10/9/2021 1:52PM

Computerized Analysis of Retinal Vascular Growth Following Intravitreal Bevacizumab Monotherapy in Retinopathy of Prematurity Until Three Years of Age

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- Jon David Hammer, MD
- Henry Nguyen
- Jacqueline Palmer
- Sarah Furtney, PhD

OBJECTIVE To measure retinal vessel growth post-intravitreal bevacizumab monotherapy (IVB) for retinopathy of prematurity (ROP) over time on serial fluorescein angiographic (FA) sessions until 3 years of age

PURPOSE Anti-VEGF's though help in inhibiting stage 3 ROP, the chronic arrest of the peripheral retinal vasculature as long-term complications has become a concern. We aim to measure the physiologic growth of the retinal vasculature over time on serial fluorescein angiographic (FA) imaging

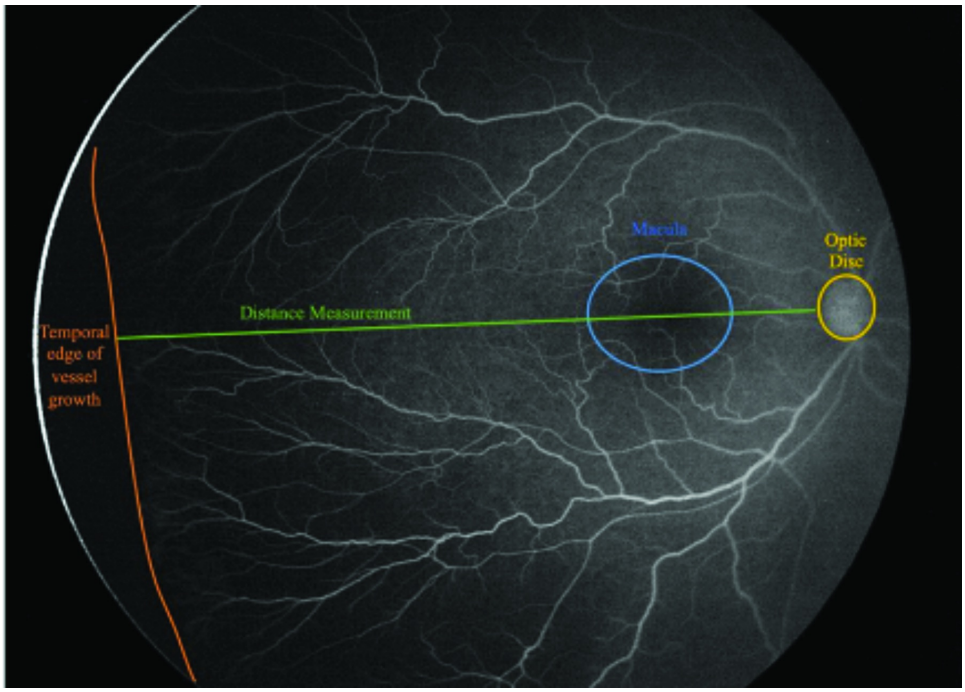
METHODS Seventy eyes in 35 infants treated for type-1 ROP were included, 63 eyes were treated with IVB and 7 eyes untreated. Serial angiographic images taken post-IVB on 4 serial examinations were analyzed starting at average 66 weeks post-menstrual age (PMA) with repeat imaging every 8 months until 3 years of age. The retinal vessel length was manually measured in ImageJ software from the temporal margin of the optic disc through the foveal center to the temporal vascular-avascular junction and vascular length at the different time points were compared.

RESULTS The mean retinal vessel length was 14.177 mm at time point #1 (66.2 weeks PMA) and 13.761 mm including all 4 FA sessions (range 44-234 weeks PMA). Paired t-tests compared the retinal vascular length of each individual eye over time and showed no

statistically significant growth from the first FA at 66.2 weeks PMA until 3 years of chronological age. From time point #2 to #1 (N=30) the difference was -0.117 ± 0.785mm (95% CI -0.416 to +0.176, p=0.42), from #3 to #1 (N=15) the difference was +0.060 ± 0.854 mm (95% CI -0.413 to +0.533, p=0.79), and from #4 to #1 (N=7) the difference was -0.404 ± 1.32 mm (95% CI -1.628 to +0.820, p=0.45). Even the eyes with recurrence (n=6) and untreated eyes (n=7) showed no significant change in vascular growth over time.

CONCLUSION Retinal vascular length measured angiographically post-IVB monotherapy in ROP showed no significant vascular growth on serial examinations from 66 weeks PMA until three years of age. The persistent chronic vascular arrest and the inhibition of normal angiogenesis with anti-VEGF monotherapy accounts for a longitudinal study for dose titration and vascular growth and recovery until adulthood.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



The retinal vessel length (green) is measured from the temporal edge of the optic disc (yellow) through the fovea center of the macula (blue) to the temporal vascular-avascular junction (orange).

Interval Change in Retinal Vessel Length Compared to Initial FA

Time Point	Retinal Vessel Length (mm) Mean ± SD	Retinal Vessel Length (mm) at Time Point #1 Mean ± SD	N	Mean difference (95% Confidence Interval)	P-value*
2	14.034 ± 0.949	14.151 ± 1.205	30	-0.117 (-0.411 to +0.176)	0.42
3	13.627 ± 1.000	13.567 ± 1.242	15	+0.060 (-0.413 to +0.533)	0.79
4	12.935 ± 0.486	13.339 ± 1.564	7	-0.404 (-1.628 to +0.820)	0.45

*2-tailed paired sample t-test

Compared individual eyes for changes in retinal vessel length over time. Three separate paired t-test analyses were performed to compare each subsequent time point (#2, #3, #4) to baseline time point #1 image.

10/9/2021 1:58PM

Ophthalmic Manifestations Associated With SARS-CoV-2 In Newborn Infants: A Preliminary Report

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- Andreas Paulo Di Luciano Rojas, MD
- Gabriela Patricia Amadeo Oreggioni, MD
- LUIS GILBERTO PEREZ CHIMAL, MD

OBJECTIVE To describe ophthalmic manifestations in newborns detected by slit-lamp examination, fundus examination, and fluorescein angiography.

PURPOSE SARS-CoV-2 has been associated with ophthalmological changes at all levels ; ocular external diseases, such as conjunctivitis, and intraocular changes, including inflammation and microvascular alterations. This is, to our knowledge, the first report of ophthalmic findings in newborn babies possibly associated with COVID-19 infection in humans

METHODS During the hospital reconversion project carried out by the federal health authorities, the hospital was designated as the regional reference center for pregnant-puerperal women and newborns with suspected COVID-19 infection. All the newborns with positive RT-PCR tests (from nasopharyngeal swabs) for SARS- CoV-2, who were isolated in a neonatal intensive care unit designed for this purpose, were included in the present cross-sectional study. All subjects received complete ophthalmic exploration, including portable slit-lamp examination, fundus examination, color fundus photography, and red-free imaging and fluorescein angiography using a contact wide-angle imaging system (RetCam 3

RESULTS Fifteen newborns (8 females [53%]) were enrolled. The mean gestational age was 35.2 weeks (range, 30-40), and the average birth weight was 2238.7 g (range, 1140–4350 g). Ten mothers were positive for SARS-CoV-2. Fundus examination was normal in 7 newborns (47%). Of the remaining 8 newborns, 2 (13%) were diagnosed with oxygen-induced retinopathy, 3 (20%) had retinopathy of prematurity (ROP), 2 (13%) had subtle cotton wool spots, and 1 (7%), born at full term, had vitreous hemorrhage.Fluorescein

angiography was performed in all patients. Of the 15, 3 (20%) had changes compatible with ROP, 2 (13%) had oxygen-induced retinopathy, 3 (20%) were reported to have patchy choroidal filling, and 3 (20%) showed peripapillary hyperfluorescence. The remaining 2 newborns (13%) had delayed retinal filling, venous laminar flow, and boxcarring.

CONCLUSION All newborns in our study had ocular manifestations, 53% had retinal findings. The mechanism of ocular injury in this study is unknown and may be related to prematurity, hemodynamic compromise, mechanical ventilation, and SARS-CoV2. We are following all the cases reported here for long-term complications.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 2:13PM

Giant Retinal Tear Detachments in LEPREL1 Mutations Mimicking Ocular Stickler Syndrome: A Condition With an Associated Nephropathy

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- Patrik Schatz, MD, PhD
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OBJECTIVE To describe the retinal features and characteristics of retinal detachments in high myopia associated with mutations in LEPREL1 gene and to report an associated nephropathy with the condition.

PURPOSE To describe the retinal features and characteristics of retinal detachments in high myopia associated with mutations in LEPREL1 gene and to report an associated nephropathy with the condition.

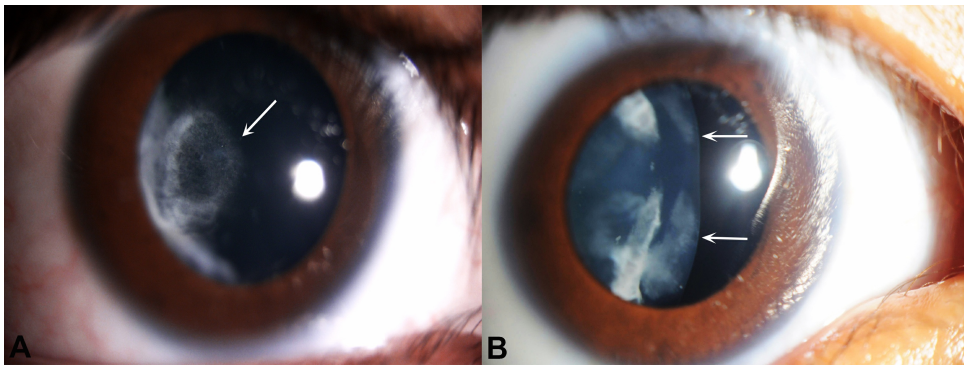
METHODS Retrospective chart review including details of ocular history, ophthalmic examination, multimodal imaging, and surgical interventions was obtained during a mean duration of 9.1 ± 4.8 years. Whenever possible, urinalysis to assess for proteinuria and hematuria was performed.

RESULTS 20 eyes of 10 patients were included. 2 patients were males and 8 patients were females. The mean age of the patients was 18.6 ± 5.5 years followed up for 9.1 ± 4.8 years. Mean axial length was 28.9 ± 1.9 mm and mean refraction was - 13.9 ± 2.8 diopters. BCVA on presentation was 0.62 ± 0.65 (Snellen = 20/80) and on last follow up was 0.45 ± 0.69 (Snellen = 20/50). Anterior segment examination revealed a posterior subcapsular cataract in 16 eyes (80%) and associated with a temporal subluxation in 5 eyes (25%). 7 eyes of 5 patients (50%) developed rhegmatogenous retinal detachments (RRD) at age of 14.14 ± 5.9 years. All eyes (100%) with RRD had giant retinal tears (GRT). Anatomical reattachment

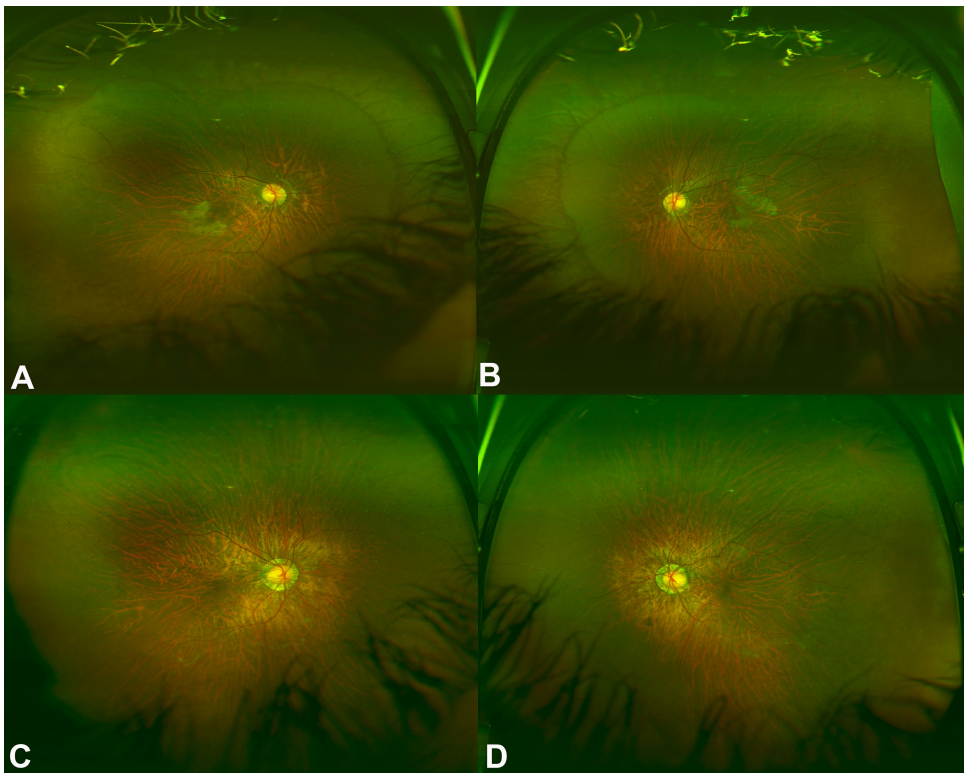
was achieved in 6 out of 7 eyes. Systemically, two siblings had marfanoid habitus. In 5 out of 7 patients tested, urinalysis showed mild proteinuria or microhematuria, or both.

CONCLUSION LEPREL1-related high myopia confers a high risk of early-onset RRD associated with GRT. Surgical interventions can achieve good anatomical and visual outcomes. Long-term follow-up is needed to assess the natural history of the associated nephropathy.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



Anterior segment features of LEPREL1 mutations: cataract and lens subluxation



High myopia in LEPREL1 mutations with a propensity to development of giant retinal tear detachment

10/9/2021 2:25PM

Clinical Features and Outcomes of Infants With Retinopathy of Prematurity Who Fail Anti-VEGF Therapy

- Lucy T Xu, MD
- David Levine, MD
- Amy Hutchinson, MD
- Prethy Rao, MD, MPH
- G. Baker Hubbard, MD

OBJECTIVE To describe characteristics and outcomes of patients with retinopathy of prematurity (ROP) who failed intravitreal anti-VEGF.

PURPOSE Anti-vascular endothelial growth factor (anti-VEGF) treatment of retinopathy of prematurity (ROP) has advantages over laser in that it can be done without general anesthesia, induces less myopia and avascular retina can still become vascularized. Success of a single dose of anti-VEGF range from 80-94%. Previous reports often do not provide detailed descriptions of the features of failed cases.

METHODS This was a retrospective case series of 211 eyes from 112 patients were treated with anti-VEGF as initial therapy for type 1 ROP at our Children's Healthcare of Atlanta between 2011-2019. We included an additional 6 eyes of 3 patients who were referred to our institution for management of failed anti-VEGF from outside institutions. We analyzed 23 eyes of 15 patients who failed anti-VEGF therapy and 194 eyes of 100 patients who had treatment success with 1 dose of intravitreal anti-VEGF. Failure was defined as recurrent plus, neovascularization, stage 4 or 5 ROP, or need for repeat treatment prior to post-menstrual age (PMA) 50 weeks.

RESULTS Among 211 eyes (112 patients) receiving initial treatment at our institution, 17 (11%) failed. An additional 6 eyes of 3 patients from outside our institution were included for a total of 23 study eyes. Failure manifested as recurrent plus in 14 eyes (58%), recurrent stage 3 in 13 eyes (54%) and retinal detachment in 5 eyes (21%). Two eyes were retreated before 50 weeks PMA for vascular arrest in zone I and one eye for vitreous hemorrhage. Median time to failure was 10.1 weeks (IQR 5.4-13.3). Treatment failures were managed with laser (13 eyes), repeat injection (4 eyes), combined injection/laser (2 eyes), pars plana vitrectomy (PPV) (2 eyes), and combined injection/PPV (2 eyes). No association was found between treatment failure and bevacizumab dose ($p = 0.31$). Follow-up of >6 months was available for 16 of 23 eyes. The retina was fully attached in 15 eyes and detached in 1 eye. Fixation behavior was present in 8 eyes.

CONCLUSION The most common manifestations of treatment failure were recurrent plus and recurrent stage 3. The failure rate at our institution was 11.0%. Most patients who failed treatment had favorable anatomic outcomes and half demonstrated fixation behavior.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 2:16PM

Clinical Spectrum of Uveal Metastasis in Korean Patients Based on Primary Tumor Origin

- Min Kim, MD, PhD, MBA, FASRS

OBJECTIVE To describe the clinical features and prognosis of patients with uveal metastasis in Korea.

PURPOSE Uveal metastasis is considered the most common intraocular malignancy in the adult population and is associated with poor survival outcomes. However, there are few studies based on mainly Asian populations. We report our experience in managing patients with uveal metastasis over 14 years in Korea, with analysis of demographics, clinical features, and survival outcomes based on primary tumor site.

METHODS Retrospective observational case series. The study included all patients who were diagnosed and managed for uveal metastasis between November 1, 2005 and November 30, 2019. Patients with lymphoproliferative disorders (lymphoma, leukemia, and other hematologic malignancies) and pathology-confirmed primary intraocular melanoma were excluded from the study. We reviewed the complete electronic medical records, including information on patient demographics, primary cancer site, clinical features, the management of uveal metastatic tumors, and survival outcomes.

RESULTS A total of 134 uveal metastases (128 choroidal, 3 iris, 3 ciliary body tumors) were diagnosed in 95 eyes of 80 patients. Mean age at diagnosis was 56 years (median 55, range 24-86), with a minor female preponderance (61%). Tumors were bilateral in 15 (19%) patients and the primary origin was established in 49 (61%) patients prior to ocular detection. The primary tumor originated in the lung (48%), breast (24%), gastrointestinal (GI) tract (10%), liver (3%), pancreas (3%), kidney (1%), cervix (1%), and nasopharynx (1%), with some remaining unknown (10%). The overall 5-year survival rate was 21%. Kaplan-Meier analysis revealed that the worst survival was found in pancreatic cancers (mean survival: 5.9 months, P=0.045) and the best with GI tract cancers (44.5 months).

CONCLUSION In conclusion, the primary tumor origin in Korean patients may differ from

those reported in primarily Caucasian population-based studies, with a much higher prevalence of lung and GI tract cancers. The overall prognosis is poor with a 5-year survival rate of 21%.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

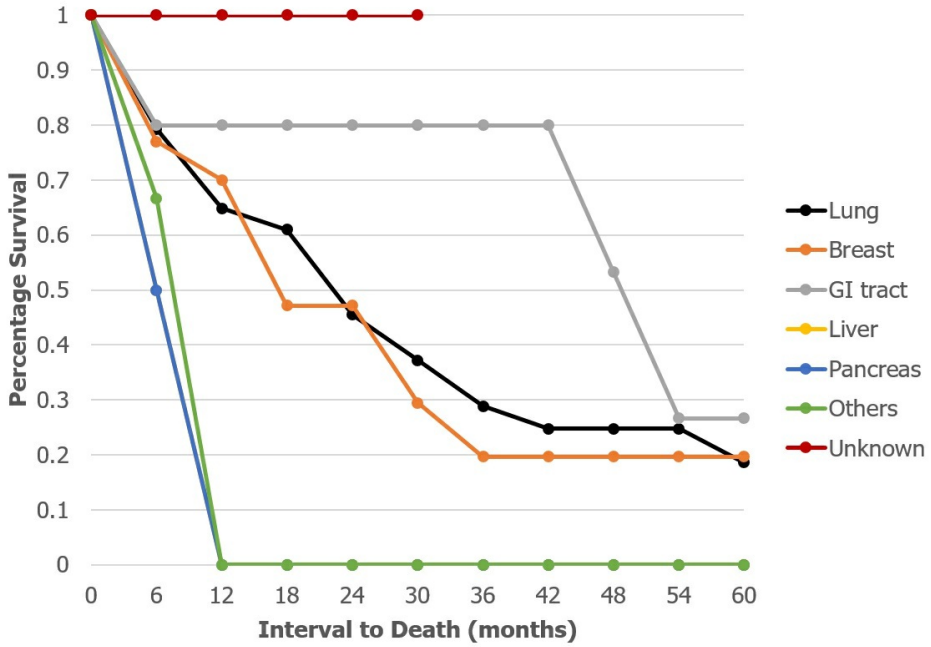


Figure 2. Kaplan-Meier analysis of time of death in patients with uveal metastasis based on primary cancer-origin site. Survival rates calculated from lung (n=37), breast (n=19), gastrointestinal (GI) tract (n=8), liver (n=2), pancreas (n=2), others (n=3), and unknown (n=8) patients. Others include patients with kidney (n=1), cervix (n=1), and nasopharynx (n=1) cancers.

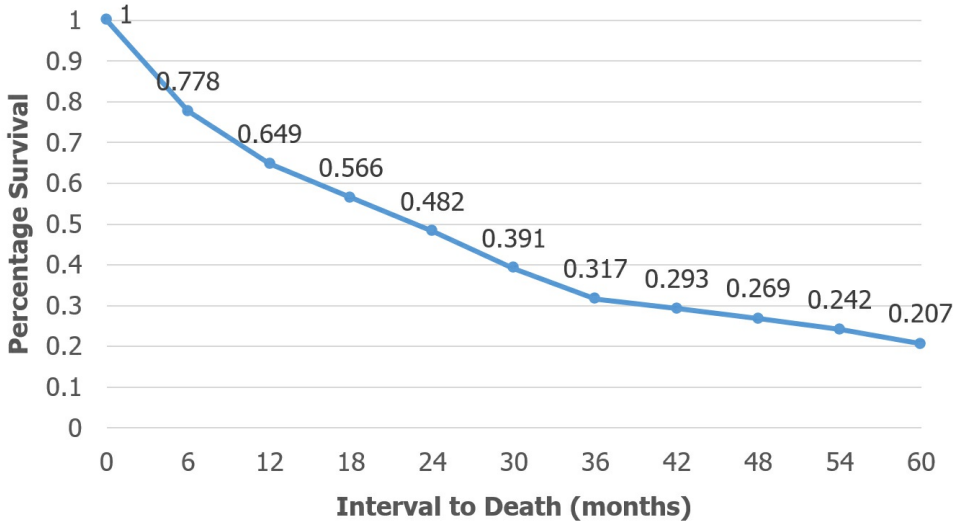


Figure 1. The overall Kaplan-Meier analysis of time of death in patients with uveal metastasis based on the total cohort with documented follow-up (n=79 patients).