Special Focus on Retinopathy of Prematurity, Original Article

Combined intravitreal ranibizumab and zone I sparing laser ablation in infants with posterior zone I retinopathy of prematurity

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Purpose: To evaluate the efficacy of combined intravitreal ranibizumab (IVR) and zone I sparing laser ablation in infants with posterior zone I Retinopathy of Prematurity (ROP). **Methods:** This was a retrospective, interventional case series including premature infants diagnosed with posterior zone I ROP (n = 24) on ROP screening. Charts and RetCam images of preterm infants with posterior zone I ROP treated with immediate IVR and zone I sparing laser ablation at 4 weeks between April 2016 and September 2019 were reviewed. Data were analyzed and tabulated using frequency and descriptive statistics to describe the demography, morphology, and treatment outcomes. Primary outcome measure was structural outcome at 6 months. It was further categorized as favorable and unfavorable. **Results:** Twenty-four infants (48 eyes) with a mean gestational age of 28.54 ± 1.98 weeks and birth weight of 1180.33 ± 280.65 grams were analyzed. Thirty-six (75%) eyes had persistent tunica vasculosa lentis and twenty-six (54.1%) eyes had iris neovascularization. All eyes had features of aggressive posterior retinopathy of prematurity (APROP) limited to posterior zone I. The mean duration between IVR and zone I sparing laser ablation was 29.62 ± 6.36 (range: 24-34) days. One infant (2 eyes) received a second IVR treatment for recurrence of plus disease and persistent new vessels close to the fovea. Laser augmentation was done in 13 (27.1%) eyes. A favorable structural outcome was seen in 45 (93.7%) eyes. **Conclusion:** Posterior zone I ROP presents as APROP. Combined IVR and zone I sparing laser ablation appears effective treatment option in these eyes.

Key words: APROP, laser ablation, posterior zone I ROP, ranibizumab, retinopathy of prematurity, zone I ROP

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Posterior zone I Retinopathy of Prematurity (ROP) is a subset of zone I ROP characterized by very posterior disease and poorly formed retinal vasculature.[1-7] A literature search revealed only 3 studies reporting outcomes in posterior zone I ROP where unfavorable outcomes following laser treatment were seen in 78.6% to 100% eyes.[3,6,7] An intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) agents is an emerging treatment option for ROP.[8,9] The RAINBOW trial reported a favorable outcome in 69% of eyes treated with intravitreal ranibizumab (IVR) as compared to 61% of eyes treated with laser treatment in zone I disease.[8] Similarly, the BEAT-ROP study documented better outcomes with intravitreal bevacizumab (IVB) monotherapy compared with conventional laser therapy, in infants with zone I ROP.[9] However, data on outcomes of anti-VEGF agents in posterior zone I disease is missing. Additionally, various studies reported reactivation of ROP ranging from 6.8% to 83% in eyes receiving anti-VEGF monotherapy for ROP.[10-13] There are also concerns regarding optimal dosage, duration of recurrence, systemic safety, proper follow-up protocol and long-term functional outcomes following anti-VEGF monotherapy.

Several studies have now been advocating combined treatment to minimize the possible disadvantage of laser ablation and intravitreal anti-VEGF monotherapy.[14-16] The rationale of a combined therapy is a possible synergistic effect of the blocking action of the existing vascular endothelial growth factor (VEGF) by anti-VEGF agents and suppression of further production of VEGF by laser ablation. Thus, a combined treatment might show a reduction in the reactivation rate and a need for repeat intravitreal anti-VEGF injection as well as achieving favorable structural outcome. Additionally, with zone I sparing peripheral laser ablation, a larger part of the central retina can be preserved. This treatment protocol may play a role in posterior zone I ROP which is the severest form of ROP. Hence, we investigated the structural outcome following combined intravitreal ranibizumab and zone I sparing laser ablation in infants with posterior zone I ROP.

Methods

A retrospective chart review was carried out for all infants diagnosed and treated for posterior zone I ROP at a tertiary eye care institute from April 2016 to September 2019. The Institutional Review Board approved the study and it adhered to the tenets of the declaration of Helsinki. All the premature infants, born at gestational age (GA) of less than 34 weeks or having birth weight (BW) less than 2000 grams, were screened for ROP. In this study, we included infants with posterior zone

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I ROP who were treated with IVR at presentation followed by zone I sparing laser ablation at 4 weeks and completed follow-up of at least 6 months. We excluded infants with incomplete records or those lost to follow-up. Aggressive posterior retinopathy of prematurity was defined in accordance with the revised International Classification of Retinopathy of Prematurity (ICROP) classification.[1,17] In addition to this, posterior zone I was defined as the area within a circle centered around the optic disc, the radius of which extends from the center of the optic disc to the center of the macula.[6,7] This area is approximately half of the area covered under zone I [Fig. 1].

At the initial screening, demographic details of the infants like name, gestational age (GA) at birth, gender, birth weight (BW) and post menstrual age (PMA) at the time of first screening were noted. Details of various risk factors like supplemental oxygen therapy, blood transfusion and post-natal infection/sepsis were gathered. Clinical characteristics like pupillary dilatation, neovascularization of the iris (NVI), tunica vasculosa lentis (TVL), clarity of the lens, vitreous haze, plus disease, optic disc, development of foveal vascularization and vessels in the periphery were studied. Retinopathy of Prematurity was documented using detailed retinal drawings on the clinical records. Our institute acquired RetCam (RetCam™ Shuttle, CLARITY, USA) in March 2019. Therefore, RetCam documentation was possible only for those babies presenting after this period.

After the diagnosis, treatment was initiated within 24 hours. Infants diagnosed with posterior zone I ROP received IVR in the operation theatre under anesthetic supervision once specially designed informed consent was signed by parents. Proparacaine hydrochloride (0.5%) eye drops was administered once 10 minutes before the injection. Lids were cleaned with 10% povidone-iodine and 5% povidone-iodine was instilled 5 minutes before the procedure followed by draping of eyes. A scrubbed operating theatre nurse held the infant's head during the procedure. The injection was administered with a 30 gauge needle 1 mm away from the limbus. All infants received 0.25 mg/0.025 ml of ranibizumab intravitreally. Topically 0.3% tobramycin eye drops were administered 4 times daily for a week. Following this injection, the infants were followed up on Day 1, Day 7 and subsequently on a weekly basis till 4 weeks. On every follow-up visit, changes in the clinical findings were noted along with signs of regression, pattern of retinal vascularization, the development of staged ROP, if any, or progression. At approximately 4 weeks follow-up, infants were scheduled to undergo zone I sparing confluent laser ablation, as the second modality of treatment. Before laser ablation was performed, the infant's eyes were dilated using 0.4% tropicamide and 2.5% phenylephrine eye drops. Laser ablation was done under topical anesthesia using 810 nm diode laser (IRIDEX ®, GERMANY) in the presence of a neonatologist at the neonatal intensive care unit (NICU) with monitoring of vital parameters. Confluent laser burns were applied on the entire avascular retina 360° beyond zone I extending up to the ora serrata. Care was taken to delineate the area of zone I and the ill-defined posterior pole with lasers spots and then proceed. Laser spots were also applied inside the vascular loops outside zone I. All the laser treatments were completed in a single sitting. Following laser ablation, infants were again followed up on a fortnightly basis for 2 months and thereafter, once every month for the next 6 months. On the follow-up visits, apart from earlier mentioned clinical parameters, special attention was paid to detect recurrence of plus disease, development of any new vessels or fibrovascular proliferation. Laser augmentation was done if signs of recurrence of disease or any skip areas was noted. Recurrence was defined as reappearance of plus disease, progression of retinal neovascularization, new pre-retinal hemorrhage or membrane formation extending into the vitreous humor from retina.[10] Treatment details including number of laser spots, number of laser sessions and complications during the follow-up period were noted. The need for the 2nd injection of IVR despite the use of laser in progressive ROP was also noted.

The structural outcome at 6 months was categorized as favorable and unfavorable. A favorable structural outcome was defined as the absence of retinal arterial and venous tortuosity and engorgement, absence of fibrovascular traction and growth of vessels towards the avascular peripheral retina. An unfavorable structural outcome was defined as progression to tractional retinal detachment (TRD) or regression with cicatricial sequelae like development of falciform retinal fold or shortening of the major arcade vessels or temporal dragging of fovea.

Statistical analysis

Data was transferred to a Microsoft Excel® spreadsheet and statistical analysis was carried out with SPSS for Windows version 16.0 (SPSS Inc, Chicago, IL). Quantitative and qualitative variables were expressed as mean ± standard deviation and percentages, respectively.

Results

This study comprised of 24 infants (48 eyes) who satisfied the inclusion criteria. [Table 1] The mean GA at birth was 28.54 ± 1.98 (range: 25-32) weeks and the mean BW was 1180.33 ± 280.65 (range: 785-2003) grams. There were 15 (62.5%) male infants. The mean PMA at the time of first ROP screening was 31.98 ± 2.03 (range: 29-36) weeks and the mean difference between GA at birth and PMA at first screening was 3.33 ± 1.0 (range: 2-7) weeks. The postnatal age of infants at first screening was 24.67 ± 8.57 (range: 14-52) days. Additional risk factors identified were supplemental oxygen therapy in 24 (100%) infants, postnatal sepsis in 6 (28.6%) infants, and blood transfusion in 4 (21%) infants.

On clinical examination, TVL was seen in 36 (75%) eyes, NVI in 26 (54.1%) eyes and poor pupillary dilatation in 24 (50%) eyes. Fovea was avascular in all eyes. All eyes had features suggestive of APROP including flat neovascularization and multiple vascular loops with intra-retinal shunts. Thirty six (75%) eyes had severe vascular dilation and tortuosity (plus disease) [Fig. 2a] whereas 12 (25%) eyes had deceptively thin caliber vessels over posterior pole ending in narrow vascular loops without any dichotomous branching [Fig. 2b].

All the infants received combined treatment. Intravitreal ranibizumab was administered within 24 hours of diagnosis. The mean duration between IVR and zone I sparing laser ablation was 29.62 ± 6.36 (range: 24-34) days. The mean number of laser spots per eye was 2856.5 ± 797.87. In 13 (27.1%) eyes, the ridge with retinal neovascularization developed temporal to the fovea at a mean of 3.15 ± 0.68 (range: 2 to 4) weeks following zone I sparing laser ablation. Therefore, laser augmentation was performed in these infants. The mean additional laser spots per eye was 482.54 ± 448.67. Overall, the mean number of laser sessions were 1.27. One infant (2 eyes) had recurrence of plus disease along with persistent flat neovascularization very close to the fovea in spite of laser augmentation. He received a second IVR injection in both the eyes following which plus disease and neovascularization regressed completely.

A favorable structural outcome at 6 months was noted in 45 (93.7%) eyes. [Fig. 3] An unfavorable structural outcome

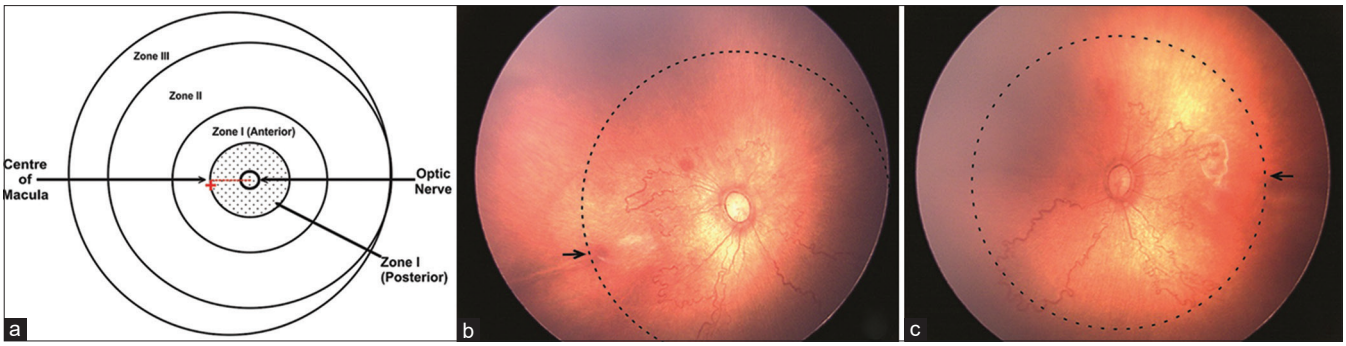

Figure 1: (a) Diagrammatic representation of various zones of retinopathy of prematurity (ROP) and posterior zone I is shown in dotted area. (b and c) RetCam images showing posterior zone I ROP within the dotted circle marking the boundary of posterior zone I

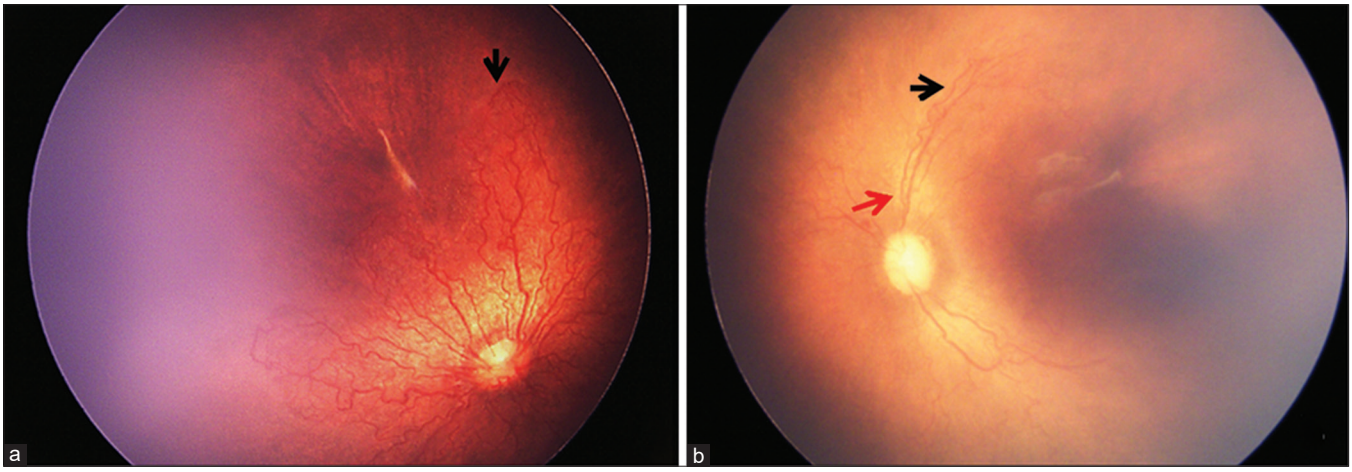

Figure 2: (a and b) RetCam features of zone I Posterior ROP: (a) Image demonstrating features of Aggressive Posterior Retinopathy of Prematurity as severe plus disease, vascular loops (black arrow) limited to zone I Posterior. (b) Image demonstrating poorly formed thin caliber tortuous vessels (red arrow) ending in peculiar tangles of smaller vessels narrow loops (black arrow)

was noted in 3 (6.3%) eyes. Infant number 8 [Table 1], (BW: 785 grams, GA: 26 weeks) had stormy postnatal period with recurrent pneumonia and candida sepsis. He was on ventilatory support for 4 months. He received IVR and zone 1 sparing laser ablation (right eye [OD]: 2629 spots and left eye [OS]: 3057 spots) while being on ventilatory support. At 1 week follow up post laser therapy, hyphema was noted in OD. He was prescribed topical prednisolone acetate 1% eye drops 4 times a day and homatropine 1% eye drops 2 times a day for 2 weeks. At 3 weeks follow up post laser, hyphema resolved but 360 degree posterior synechiae and total cataract was noted in OD. At this visit infant was still on ventilatory support and continued to be in NICU setup for next 4 weeks. Infant was discharged at 8 weeks post laser therapy and referred to our base hospital for further ocular management. Ocular ultrasonography of OD revealed tractional retinal detachment. Despite undergoing pars plana lensectomy and vitrectomy at higher center, the eye developed phthisis bulbi. The left eye of the same infant showed a favorable structural outcome, with complete regression of ROP.

Infant number 16 (BW: 1050 grams, GA: 29 weeks) had multiple risk factors including supplementary oxygen, anemia (Hb: 8 gram%) and repeated blood transfusions. At first ROP screening both eyes (OU) had non-dilating pupils and NVI. She received IVR and zone I sparing laser ablation (OD: 4265 and OS: 4204 spots). During zone I sparing laser ablation, wedge shaped avascular area temporal to fovea within zone I was left unlasered. At 3 weeks follow up following primary laser, wedge shaped avascular area persisted with development of flat neovascularization in OU. Option of second IVR was given to parents but they did not consented. Hence, laser augmentation (OD: 320 and OS 280) was done. At 2 weeks post laser augmentation, neovascularization persisted in OD whereas it started regressing in OS. No skip areas were noted at this visit. At 4 weeks post laser augmentation, OD progressed to Stage 4 B. The patient was counselled for lens sparing vitrectomy but the parents refused any further surgical intervention. The left eye of the same infant showed a favorable structural outcome, with complete regression of neovascularization following laser augmentation.

Infant number 17 (BW: 900 grams, GA: 29 weeks) had delayed presentation at first ROP screening (PMA: 36 weeks). He also had non-dilating pupils and florid NVI. Additionally, OD had pre-retinal bleed at presentation. He received IVR and zone I sparing laser ablation (OD: 4248 and OS: 3961 spots). At follow up 2 and 4 weeks post laser ablation, pre-retinal bleed in OD decreased but still persisted. At 6 weeks, pre-retinal fibrosis was noted temporal to macula. At follow up 10 week, post laser, stage 4A was noted in OD. [Fig. 4a] Child underwent lens sparing vitrectomy at higher center. Following surgery, he has been on regular follow up and had good structural outcome. The left eye of the same infant showed a favorable structural outcome, with complete regression of ROP. [Fig. 4b]

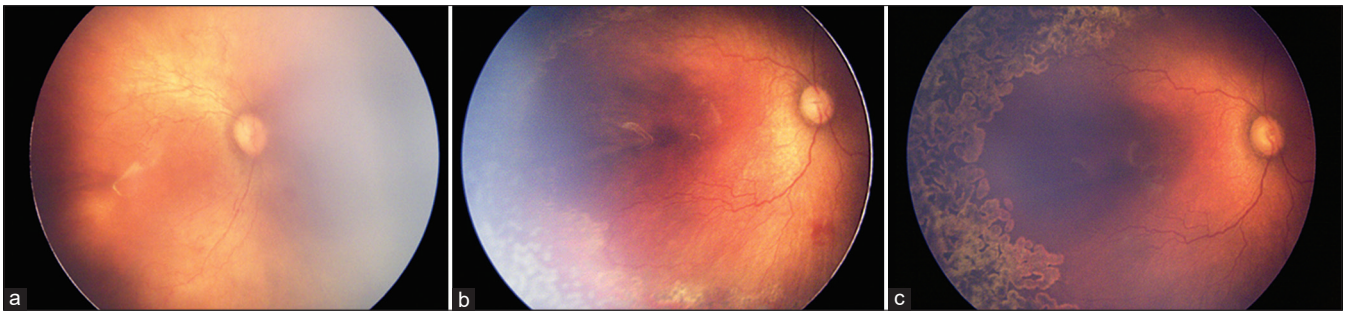

Figure 3: (a-c) A male infant with birth weight 875 gm and period of gestational age 28 weeks presented with posterior zone I ROP. (a) Retcam image obtained at PMA 31 weeks demonstrating poorly formed thin caliber tortuous vessels, vascular loops, and avascular fovea. (b) Image obtained at PMA 38 weeks after IVR and confluent laser ablation. (c) Image obtained at PMA 48 weeks showing regressed ROP with confluent laser scars beyond zone I

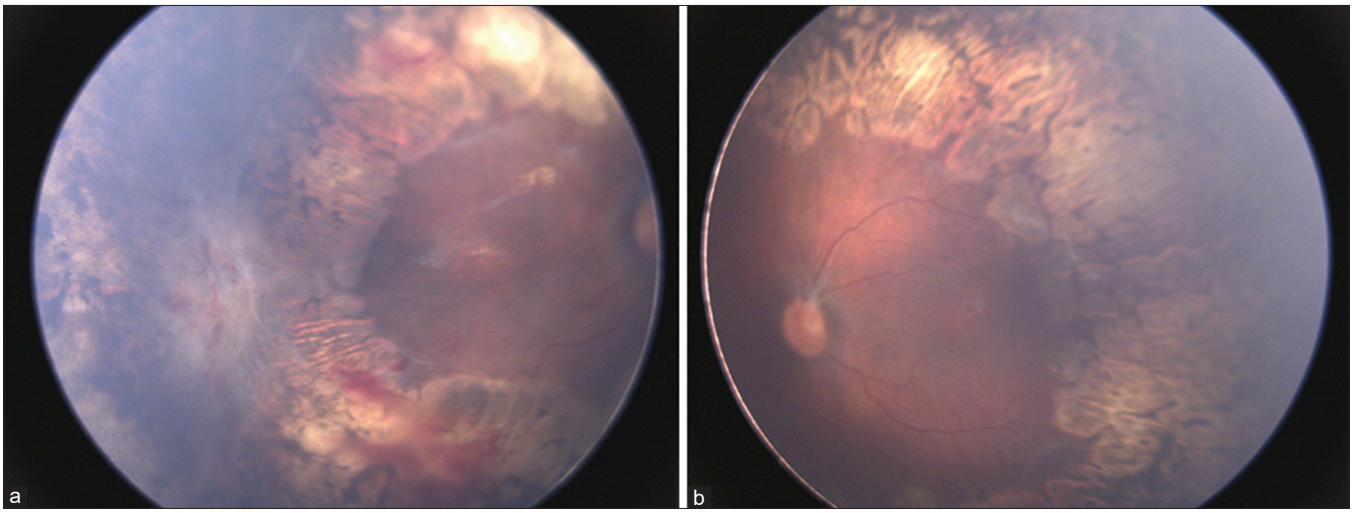

Figure 4: (a) RetCam image of infant number 17 demonstrating fibrovascular proliferation with underlying tractional retinal detachment in temporal quadrant and vitreous hemorrhage. (b) Image of OS showing regressed ROP along with confluent laser scars

Discussion

Posterior zone I ROP is considered to be the severest type of ROP. Very few studies have analyzed treatment outcomes in posterior zone I ROP.[3,6,7] Two of these studies reported unfavorable outcomes in 100% eyes while Katoch *et al*. documented poor outcomes in 78.6% of eyes with laser treatment. The present study reports the largest data of the posterior zone I ROP where we treated these eyes with intravitreal ranibizumab at presentation followed by zone I sparing laser ablation at 4 weeks. Despite the severest form of ROP, we achieved favorable structural outcomes using the combined modality of treatment in 93.7% of eyes.

Posterior zone I is not described in ICROP classification.[1] Kychenthal *et al*. first defined posterior zone I as the area within a circle centered around the optic disc, the radius of which extends from the center of the optic disc to the center of the macula.[7] As this area is approximately half of zone I, some studies have mentioned this as zone half ROP instead of posterior zone I ROP.[6,7] For uniform documentation this needs to be classified when new revision of ICROP classification is undertaken.

Various difficulties encountered in recognition of posterior zone I ROP include hazy cornea in extremely premature infants, poorly dilating pupils due to TVL and NVI, a virtually non-existent capillary network, deceptively thin caliber vessels and absence of a classical ridge. This may cause confusion regarding diagnosis of plus disease leading to errors in treatment and ultimately poor outcomes. Since, most of these extremely premature infants are sick requiring ventilatory support or oxygen therapy, pediatricians are also anxious to conduct ROP screening in their initial weeks. In our study, the mean age of infants at the time of first screening was 3.33 ± 1.0 weeks. This is one week before the western guidelines for first ROP screening.[18,19] Katoch *et al*. reported that 75% of eyes in their study had non-dilating pupils and NVI whereas we found NVI and poorly dilating pupils in 54.1% and 50% of eyes, respectively.[6] This difference could be because we carried out early screening in our study. Therefore, in most of the eyes diagnosis was done before the start of fibrovascular proliferation and this may have played an important role in achieving favorable outcomes in our study.

Retinal vascularization in zone I develops by vasculogenesis whereas vessels in zones II and III develop by angiogenesis.[20] Vasculogenesis is the initial process by which vascularization starts at the optic disc at around 14 weeks of gestation and completes by 21 weeks of gestation. Fovea remains avascular till 25 weeks of gestation and development starts from 26 weeks by angiogenesis. In the present study, mean PMA at the first screening was 31.98 ± 2.03 weeks. Despite high PMA, we observed absence of foveal vascularization in all infants and

Table 1: Patient characteristics of infants with posterior zone I ROP

Infant number	Sex	GA (weeks)	BW (grams)	Post-natal age at first screening (Days)	PMA at first screening (Weeks)	Eye	TVL	NVI	Non-Dilating Pupil	Interval between IVR and laser (Days)	Time between Primary and supplemental laser ablation (Weeks) (if any)	Follow up period (months)	Outcome
1	F	27	1200	23	30	OD	A	P	A	29	-	18	1
						OS	A	P	A				1
2	M	26	830	21	29	OD	P	A	P	26	4	14	1
						OS	P	A	P		4		1
3	F	27	1155	23	30	OD	P	A	P	30	-	12	1
						OS	P	A	P				1
4	F	30	1150	20	33	OD	P	P	A	32	3	15	1
						OS	P	P	A		3		1
5	F	29	960	36	34	OD	P	P	P	29	-	14	1
						OS	P	P	P				1
6	M	27	1245	19	30	OD	P	P	A	26	-	13	1
						OS	P	P	A		3		1
7	F	32	1560	17	35	OD	P	A	P	30	-	11	1
						OS	P	A	P				1
8	M	26	785	39	31	OD	P	A	A	27	-	10	2
						OS	P	A	A				1
9	F	32	1770	20	35	OD	P	A	A	32	-	11	1
						OS	P	A	A				1
10	M	30	1300	22	33	OD	P	P	P	27	3	10	1
						OS	P	P	P		3		1
11	F	30	1415	20	33	OD	A	A	A	31	-	10	1
						OS	A	A	A				1
12	M	30	1100	20	33	OD	A	A	A	29	-	11	1
						OS	A	A	A				1
13	M	30	1200	23	33	OD	P	P	P	34	-	15	1
						OS	P	P	P				1
14	M	32	2003	14	34	OD	P	P	A	31	-	12	1
						OS	P	P	A				1
15	M	25	900	35	29	OD	P	A	P	24	4	9	1
						OS	P	A	P		4		1
16	F	29	1050	16	31	OD	P	P	P	33	3	7	2
						OS	P	P	P		3		1
17	M	29	900	52	36	OD	A	P	P	30	-	6	2
						OS	A	P	P				1
18	M	28	875	23	31	OD	P	A	A	29	2	6	1
						OS	P	A	A		2		1
19	M	28	1070	20	31	OD	P	A	A	33	-	6	1
						OS	P	A	A				1
20	M	26	1100	23	29	OD	P	P	P	31	-	6	1
						OS	P	P	P				1
21	M	27	1185	20	30	OD	P	P	P	31	-	6	1
						OS	P	P	P				1
22	M	29	1145	30	33	OD	A	P	P	29	-	6	1
						OS	A	P	P				1
23	M	28	1280	30	32	OD	P	P	A	29	-	6	1
						OS	P	P	A				1

Contd...

Table 1: Contd...

Infant number	Sex	GA (weeks)	BW (grams)	Post-natal age at first screening (Days)	PMA at first screening (Weeks)	Eye	TVL	NVI	Non-Dilating Pupil	Interval between IVR and laser (Days)	Time between Primary and supplemental laser ablation (Weeks) (if any)	Follow up period (months)	Outcome
24	F	28	1150	26	32	OD	A	A	A	29	-	6	1
						OS	A	A	A				1

F: Female, M: Male, GA: Gestational Age, BW: Birth Weight, PMA: Post Menstrual Age, TVL: Tunica Vasculosa Lentis, NVI: Neovascularization of Iris, A: Absent, P: Present, IVR: Intravitreal Ranibizumab, Outcome: 1- Favorable outcome, 2- Unfavorable outcome

retinal vascularization was restricted to posterior zone I at the time of the first screening. Therefore, apart from a defect in vasculogenesis, factors like unblended oxygen administration may account for severe capillary dropout in zone I disease. Shah *et al*. reported oxygen exposure led to a loss of the vascularized retina as well as retraction of capillary networks from zone II to zone I or zone I anterior to zone I posterior.[21] Since all infants in this cohort were from level II NICUs, it is possible that they might have received prolonged unmonitored oxygen resulting in severe vaso-obliteration.

Studies have shown that zone I disease is less responsive to laser therapy as compared to zone II.[3,6,7,22] The Early Treatment for Retinopathy of Prematurity study reported unfavorable outcomes in 55.2% of eyes with zone I ROP treated with laser monotherapy.[5] Previous studies reported 78.6% to 100% unfavorable outcomes in eyes with posterior zone I ROP treated with laser alone.[3,6,7] Possible explanations for poor outcomes in zone I disease with laser therapy are a) laser treatment leads to destruction of neurons and source of VEGF 165 thus taking away hypoxic stimulus for VEGF production, b) zone I ROP may be driven by molecular signals other than VEGF or c) source of VEGF like vitreal macrophages are responsible for lack of effectiveness of laser therapy in zone I disease.[22] Recently, a few studies have reported the role of anti-VEGF agents in treatment of zone I ROP.[10-12,21] Shah *et al*. in their series of zone I APROP reported growth of capillary networks up to zone II as well as opening up of thrombosed vessels on fluorescein angiogram in eyes treated with intravitreal bevacizumab (IVB).[21] Padhi *et al*. reported three phases of vascular changes following IVB in eyes with zone I ROP mainly phase 1: rapid regression of plus disease; phase 2: slow vascular development and lastly, phase 3: there may be complete regression on follow-up or progression to rebound/recurrent ROP.[23]

Various studies have reported a recurrence of ROP following intravitreal anti-VEGF injection ranging from 6.8% to 83%.[10-13] In a large series of 626 eyes of 331 premature infants with ROP treated with IVR, the rate of recurrence with type I prethreshold ROP was 15.9%, 38.2% with threshold ROP and 66.7% with APROP.[12] The recurrence rate was significantly higher in zone I (61.6%) ROP than zone II ROP (31%). Also, the mean time to recurrence was 8.57 ± 3.73 weeks and it occurred as early as 4 weeks. Wong *et al*. observed 83% of eyes treated with IVR for zone I or posterior zone II diseases had reactivation of ROP after the initial response to treatment with a mean treatment to reactivation interval of 5.9 weeks.[13] Although various studies have shown a better systemic safety profile of ranibizumab over bevacizumab, the possibility of reactivation of ROP is higher and earlier with ranibizumab.[24-29] According to Rainbow trial, the elimination rate of ranibizumab from the eye was faster in infants when compared to adults ($t_{1/2}$: 5.6 [infants] vs 8.6 days [adults].[30,31] This could be due to several factors that includes structural difference in tissues, shorter vitreous diffusion pathway within smaller eye and reduced blood-retina vessel barrier function in active ROP. Kim *et al*. reported excellent anatomical outcomes with combined IVB and zone I sparing laser photocoagulation in zone I ROP.[16] All eyes showed prompt regression of neovascular pathology and plus disease without recurrence in their series. Katoch *et al*. studied treatment outcome in posterior zone I ROP where 5 of 6 (83.3%) eyes receiving combined treatment with IVB followed by laser photocoagulation had favorable outcome while only 7 of 50 (14%) eyes treated with laser monotherapy had favorable outcome.[6] From above evidences combined treatment looks promising approach while managing these eyes with posterior zone I ROP but the guidelines regarding timing of laser therapy following IVR are not available. Hence, considering posterior zone I ROP as severest form of ROP with very high and early recurrences as well as from above evidences, we decided to planned zone I sparing laser treatment at 4 weeks following IVR in all infants with posterior zone I ROP.

Combined IVR with zone I sparing laser photocoagulation in posterior zone I ROP have many advantages.[14-16] It reduces the number of injections needed since only a minimal section of the retina is vascularized in posterior zone I ROP. Hence, if anti-VEGF monotherapy is planned, more than 2 anti-VEGF injections might be required till the retina is completely vascularized.[32] Secondly, the persistent area of peripheral avascular retina can lead to late exudative and tractional consequences which can be prevented by performing early laser. Infants receiving IVR monotherapy require close follow ups to identify recurrences and might even require examination under anesthesia after a certain age. This is especially important in developing countries like India where follow up is big challenge and dropout rate is high. Missing recurrence in between follow up visit could lead to development of rapid retinal detachment in posterior zone I disease.

The limitations of our study are that it is a retrospective study from a single institution with limited follow-up. As we performed laser ablation on all patients following IVR at 4 weeks, we could not include a control group of IVR monotherapy or another group where laser ablation could have been delayed till time of recurrence after IVR. It would be interesting to see the pattern of recurrence in these eyes with posterior zone I ROP. Secondly, fundus fluorescein angiography was not performed in these eyes. Hence, nature of foveal vascularization can only be presumed. Lastly, refractive outcomes of the patients are not mentioned. Nevertheless, the present study has many strengths that include the largest cohort of infants with posterior zone I ROP receiving uniform treatment protocol. Importantly, in eyes where reported favorable outcomes in previous studies ranged from 0 to 21.4%, we could document favorable outcomes of 93.7% with IVR and zone I sparing laser ablation.

Conclusion

In conclusion, posterior zone I ROP presents as APROP and high index of suspicion is a must for early diagnosis. Combined treatment with IVR and zone I sparing laser ablation appears an effective treatment approach in eyes with posterior zone I ROP.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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