. The severity of intraoperative hemorrhage was then evaluated and recorded. Postoperatively all patients were regularly examined on the first day, after 1 week and then monthly for 3 months. The examination included BCVA, anterior segment examination, IOP and dilated fundus examination to detect postoperative vitreous hemorrhage and to evaluate the state of the retina. Silicone oil was removed 3 months postoperatively, and colored fundus photography was performed 1 month after silicone oil removal.

Data was statistically represented in terms of range, mean, standard deviation (±SD) and percentages. Comparisons were done using Student's t test comparing parametric data. For comparing nonparametric data, the χ^2 ($\times 2$) test was performed. Yates correction was used instead when frequency was less than 10. Correlation between various variables was done using Pearson correlation coefficient (r) with graphic representation using linear regression. A p value less than 0.05 was considered significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corp., N.Y., USA) and SPSS (Statistical Package for the Social Sciences) and statistical programs (SPSS Inc., Chicago, Ill., USA).

Results

Our study was performed on 20 eyes (18 patients) suffering from PDR requiring pars plana vitrectomy for the following reasons: TRD affecting the macula, combined T + RRD and FVT covering and distorting the macula.

Patient Data

Age ranged from 23 to 67 years with a mean of 47.7 ± 10.39 years. The male:female ratio was 2:3. From the 18 patients, 11 patients (11 eyes) had insulin-dependent dia-

Table 1. Patients' demographics, diabetes mellitus, hypertension and retinopathy profile, pre- and postoperative BCVA in logMAR, operative bleeding and technique

Case	Age years	Sex	Type of DM	DM years	HT	Dx	NV		BCVA (pre-/postoperative day 1, week 1, months 2, 3)	Operative bleeding		Membrane dissection
							before injection	after injection		intraop.	postop.	
1	37	F	IDDM	20	–	TRD/RRD	severe NVD/ NVE	mild NVD/ resolved NVE	2.00/1.30, 1.10, 0.80, 0.80	minimal	absent	bimanual
2	51	F	IDDM	25	+[1]	TRD/RRD	severe NVD/ NVE	mild NVD/ resolved NVE	1.60/2.20, 1.80, 1.10, 1.10	minimal	mild on ON	bimanual
3	23	F	IDDM	13	–	TRD macula, SH Hge	severe NVD/ NVE	mild NVD/ mild NVE	1.10/0.80, 0.60, 0.50, 0.50	minimal	mild para-ON	unimanual
4	67	M	IDDM	38	–	TRD, massive SH Hge	severe NVD/ NVE	mild NVD/ resolved NVE	0.90/1.30, 1.10, 0.90, 0.90	minimal	absent	unimanual
5	41	M	IDDM	15	–	TRD macula	severe NVD/ NVE	mild NVD/ resolved NVE	1.60/1.80, 1.30, 1.10, 1.10	minimal	absent	unimanual
6	40	F	IDDM	12	–	TRD/RRD	severe NVD/ NVE	mild NVD/ resolved NVE	1.00/1.60, 1.30, 1.00, 1.00	minimal	absent	bimanual
7	51	M	NIDDM	10	+	TRD macula	severe NVD/ NVE	mild NVD/ mild NVE	1.60/1.90, 1.10, 1.10, 1.10	minimal	absent	unimanual
8	46	M	IDDM	18	–	TRD macula	severe NVD/ NVE	mild NVD/ mild NVE	0.50/0.80, 0.50, 0.30, 0.30	minimal	absent/lower tear	unimanual
9	37	F	IDDM	11	–	TRD macula	severe NVD/ NVE	mild NVD/ mild NVE	1.30/0.80, 0.50, 0.50, 0.50	minimal	vitreous Hge	unimanual
10	40	F	IDDM	10	–	TRD macula	severe NVD/ NVE	mild NVD/ resolved NVE	0.80/1.90, 1.60, 0.80, 0.80	minimal	absent	unimanual
11	55	M	NIDDM	9	–	TRD/RRD	severe NVD/ NVE	mild NVD/ resolved NVE	1.60/1.90, 1.30, 1.00, 1.00	minimal	absent/rFV ON	bimanual
12	55	M	NIDDM	9	–	TRD macula	severe NVD/ NVE	mild NVD/ resolved NVE	1.30/1.80, 1.30, 1.00, 1.00	minimal	absent	unimanual
13	36	M	IDDM	20	–	TRD macula	severe NVD/ NVE	mild NVD/ mild NVE	2.00/1.80, 1.30, 1.00, 1.00	minimal	absent	unimanual
14	56	F	NIDDM	10	–	TRD macula	severe NVD/ NVE	mild NVD/ mild NVE	1.60/1.80, 1.30, 1.10, 1.10	minimal	vitreous Hge	unimanual
15	54	M	NIDDM	11	–	TRD macula	severe NVD/ NVE	severe NVD/ mild NVE	1.30/1.90, 1.60, 1.10, 1.10	minimal	absent	unimanual
16	57	F	NIDDM	11	–	FV macula	severe NVD/ NVE	mild NVD/ resolved NVE	1.30/1.90, 1.60, 1.10, 1.10	marked (D)	absent	bimanual
17	57	F	NIDDM	11	–	FV macula	severe NVE	mild NVE	1.90/1.60, 1.30, 1.00, 1.00	minimal	absent	bimanual
18	55	F	NIDDM	13	–	TRD macula	severe NVD/ NVE	mild NVD/ resolved NVE	1.90/2.00, 2.00, 3.00 (PL), 3.00 (PL)	marked (D)	absent	unimanual
19	42	F	IDDM	15	–	TRD macula	severe NVD/ NVE	mild NVD/ resolved NVE	2.00/1.80, 1.60, 1.30, 1.30	minimal	absent	unimanual
20	54	F	NIDDM	12	–	TRD macula	severe NVD/ NVE	severe NVD/ resolved NVE	1.90/2.00, 1.80, 1.60, 1.60	marked (D)	absent	unimanual

DM = Diabetes mellitus; HT = hypertension; Dx = diagnosis; NV = neovessels; BCVA: Best Corrected Visual Acuity in logMAR; IDDM = insulin-dependent diabetes mellitus; NIDDM = non-insulin-dependent diabetes mellitus; RRD = rhegmatogenous retinal detachment; NVD = neovascularization at the disk; NVE = neovascularization elsewhere; ON = optic nerve; SH = subhyaloid; Hge = hemorrhage; rFV = recurrent fibrovascularization; PL = perception of light; D = diathermy.

Eyes No. 11 and 12 represent the right and left eyes of the same male patient, and No. 16 and 17 are for the same female patient.

[1] Patient with open heart surgery.

betes mellitus (type 1), and 7 patients (9 eyes) had non-insulin-dependent diabetes mellitus (type 2). The duration of diabetes ranged from 9 years up to 38 years, with a mean of 14.65 ± 6.97 years. Two patients had a history of hypertension of whom 1 had a history of open heart surgery while the rest of them had no history of hypertension. Preoperatively, the 20 eyes presented with preoperative visual acuities ranging from 2 to 0.5 logMAR. The mean for preoperative BCVA was 1.460 ± 0.439 logMAR (table 1).

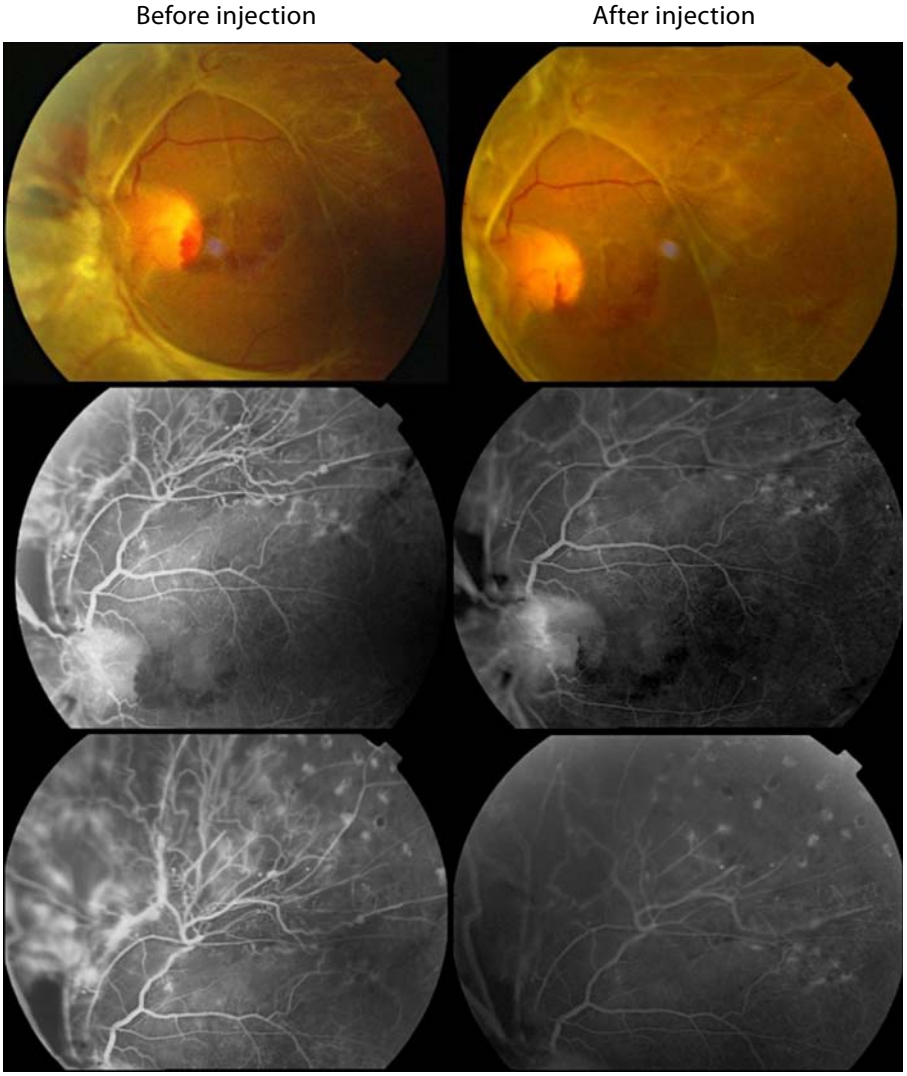

Fig. 1. Case 1: T + RRD, showing pre- and post-Avastin injection changes in fibrovascularization size and activity on colored and fluorescein angiography, respectively.

All eyes had clear media with no dense cataract or dense vitreous hemorrhage allowing preinjection and postinjection FFA to be done. FFA showed PDR with fibrovascular proliferations and late leakage in all of them. Nineteen eyes (95%) showed severe neovascularizations at the disk (NVDs; more than 1/3 disk area) and severe neovascularizations elsewhere (NVEs; more than 1/2 disk area), while 1 eye (5%) had only severe NVEs (table 1).

Colored fundus photography and FFA were done about 5 days after injection and showed significant regression of neovascularization (fig. 1). Twelve eyes had mild NVDs with resolved NVEs (60%), 6 eyes had mild NVDs with mild NVEs (30%), 1 eye had severe NVDs with mild NVEs (5%) and 1 eye had only mild NVEs (5%). There was also a significant decrease in neovessel leakage, no sign of fresh bleeding and no increase in the extent of TRD (table 1).

Pars Plana Vitrectomy

The duration between injection and vitrectomy varied from 5 to 14 days. Intraoperatively the following was noticed. (1) Three eyes (15%) showed marked bleeding requiring intraocular endodiathermy during delamination. The remaining 17 eyes (85%) showed minimal bleeding just requiring raising the infusion bottle or touching the bleeding points with a blunt-tipped instrument. This was statistically highly significant (χ^2 test: $p < 0.0001$). (2) Most epicenters were peeled with blunt dissection. (3) Removal of all epiretinal FVT was successful. Bimanual delamination was done for 6 eyes (30%) while in the remaining 14 eyes (70%) unimanual delami-

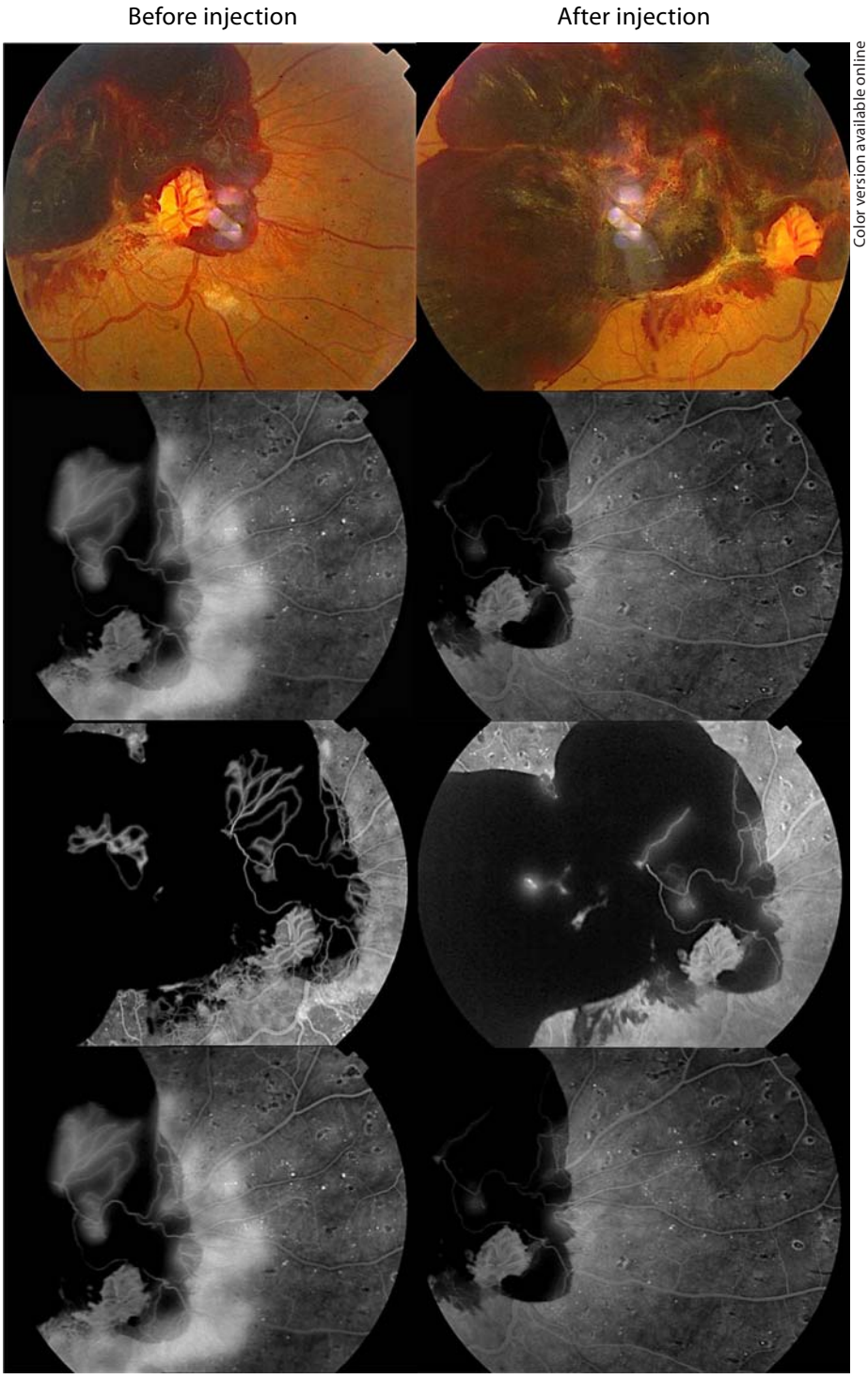

Fig. 2. Case 3: TRD involving the macula with subhyaloid hemorrhage, showing pre- and post-Avastin injection changes in fibrovascularization size and activity on colored and fluorescein angiography, respectively.

nation was done. (4) Combined phacovitrectomy was done for 11 eyes (55%).

All the eyes were examined postoperatively for the incidence of postoperative bleeding (fig. 2). Four out of the 20 eyes (20%) had postoperative bleeding which was minimal and resolved during the follow-up period (3 months). One eye showed recurrent FVT and 1 eye showed an inferior retinal tear.

All eyes were followed for up to 3 months for the functional outcome guided by the BCVA. Postoperative mean

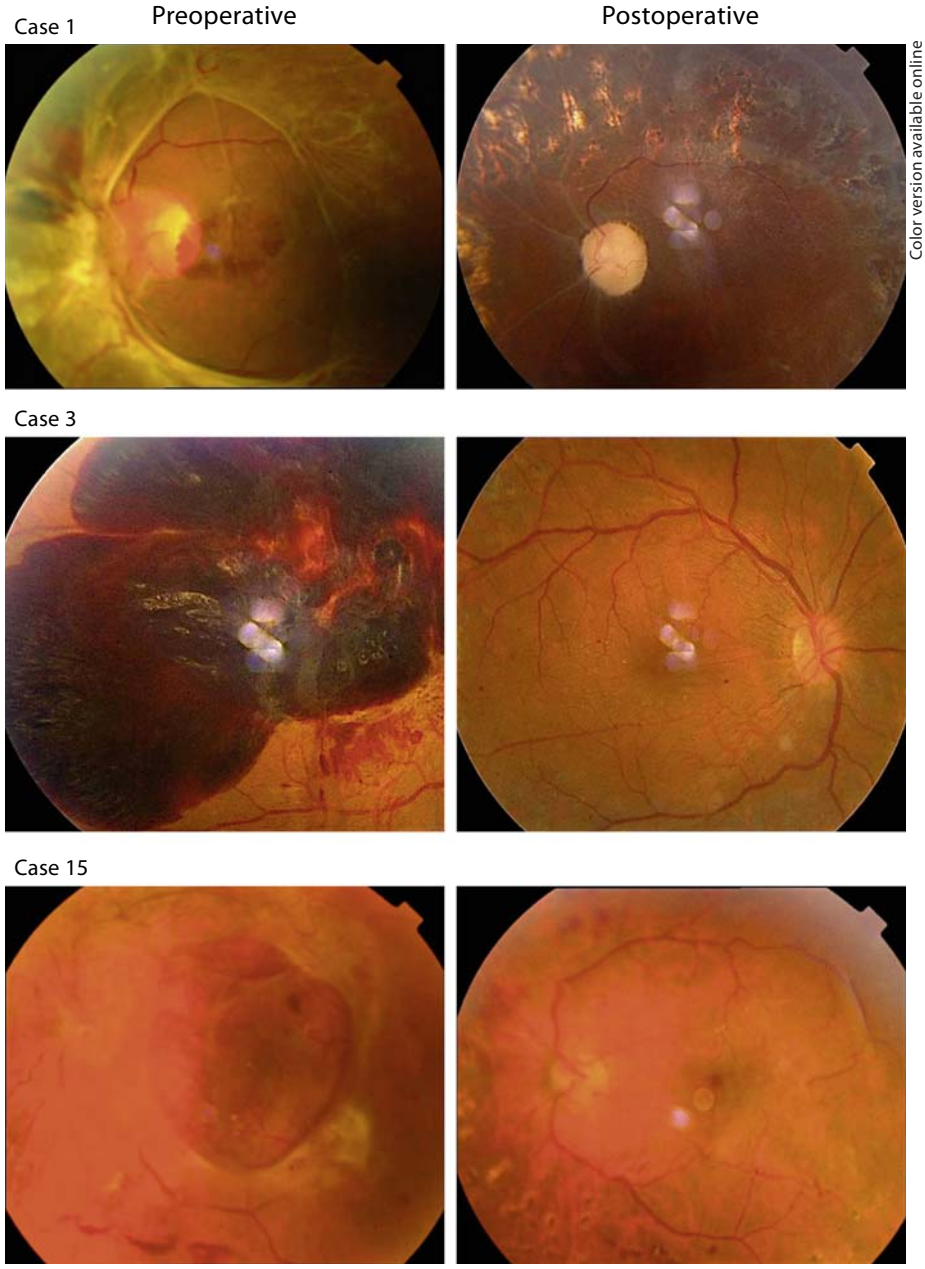

Fig. 3. Pre- and postoperative colored fundus photography of cases 1, 3 and 15.

BCVA was 1.645 ± 0.422, 1.300 ± 0.413, 1.065 ± 0.538 and 1.065 ± 0.538 logMAR for day 1, week 1, and months 2 and 3, respectively, and this was only statistically significant at months 2 and 3 when compared to preoperative BCVA (paired Student's t test: p = 0.078, 0.123, 0.002 and 0.002, respectively). About 65% of the eyes (n = 13) had a significant gain in BCVA (15 letters or more), 15% (n = 3) had a nonsignificant gain in BCVA (less than 15 letters), 15% (n = 3) of the eyes had no change in BCVA and 5% (patient 18) had a finally worse BCVA.

Discussion

Since the early reports [1–3] regarding the use of bevacizumab to elicit rapid regression of retinal neovascularization in eyes with PDR, its use in the management of different aspects of this disease has expanded. Several reports of the preoperative use of bevacizumab to facilitate surgery and improve outcomes in diabetics have shown a significant benefit [4–18]. In 2006, Chen and Park [4] were the first to describe the use of preoperative intravit-

real bevacizumab injection for severe PDR in a 27-year-old man. In their report, vitrectomy was performed after 7 days with all epiretinal fibrovascular membranes successfully removed, minimal bleeding during segmentation and delamination of the membranes, suggesting regression of the recently active neovascular complex [4].

Several other studies were done later on [5–18], of which only 3 were randomized controlled clinical trials [12, 14, 18]. Studies [5–7, 9, 14–16] investigating the visual outcomes in these cases showed visual benefits except one by Lo et al. [11]. However, in this retrospective comparative study by Lo et al. [11], patients in the bevacizumab group were significantly younger and more likely to have 20-gauge instrumentation than those patients in the non-bevacizumab group, which might explain the absence of visual gains. In general, the percentage of patients experiencing visual gains in the reported studies ranged from 38% in the early postoperative period [5] to 87% in the late postoperative period [7]. The preoperative BCVA in these cases ranged from 1.6 to 1.88 logMAR, and the postoperative BCVA ranged from 0.4 to 1.1 logMAR [6, 9, 16].

All reported studies [5–18] agreed on the benefits of preoperative intravitreal bevacizumab in reducing the rates of intraoperative bleeding in these patients. However, the rate of intraoperative bleeding has been extremely variable among reported studies (range 8.3–90%) [6, 8, 10, 11, 14, 18]. This might be explained by the different methodology used in each study for defining and grading intraoperative bleeding as well as by the difference in severity and complexity of cases operated upon in each study. In addition, the rate of use of endodiathermy to stop the intraoperative bleeding was less variable and ranged from 1.5 to 18% [6, 18]. On the other hand, most reported studies [5–7, 9, 10, 12–18] agreed on the benefits of preoperative intravitreal bevacizumab in reducing the rates of postoperative bleeding in these patients. However, in 2 separate reports by Yang et al. [8] and Lo et al. [11], there were no significant benefits in the rate of reduction of postoperative recurrent vitreous hemorrhage. The rate of postoperative vitreous hemorrhage ranged from none in some studies [7, 8] to 39% of patients in others [5].

In our study, we chose to evaluate the benefit of pretreatment with bevacizumab on eyes undergoing vitrectomy for complex complications of diabetic retinopathy. About 65% of the eyes (n = 13) had a significant gain in BCVA, 15% (n = 3) had nonsignificant gains, 15% (n = 3) had no change and 5% (n = 1) had a finally worse BCVA. This means that 80% of our study eyes experienced visual gains at 3 months, which correlates well with previously reported percentages [5–7, 9, 14–16]. Eighteen eyes had a dramatic reduction in size and activity of NVDs and NVEs 1 week following the injections, and eyes No. 15 and 20 had only a mild reduction in neovascularizations (fig. 3).

Most eyes (85%, n = 17) had only minimal intraoperative bleeding, while 3 eyes (15%) had marked intraoperative bleeding requiring endodiathermy. Those 3 eyes belonged all to nonhypertensive female patients with non-insulin-dependent diabetes mellitus for 11–13 years and all 3 had a final BCVA gain at 3 months. It is worth noting also that the 3 eyes with marked intraoperative bleeding are among the 16 eyes that did not have any vitreous, retinal and/or optic nerve bleeding in the postoperative period. The severity and complexity of our cases, where 18 out of the 20 eyes had TRD of which 4 had combined T + RRD, might partly explain the presence of intraoperative bleeding in all cases. However, most intraoperative bleedings were minimal as seen by the need to use endodiathermy in only 15% of eyes, which again correlates well with previous reported rates [6, 18].

Two eyes had postoperative vitreous hemorrhage and 2 had bleeding at the optic nerve head. All 4 eyes with postoperative bleeding belonged to 4 female patients with a final BCVA gain at 3 months. Three of them had insulin-dependent diabetes mellitus, and 1 patient was hypertensive with a history of previous open heart surgery and a diabetes disease duration of 25 years.

Although the number of patients in this study sample is small, yet we can conclude few trends about the factors that might influence the visual prognosis. Four eyes of 4 patients did not experience any visual gains. There were no major changes in the age or gender structures for these 4 patients when compared with the rest of the 20 patients (3 females and 1 male and age range 40–67 years). Also none of these patients had postoperative bleeding, only 1 had marked intraoperative bleeding, none of them was hypertensive, 3 had insulin-dependent diabetes mellitus, and only 1 had a disease duration of more than 15 years (38 years). In addition, 3 of these patients had a BCVA logMAR of 1 or less at baseline, which might have given a little room for further visual improvement, as the other patients with visual gains had a BCVA of more than 1 logMAR at baseline.

Preoperative injection of bevacizumab in eyes with TRD and T + RRD appears to facilitate surgery, and improve visual outcomes. Fewer postoperative complications were seen, and fewer postoperative procedures were required. However, our study is limited by the small sample size (only 20 eyes) and the absence of a control group. Finally, large prospective, randomized studies are needed to further evaluate this treatment modality.

References

1 Avery RL, Pearlman J, Pieramici DJ, Rabena MD, Castellarin AA, Nasir MA, Giust MJ, Wendel R, Patel A: Intravitreal bevacizumab (Avastin) in the treatment of proliferative diabetic retinopathy. Ophthalmology 2006; 113:1695.

2 Jorge R, Costa RA, Calioli D, Cintra LP, Scott IU: Intravitreal bevacizumab (Avastin) for persistent new vessels in diabetic retinopathy (IBEPE study). Retina 2006;26:1006–1013.

3 Spaide RF, Fisher YL: Intravitreal bevacizumab (Avastin) treatment of proliferative retinopathy complicated by vitreous hemorrhage. Retina 2006;26:275–278.

4 Chen E, Park CH: Use of intravitreal bevacizumab as a preoperative adjunct for tractional retinal detachment repair in severe proliferative diabetic retinopathy. Retina 2006;26: 699–700.

5 Yeoh J, Williams C, Allen P, Buttery R, Chiu D, Clark B, Essex R, McCombe M, Qureshi S, Campbell WG: Avastin as an adjunct to vitrectomy in the management of severe proliferative diabetic retinopathy: a prospective case series. Clin Exp Ophthalmol 2008;36: 449–454.

6 Rizzo S, Genovesi-Ebert F, Di Bartolo E, Vento A, Miniaci S, Williams G: Injection of intravitreal bevacizumab (Avastin) as a preoperative adjunct before vitrectomy surgery in the treatment of severe proliferative diabetic retinopathy (PDR). Graefes Arch Clin Exp Ophthalmol 2008;246:837–842.

7 El-Batarny AM: Intravitreal bevacizumab as an adjunctive therapy before diabetic vitrectomy. Clin Ophthalmol 2008;2:709–716.

8 Yang CM, Yeh PT, Yang CH, Chen MS: Bevacizumab pretreatment and long-acting gas infusion on vitreous clear-up after diabetic vitrectomy. Am J Ophthalmol 2008;146:211–217.

9 Romano MR, Gibran SK, Marticorena J, Wong D, Heimann H: Can a preoperative bevacizumab injection prevent recurrent postvitrectomy diabetic vitreous hemorrhage? Eye 2009;23:1698–1701.

10 Yeh PT, Yang CM, Lin YC, Chen MS, Yang CH: Bevacizumab pretreatment in vitrectomy with silicone oil for severe diabetic retinopathy. Retina 2009;29:768–774.

11 Lo WR, Kim SJ, Aaberg TM Sr, Bergstrom C, Srivastava SK, Yan J, Martin DF, Hubbard GB 3rd: Visual outcomes and incidence of recurrent vitreous hemorrhage after vitrectomy in diabetic eyes pretreated with bevacizumab (Avastin). Retina 2009;29:926–931.

12 da R Lucena D, Ribeiro JA, Costa RA, Barbosa JC, Scott IU, de Figueiredo-Pontes LL, Jorge R: Intraoperative bleeding during vitrectomy for diabetic tractional retinal detachment with versus without preoperative intravitreal bevacizumab (IBeTra study). Br J Ophthalmol 2009;93:688–691.

13 Yeung L, Liu L, Wu WC, Kuo YH, Chao AN, Chen KJ, Yang KJ, Chen TL, Lai CC: Reducing the incidence of early postoperative vitreous hemorrhage by preoperative intravitreal bevacizumab in vitrectomy for diabetic tractional retinal detachment. Acta Ophthalmol 2009, E-pub ahead of print.

14 Ahmadieh H, Shoeibi N, Entezari M, Monshizadeh R: Intravitreal bevacizumab for prevention of early postvitrectomy hemorrhage in diabetic patients: a randomized clinical trial. Ophthalmology 2009;116: 1943–1948.

15 Oshima Y, Shima C, Wakabayashi T, Kusaka S, Shiraga F, Ohji M, Tano Y: Microincision vitrectomy surgery and intravitreal bevacizumab as a surgical adjunct to treat diabetic traction retinal detachment. Ophthalmology 2009;116:927–938.

16 Modarres M, Nazari H, Falavarjani KG, Naseripour M, Hashemi M, Parvaresh MM: Intravitreal injection of bevacizumab before vitrectomy for proliferative diabetic retinopathy. Eur J Ophthalmol 2009;19:848–852.

17 Ishikawa K, Honda S, Tsukahara Y, Negi A: Preferable use of intravitreal bevacizumab as a pretreatment of vitrectomy for severe proliferative diabetic retinopathy. Eye (Lond) 2009;23:108–111.

18 Di Lauro R, de Ruggiero P, di Lauro R, di Lauro MT, Romano MR: Intravitreal bevacizumab for surgical treatment of severe proliferative diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol 2010;248:785–791.

19 Romano MR, Gibran SK, Marticorena J, Wong D, Heimann H: Can an intraoperative bevacizumab injection prevent recurrent postvitrectomy diabetic vitreous hemorrhage? Eur J Ophthalmol 2009;19:618–621.

20 Yeh PT, Yang CH, Yang CM: Intravitreal bevacizumab injection for recurrent vitreous hemorrhage after diabetic vitrectomy. Acta Ophthalmol 2010, E-pub ahead of print.