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Outcomes after Intravitreal Bevacizumab versus Laser Photocoagulation for Retinopathy of Prematurity

A 5-Year Retrospective Analysis

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Purpose: To determine the relative effectiveness, major complications, and refractive errors associated with intravitreal bevacizumab (IVB) versus panretinal photocoagulation (PRP) to treat type 1 retinopathy of prematurity (ROP).

Design: Retrospective case series.

Participants: Consecutive infants with type 1 ROP who received either IVB or PRP and had at least 6 months of follow-up.

Methods: The data from infants treated with either IVB or PRP for type 1 ROP between 2008 and 2012 were recorded from 2 medical centers in Atlanta, Georgia.

Main Outcome Measures: Recurrence rate, complication rate, and refractive error.

Results: A total of 54 eyes (28 patients) with type 1 ROP were evaluated: 22 eyes (11 patients) received IVB, and 32 eyes (17 patients) received PRP. Among the 22 eyes treated with IVB, 16 eyes had zone I ROP and 6 eyes had posterior zone II ROP. The number of zone I and II ROP eyes treated with PRP were 5 and 27, respectively. Mean gestational age, birth weight, postmenstrual age at initial treatment, and follow-up period for the infants receiving IVB were 24.2 weeks, 668.1 g, 35.1 weeks, and 21.7 weeks, respectively, and for the infants receiving PRP, these were 24.8 weeks, 701.4 g, 36.1 weeks, and 34.5 weeks, respectively. Retinopathy of prematurity recurred in 3 (14%) of 22 IVB-treated eyes and in 1 (3%) of 32 PRP-treated eyes. Neither retinal detachment nor macular ectopia developed in any of the IVB-treated eyes. In PRP-treated eyes, retinal detachment developed in only 1 eye and macular ectopia developed in 5 eyes. Mean spherical equivalent and postgestational age at the last refraction for IVB-treated eyes were −2.4 diopters (D) and 22.4 months, respectively, and for PRP-treated eyes, these were −5.3 D and 37.1 months, respectively. Mean spherical equivalent for zone I ROP eyes treated with IVB and PRP were −3.7 D and −10.1 D, respectively, and for zone II ROP eyes, these were 0.6 D and −4.7 D, respectively.

Conclusions: Both IVB and PRP are effective treatment options for type 1 ROP with low complication rates. IVB was associated with less myopia than PRP, although longer follow-up was available for PRP. *Ophthalmology 2015;122:1008-1015 © 2015 by the American Academy of Ophthalmology.*

Retinopathy of prematurity (ROP) is a leading cause of blindness in children worldwide. It is a proliferative vascular disorder of the retina that exclusively affects premature infants. Although the pathogenesis of ROP is not completely understood, one of the causative factors leading to ROP is dysregulation of vascular endothelial growth factor (VEGF),[1] leading to abnormal vasculogenesis and neovascularization.[2–4]

Panretinal photocoagulation (PRP) has been used for the last 2 decades to treat ROP. However, the side-effect profile of PRP is substantial, including permanent destruction of a considerable portion of the retina, visual field loss, and high myopia.[5–11] Moreover, despite treatment with PRP, some eyes progress to retinal detachment. In recent years, the VEGF inhibitors like bevacizumab,[12] which have been used effectively to treat other types of retinopathies like age-related macular degeneration and diabetic retinopathy,[13–17] have been used off-label to treat ROP.[18–24]

Although the BEAT-ROP (Bevacizumab Eliminates the Angiogenic Threat of Retinopathy of Prematurity) study[25] showed improved outcomes with intravitreal bevacizumab (IVB) compared with PRP for zone I ROP, confirmatory studies are lacking. Although recent studies have assessed the effectiveness of IVB or PRP to treat ROP, only a single treatment method was analyzed, and no direct comparison was made between IVB and PRP.[23–27] Moreover, many of these studies were conducted in developing countries in which patient profiles differ significantly from those of the patients in the BEAT-ROP study.

This study compared the clinical outcome of babies with type 1 ROP treated with IVB versus PRP. The infants in this

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study had similar patient characteristics to the infants enrolled in the BEAT-ROP study,[25] but had a longer follow-up period.

Methods

After approval from the Institutional Review Board at Emory University School of Medicine, we conducted a retrospective chart review of infants who underwent treatment for type 1 ROP to assess and compare the use of IVB (Avastin; Genentech, Inc., South San Francisco, CA) versus PRP. Included in the study were consecutive infants with type 1 ROP who received either IVB or PRP between January 2008 and December 2012 at Children's Healthcare of Atlanta at Egleston Hospital and Emory Midtown Hospital in Atlanta, Georgia, and had at least 6 months of follow-up. From January 2008 through January 2011, patients with either zone I or zone II type 1 ROP were treated exclusively with PRP. After the publication of the BEAT-ROP study in 2011, we also offered IVB to patients with either zone I or posterior zone II type 1 ROP as an alternative to PRP. However, starting in October 2011 after the publication of several studies raising awareness of potential, deleterious systemic effects from IVB, we offered IVB exclusively to zone I ROP patients. Infants whose ROP met the criteria for type 1 ROP, as defined by the Early Treatment for Retinopathy of Prematurity study as zone I with any stage with plus disease, zone I with stage 3 without plus disease, and zone II with stage 2 or 3 with plus disease, were treated.[28] After the treatment with either IVB or PRP, each infant initially was examined every 1 to 2 weeks until the ROP regressed completely, and in the case of IVB, until the retinal vessels extended into zone III. Subsequently, each infant was examined less frequently in a gradual fashion, from every 4 weeks to every 3 to 6 months. For IVB, a lid speculum first was placed in the eye and then 2 to 3 drops of tetracaine 0.5% were placed into the eye. The eye was sterilized with 10% povidone solution with a swab. An injection of bevacizumab 0.625 mg (0.025 ml solution) was performed through the pars plicata using a 30-gauge needle, aiming the needle directly toward the optic nerve in direction of visual axis. For PRP, the infant was intubated and sedated under the supervision of an attending neonatologist. An indirect laser at wavelength 810 nm then was used to apply photocoagulation to the entire avascular retina. The screening and treatment were administered by 2 experienced, attending physicians, one of whom specializes in vitreoretinal surgery (G.B.H.) and the other in pediatric ophthalmology (A.K.H.).

The following characteristics were recorded for each patient in the study: estimated gestational age at birth, birth weight, gender, ROP zone, ROP stage, race of the mother, comorbidities, 1- and 5-minute Apgar scores, mean age at treatment, and follow-up period. The clinical status of the retina at the last dilated fundus examination was noted for each patient, and the status was classified as attached with no dragging or macular ectopia, attached with macular ectopia, attached with dragging, detached stage 4, detached stage 5, and others. The main outcome measures included ROP recurrences requiring retreatment or progressing to retinal detachment, or both; major complications associated with each treatment group; and refractive errors. We defined recurrence as any of the following: recurrent plus disease, recurrent neovascularization, or progression of traction despite treatment. The time from the initial treatment to the recurrence, the type of treatment administered after the recurrence, and the clinical outcome were recorded for each recurrence. Major complications were defined as corneal opacity requiring corneal transplant, lens opacity requiring cataract surgery, preretinal or intravitreal hemorrhage requiring vitrectomy, and ROP crunch (rapid progression to tractional retinal detachment after IVB). Intraocular pressure (IOP) was not measured routinely for each patient, but when there were visible signs of increased IOP, such as corneal clouding and mucoid discharge, IOP was calculated based on the average of 3 separate Tono-Pen (Reichert, Depew, NY) measurements. The refractive error data comprised spherical power, cylindrical power, spherical equivalent, and age at examination. Cycloplegic refractions were performed after instilling 1 drop of a mixture of 1% cyclopentolate, 1% tropicamide, and 2.5% phenylephrine in each eye and then waiting 30 to 40 minutes for cycloplegia to be achieved.

For statistical analyses, the t test for independent means, the Mann−Whitney rank-sum test, the chi-square test, and the Fisher exact test were used. A P value less than 0.05 was considered statistically significant. Numerical data are expressed as mean ± standard deviation unless otherwise stated.

Results

Of 39 infants who were treated for type 1 ROP from January 2008 through December 2012, 11 infants had fewer than 6 months of follow-up and were excluded from this study. A total of 54 eyes from 28 patients were included in this study (Table 1). The composition of the maternal race for the IVB group and PRP was similar. The IVB group comprised 45% black persons, 27% white persons, 0% Hispanic persons, 18% Asians, and 9% persons of other racial or ethnic backgrounds, whereas the PRP group comprised 41% black persons, 35% white persons, 23% Hispanic persons, and 0% Asians. Twenty-two eyes from 11 patients were treated with IVB (Fig 1), and 16 of 22 eyes (8 patients) had zone I ROP, whereas 6 of 22 eyes (3 patients) had zone II ROP. Twenty of 22 eyes treated with IVB had stage 3 ROP and 2 of 22 eyes had stage 2 ROP. All 22 eyes treated with IVB had plus disease. Thirty-two eyes from 17 patients were treated with PRP (Fig 2) and 5 of 32 eyes (3 patients) had zone I ROP, whereas 27 of 32 eyes (14 patients) had zone II ROP. All 32 eyes treated with PRP had stage 3 ROP. Among the 32 eyes treated with PRP, 31 of 32 had plus disease and 1 of 32 had zone I stage 3 pre-plus ROP. Regression of the disease was seen within 48 hours in the IVB-treated eyes and within 1 to 2 weeks in the PRP-treated eyes. The mean time from the initial treatment to reach zone III for the IVB-treated eyes was 5.5±1.8 months (range, 2.2−7.4 months). At the last dilated fundus examination, 22 (100%) of 22 eyes treated with IVB had an attached retina with no macular ectopia, whereas among 32 eyes treated with PRP, 26 (81%) of 32 eyes had an attached retina with no macular ectopia, 5 (16%) of 32 eyes had an attached retina with macular ectopia, and 1 (3%) of 32 eyes progressed to stage 5 retinal detachment. Only 1 eye in 2 patients of the 17 ROP patients treated with PRP was included in the study. In 1 patient, 1 eye had zone III stage 2 ROP without plus disease and did not require treatment. In another patient, 1 eye had zone II pre-plus ROP, which was treated with PRP based on the patient's family preference, but did not meet the criteria for type 1 ROP, and the data from that eye were omitted from the study.

A total of 4 eyes, all of which had zone I ROP, had recurrence (Table 2). Retinopathy of prematurity recurred in 3 (19%) of 16 zone I ROP eyes initially treated with IVB and in 1 (20%) of 5 zone I ROP eyes initially treated with PRP. There was no significant difference in the recurrence rate between the 2 groups ($P = 1.0$). In all 3 recurrence cases in the IVB group, ROP regressed. Two cases were retreated with IVB, whereas for the third case, PRP was used as the second treatment. The average time between the initial IVB and additional treatment was 9.0±5.7 weeks (range, 2.4−12.3 weeks), and the mean age at which the recurrence took place was 45.0±6.3 weeks postmenstrual age (range, 37.7−48.6 weeks). In the PRP group,

Table 1. Characteristics of Retinopathy of Prematurity Patients Receiving Intravitreal Bevacizumab or Panretinal Photocoagulation

	Intravitreal Bevacizumab	Panretinal Photocoagulation	*P* Value
No. of eyes (patients)	22 (11)	32 (17)	
Zone 1	16 (8)	5 (3)	
Zone 2	6 (3)	27 (14)	
Mean birth age (wks)	24.2±1.0 (23–26)	24.8±1.2 (23–28)	
Zone 1	24.3±1.0 (23–26)	24.4±0.0 (24–24)	0.70
Zone 2	24.0±1.0 (23–25)	24.9±1.3 (23–28)	0.26
Mean birth weight (g)	668.1±127.3 (473–850)	701.4±118.8 (525–970)	
Zone 1	667.6±117.4 (515–850)	697.7±89.6 (629–799)	0.70
Zone 2	669.3±181.2 (473–830)	702.2±127.0 (525–970)	0.71
Male gender (%)	55	76	0.24
Zone 1	63	100	
Zone 2	33	71	
Mother's race (%)			0.13
Black	45	41	
White	27	35	
Hispanic	0	23	
Asian	18	0	
Other	9	0	
Comorbidities (%)			0.21
Intraventricular hemorrhage	64	47	
Grade I	27	0	
Grade II	18	12	
Grade III	9	18	
Grade IV	1	18	
Necrotizing enterocolitis requiring surgery	73	59	
Sepsis with positive cultures	45	41	
Patent ductus arteriosus corrected with ligation	18	18	
Mean Apgar score at 1 min	3.1±2.5 (1–8)	3.8±2.1 (1–7)	
Zone 1	3.5±2.9 (1–8)	5.0±2.0 (3–7)	0.43
Zone 2	2.0±1.0 (1–3)	3.6±2.1 (1–7)	0.23
Mean Apgar score at 5 min	5.8±2.0 (2–8)	6.3±2.4 (1–9)	
Zone 1	6.3±1.8 (4–8)	7.3±1.5 (6–9)	0.37
Zone 2	4.7±2.5 (2–7)	6.1±2.6 (1–9)	0.31
Mean age at treatment (PMA)	35.1±2.2 (31.7–38.0)	36.1± 2.3 (32.7–39.9)	
Zone 1	34.9±2.2 (31.7–38.0)	33.6±0.8 (32.7–34.1)	0.76
Zone 2	35.5±2.7 (32.4–37.6)	37.4±2.0 (33.4–39.9)	0.58
Follow-up period (mos)	21.7±8.8 (9.8–33.7)	34.5±20.4 (6.8–72.8)	
Zone 1	19.1±8.1 (9.8–33.7)	38.6±20.7 (14.9–52.8)	0.04
Zone 2	28.8±7.5 (20.2–33.7)	33.7±21.0 (6.8–72.8)	0.52

PMA = postmenstrual age.
Data are mean ± standard deviation (range) unless otherwise indicated.

1 infant had a recurrence 2.6 weeks after the initial treatment at 35.3 weeks postmenstrual age. This patient had progression to traction detachment because of fibrosis and blood after laser. There were no skip areas and no additional laser treatment was performed. Laser was applied only to the avascular retina and not posterior to the ridge. Fibrosis and traction developed in the eye in association with blood in the first few weeks after laser, and the eye underwent vitrectomy, but the eye progressed to stage 5 despite this intervention.

Preretinal or vitreous hemorrhage occurred in 4 (18%) of 22 eyes treated with IVB, but none of them involved the visual axis or required vitrectomy. No corneal or lenticular opacities, vascular sheathing, or ROP crunch were identified, and no systemic effects related to IVB were reported. In eyes treated with PRP, preretinal or vitreous hemorrhage not involving the visual axis or requiring vitrectomy occurred in 3 (9%) of 32 eyes. Signs of increased IOP, including corneal clouding and mucoid discharge, developed in 1 eye several weeks after PRP, which prompted the evaluation for and discovery of ocular hypertension. Corneal or lenticular opacities did not develop in any eyes.

Refractive error data were available for 49 (93%) of 54 eyes from 26 (93%) of 28 patients (Table 3). Twenty eyes in 10 patients were treated with IVB, and 14 (70%) of 20 eyes had zone I ROP, whereas 6 (30%) of 20 eyes had posterior zone II ROP. Twenty-nine eyes in 16 patients were treated with PRP; 4 (14%) of 29 eyes had zone I ROP, and 25 (86%) of 29 eyes had zone II ROP. The mean postgestational age at which the latest refractive data were available was 22.4±8.1 months (range, 11.8–36.6 months) for the infants treated with IVB and 37.1±19.8 months (range, 9.6–76.2 months) for the infants treated with PRP. The average spherical power, cylindrical power, and spherical equivalent were −3.0±3.7 diopters (D; range, −9.5 to 2.5 D), 1.0±0.8 D (range, 0–2.5 D), and −2.4±3.5 D (range, −8.9 to 2.5 D), respectively, for the infants in the IVB group and −6.1±5.6 D (range, −17.5 to 1.8 D), 1.6±1.5 D (range, 0–5 D), and −5.3±5.4 D (range, −16.5 to 1.8 D), respectively, for the infants in the PRP group. The mean spherical power, mean cylindrical power, and mean spherical equivalent were not significantly different between zone I ROP eyes treated with IVB versus PRP ($P = 0.09$, $P = 0.13$, and $P = 0.41$, respectively). However, in babies with zone II ROP,

Figure 1. Pretreatment and posttreatment fundus photographs showing the retina after intravitreal bevacizumab. **A**, Plus disease with prominent tortuosity and congestion of the retinal vessels are observed before treatment in the left eye of a patient with type 1 retinopathy of prematurity. **B**, Two weeks after treatment, the retinal vessels appear significantly less tortuous and congested.

the mean spherical power and mean spherical equivalent were significantly greater in the infants treated with PRP than in those treated with IVB ($P = 0.004$ and $P = 0.002$, respectively). The mean cylindrical power was not significantly different between the 2 groups for zone II ROP ($P = 0.19$). For ROP eyes treated with IVB and PRP, mean spherical equivalent was significantly more severe in zone I than in zone II ($P = 0.007$ and $P = 0.03$, respectively).

Discussion

We found that eyes with type 1 ROP had similarly low recurrence and complication rates after treatment with either IVB or PRP. Moreover, we observed myopic refractive errors in eyes with zone I ROP in both the IVB and PRP treatment groups.

Both IVB and PRP are effective treatment options for ROP. Studies assessing the effectiveness of IVB in treating zone I and II ROP have shown similarly low recurrence rates (6%−10%) (Table 4).[23−25] Likewise, recurrence rates of zone I and zone II ROP after treatment with PRP coincide with our results.[26,27] One study reported treating161 eyes with zone I ROP with PRP, and after a mean follow-up of 10.3 months, ROP recurred in only 13 (7.7%) of 169 eyes.[26] Moreover, another study reported that ROP recurred in only 19 (17.4%) of 109 eyes with zone I or II ROP treated with PRP after 6 months or longer of follow-up.[27] However, the BEAT-ROP study showed significantly higher recurrence

Figure 2. Pretreatment and posttreatment fundus photographs showing the retina after pan-retinal photocoagulation (PRP). **A**, Plus disease with prominent tortuosity and congestion of the retinal vessels are observed in the left eye of a patient with type 1 retinopathy of prematurity before treatment. **B**, The retinal vessels appear significantly less tortuous and congested 2 weeks after PRP.

Table 2. Retinopathy of Prematurity Recurrence Rates in Intravitreal Bevacizumab and Panretinal Photocoagulation Groups

Group	No. of Eyes with Recurrence (%)	Type	Outcome
IVB	3/22 (14)		
Zone 1	3/16 (19)	Plus (n = 2); NVI (n = 1)	Regressed after laser photocoagulation (n = 2); regressed after second IVB (n = 1)
Zone 2	0/6 (0)		
PRP	1/32 (3)		
Zone 1	1/5 (20)	RD	Stage 5 RD
Zone 2	0/27 (0)		

IVB = intravitreal bevacizumab; NVI = neovascularization of the iris; PRP = panretinal photocoagulation; RD = retinal detachment.

rate after PRP versus IVB (22% vs. 4% overall; 35% vs. 3.2% for zone I ROP). These recurrence rates are much higher than what we report in the present study, although the patient characteristics of our study and the BEAT-ROP study are similar.[25] Although a few studies have reported a high recurrence rate (21%–78%) in eyes with zone I ROP eyes treated with PRP,[29–31] these studies treated eyes with threshold ROP, which is associated with a higher recurrence rate than eyes with type 1 ROP.[28]

Although our study was not powered to evaluate safety, we did not detect significant complications with either IVB or PRP. In our study, similar rates of preretinal or vitreous hemorrhages were noted after treatment with IVB and PRP, and none of these hemorrhages involved the visual axis or required a vitrectomy. These results are in sharp contrast to those reported in the BEAT-ROP study that showed significantly higher complication rates in the PRP-treated group compared with the IVB-treated group. The reasons for the discrepancy between the results from our study and the BEAT-ROP study are not entirely clear. It is possible that the ethnic composition could play a role, because most of the BEAT-ROP patient population was Hispanic, whereas our study comprised mainly non-Hispanics. Nonetheless, the use of IVB to treat ROP is not without shortcomings or potentially harmful consequences. For example, an optimal dose of IVB for treating ROP has yet to be established.[32,33] Moreover, intravitreal IVB has been shown to suppress systemic VEGF levels significantly for at least 2 weeks in infants with ROP,[34] which may result in deleterious systemic effects. In addition, the long-term ocular effects of IVB in infants are not known.

Our study included 3 infants with posterior zone II ROP who were treated with IVB. After the publication of the results of the BEAT-ROP study, but before October 2011, we offered IVB to patients with either zone I or posterior zone II type 1 ROP as an alternative to conventional PRP. Occasionally, IVB was chosen over PRP in a patient whose systemic status was considered too fragile to withstand laser treatment. All had been counseled appropriately as to the known and unknown risks of IVB. However, after the release of several publications that raised awareness of decreased systemic VEGF levels in patients receiving IVB,[34–36] we offered only IVB to infants with zone I ROP.

Both IVB-treated and PRP-treated ROP eyes were associated with myopic refractive errors. Our results from eyes treated with PRP are consistent with those published in other studies that showed mean myopic refractive errors ranging from −2.3 to −6.7 D.[5–8,11,37–40] Although the number of studies reporting refractive error data for IVB-treated eyes is limited, 2 studies showed a mean myopic refractive error

Table 3. Refractive Errors in Retinopathy of Prematurity Infants after Treatment with Intravitreal Bevacizumab or Panretinal Photocoagulation

	Intravitreal Bevacizumab	Panretinal Photocoagulation	P Value
Mean spherical power			
Zone 1	−4.3±3.4 (−9.5 to 0)	−11.2±11.0 (−17.5 to 1.5)	0.09
Zone 2	0.3±2.0 (−2.0 to 2.5)	−5.5±4.6 (−16.3 to 0)	0.004
Mean cylindrical power			
Zone 1	1.2±0.8 (0–2.5)	2.1±1.1 (1.0–3.25)	0.13
Zone 2	0.6±0.8 (0–1.75)	1.6±1.6 (0–5.0)	0.19
Mean spherical equivalent			
Zone 1	−3.7±3.3 (−8.9 to 0.3)	−10.1±10.5 (−16.5 to 2.0)	0.41
Zone 2	0.6±1.7 (−1.1 to 2.5)	−4.7±4.6 (−16 to 0)	0.002
Mean age at last refraction (mos)			
Zone 1	18.4±5.1 (11.8–25.1)	52.8±2.4 (50.7–54.8)	0.004
Zone 2	31.5±6.3 (23.4–36.6)	34.6±20.2 (9.6–76.2)	1.0

Data are mean ± standard deviation (range) unless otherwise indicated.

Table 4. Comparison of the Present Study with Other Published Studies Reporting the Results of Treating Type 1 Retinopathy of Prematurity

Study	Location	Treatment Type	No. of Eyes	No. of Eyes in Zone 1 (%)	Race	Mean Postmenstrual Age at Birth (wks)	Mean Postmenstrual Age at Treatment (wks)	Mean Birth Weight (g)	Follow-up (mos)	Recurrence Rate, No. (%)
Mintz-Hittner et al,[25] 2011	United States									
		IVB	75	33 (44)	Mixed	24.4	35.1	652.1	~5	4/70 (6)
		Laser	75	34 (44)	Mixed	24.4	34.8	669.3	~5	19/73 (26)
Jalali et al,[26] 2011	India	Laser	161	161 (100)	Asian	29.6	34.6	1228	10.3	13/169 (7.7)
Sanghi et al,[27] 2013	India	Laser	109	39 (36)	Asian	30.2	35.3	1392.8	≥6	19/109 (17.4)
Wu et al,[23] 2013	Taiwan	IVB	162	17 (10)	Asian	26.3	36.6	930.1	13.7	14/162 (9)
Present study	USA									
		IVB	22	16 (73)	Mixed	24.2	35.1	668.1	21.7	3/22 (14)
		Laser	32	5 (16)	Mixed	24.8	36.2	701.4	32.5	1/32 (3)

IVB = intravitreal bevacizumab.

of −1.8 D and −1.1 D at 5 and 2.5 years of age, respectively.[11,41] Another study reported minimal refractive errors (mean spherical equivalent of −0.1 D) in IVB-treated eyes at a mean age of 1.5 years.[23] Interestingly, in zone II ROP eyes treated with IVB in our study, the mean spherical equivalent refractive error was 0.6 D, which was significantly different from the mean refractive error in zone II ROP eyes treated with PRP (−4.7 D), although the mean refractive error between zone I ROP eyes treated with IVB versus PRP was not significantly different. This result suggests that zone I disease may be an independent risk factor for high refractive errors even for IVB-treated eyes.

Although the mean age for the last refraction for zone II ROP eyes was similar in both groups, the mean age for the last refraction was significantly higher in zone I ROP eyes treated with PRP than in those treated with IVB. The discrepancy is primarily because we did not start treating eyes with zone I ROP with IVB until the publication of the results of the BEAT-ROP study.[25] Therefore, more recent cases of zone I ROP were treated with IVB, whereas older cases of zone I ROP were treated with PRP.

This study has a number of limitations. First, it was a retrospective study and as a result, the follow-up period was variable and appropriate controls could not be implemented into the study design. Second, the sample size was small, limiting the power of the findings, which might have underestimated the difference in myopia in PRP- versus IVB-treated eyes, which was recently reported to be significantly worse in PRP-treated eyes of the infants in the BEAT-ROP study.[11] Third, the generalizability of our results may be limited given that the distribution of zone I and zone II disease differed between the PRP and IVB groups. Finally, at the time of this study, we did not routinely perform fluorescein angiography. Delayed development of the retinal vasculature is a potential problem in ROP eyes treated with IVB. Unlike in PRP-treated eyes, late recurrences may occur in IVB-treated eyes after several months of regression. In our IVB-treated group, no difference in outcome was observed 7.4 months after treatment. Because our follow-up threshold was 6 months, we could have missed recurrence in some patients if there were much-delayed vascularization. However, the strengths of this study include its consecutive design with relatively few patients lost to follow-up, the mean follow-up being longer than 2 years, and all patients being treated at only 2 hospitals, both of which used the same treatment protocols. Nevertheless, future studies with prospective designs and large sample sizes are needed to confirm our results.

In conclusion, no difference in outcome was observed between type 1 ROP eyes treated with IVB versus PRP in this study. Both IVB and PRP seem to be effective methods to treat type 1 ROP with low complication and recurrence rates. Retinal detachment developed after treatment in only 1 patient treated with PRP. IVB was associated with less myopia than PRP in our study, although longer follow-up is needed to confirm this finding.

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Abbreviations and Acronyms:
BEAT-ROP = Bevacizumab eliminates the Angiogenic Threat of Retinopathy of Prematurity; **D** = diopters; **IOP** = intraocular pressure; **IVB** = intravitreal bevacizumab; **PRP** = panretinal photocoagulation; **ROP** = retinopathy of prematurity.

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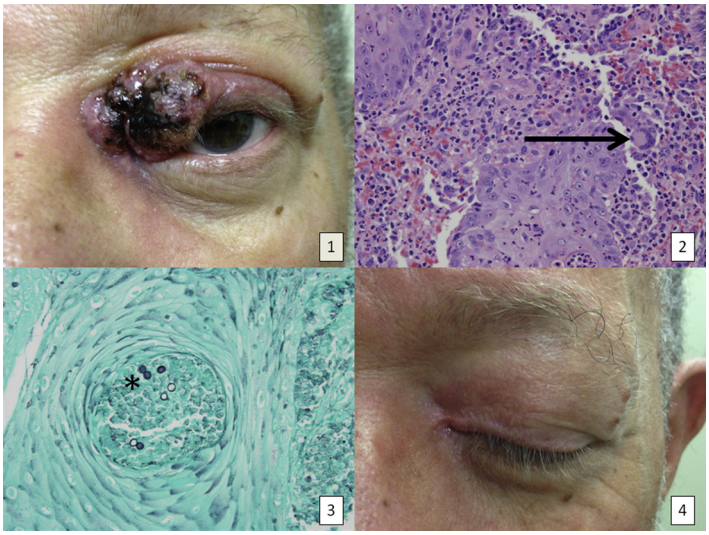
Pictures & Perspectives



Blastomycosis in the Eyelid of a Native Chicagoan

Cutaneous blastomycosis in a 66-year-old healthy man, who presented with a rapidly enlarging warty lesion of his left upper eyelid (Fig 1). A shave biopsy revealed acute and granulomatous inflammation with giant cells (*arrow*) after hematoxylin and eosin staining (Fig 2). Systemic workup was negative for disseminated disease. Special staining with Gomori's methenamine silver demonstrated broad-based budding organisms (Fig 3, *asterisk*). Treatment with oral itraconazole resulted in full resolution of the lesion within 2 months (Fig 4).

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