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Macular Microvasculature Observations in Two Infants with Treated Retinopathy of Prematurity

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Retinopathy of prematurity (ROP) is characterized by abnormal vascular development in the retinal periphery.[1,2] Here we report macular microvascular anomalies visualized in two infants with treated ROP using an investigational portable optical coherence tomography angiography (OCT-A) system (Spectralis HRA+OCT with Flex and OCT-A module, Heidelberg Engineering, Heidelberg, Germany) with age-appropriate manual segmentation[3].

Report of Cases

A Caucasian female born at 24 weeks gestational age (GA) (birth weight 410g) had intravitreal bevacizumab injection in both eyes (35 weeks postmenstrual age, PMA) for Zone II stage 3 ROP, subsequent laser photocoagulation of avascular retina in both eyes, and later vitreoretinal surgery in the right eye for vitreous hemorrhage. Examination under anesthesia (EUA) was performed at 73 weeks PMA. Research OCT-A imaging of the left eye (Zone II stage 3 regressed) showed absence of the foveal avascular zone (FAZ) associated with lack of the foveal pit on the structural OCT scans[4]. The superficial vascular complex (SVC), which we defined as flow signal between the internal limiting membrane

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Contributions and Access to data:

S. Tammy Hsu – *Study concept and design, Acquisition, analysis, and interpretation of data; Drafting of the manuscript; Critical revision of the manuscript for important intellectual content;* ,

Xi Chen - *Study concept and design, analysis and interpretation of data, Drafting of the manuscript; Critical revision of the manuscript for important intellectual content;*

Robert J. House - *Acquisition of data; Critical revision of the manuscript for important intellectual content;*

Michael P. Kelly - *Acquisition of data; Critical revision of the manuscript for important intellectual content;*

Cynthia A. Toth - *Study concept and design; acquisition of data; Critical revision of the manuscript for important intellectual content; Study supervision*

Lejla Vajzovic - *Study concept and design, acquisition of data; Critical revision of the manuscript for important intellectual content; Obtained funding; Study supervision*

Lejla Vajzovic had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

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(ILM) and the lower boundary of the inner plexiform layer (IPL), showed an irregular, angular vascular pattern with several large vessels diving into the inner nuclear layer, an area considered deep vascular complex (DVC) territory (Figure 1).

A Caucasian male born at 24 weeks GA (birth weight 610g) had prior laser photocoagulation for Zone II stage 3 ROP (37 weeks PMA) and developed Zone II stage 4A ROP with plus disease in both eyes at 40 weeks PMA. Structural OCT in the left eye during EUA showed attached macula with a central foveal cystoid space, the boundaries of which corresponded to a small FAZ. OCT-A showed a developed SVC with vessels that appeared to be located deeper than expected within the boundaries that define the SVC, as well as a lack of flow across the corresponding central macula in the DVC (Figure 2).

Discussion

Here we report depth-resolved macular microvascular anomalies in two eyes after treatment of type I ROP: (1) Violation of vascular stratification, with large superficial vessels diving from IPL into INL; (2) Deeper SVC vessels located closer to the IPL associated with (3) incomplete perifoveal DVC development. These findings, not previously reported in children or adults with history of ROP (PubMed search on March 13, 2018: “retinopathy of prematurity” and “optical coherence tomography angiography”), suggest that the retinal perifoveal microvasculature may undergo an active developmental and remodeling process during the critical postnatal period of ROP pathogenesis. Of note, these findings are based on a single imaging session each in two infants, both of whom received ROP treatments prior to imaging. Thus, it is difficult to judge if the incomplete development of the DVC relative to the SVC and the deeper SVC localization are physiological, pathological, or related to treatment or perfusion status, especially with a lack of age-matched controls.

Depth-resolved visualization using OCT-A provides an opportunity to observe the development of perifoveal microvasculature in detail. However, as the overall thickness of the developing retina in infants is different from the adult retina[3,5], and the developmental timeline and location of the superficial and deep vascular layers have yet to be explored, the segmentation criteria of SVC and DVC in infants would seem to warrant further study. Further analysis on a larger sample size is needed in order to determine the ideal vascular boundaries for premature infants.

The advent of supine retinal imaging and OCT-A has allowed visualization of vascular details not seen on traditional table-top imaging[2,6]. The findings in this report may guide future research of human retinal vascular development, and alert us to macular changes in infants with ROP.

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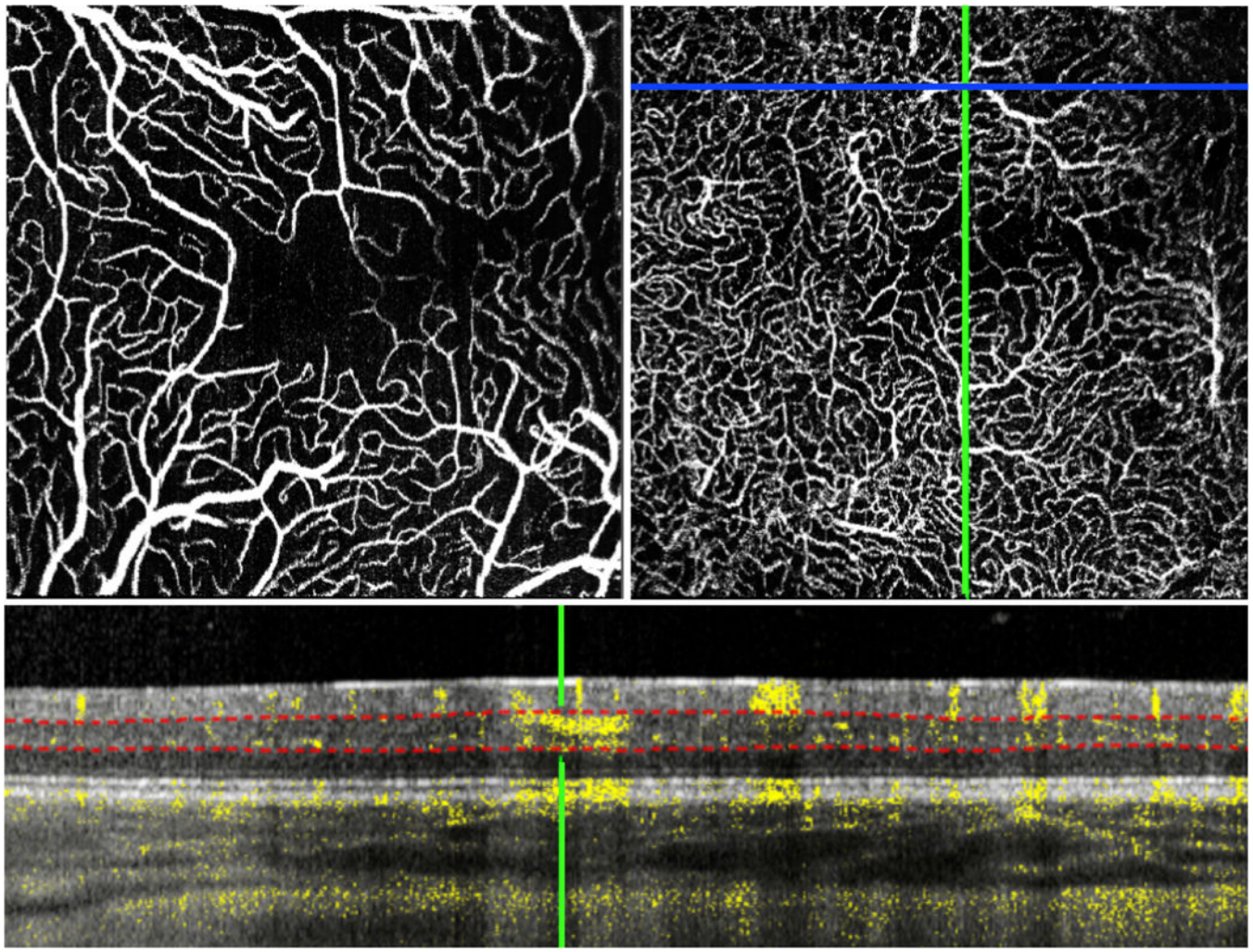

Figure 1.

The macula of left eye of an infant with stage 3 ROP, regressed after bevacizumab treatment, imaged at 73 weeks postmenstrual age showed an irregular angular vessel pattern with several large vessels in the superficial vascular complex (A) diving down into the deeper layers of the retina (examples circled in red in B and C). A B-scan shows one of these diving vessels (red arrow at the green crosshair) penetrating into the inner nuclear layer. Red dotted lines indicate the manually placed segmentation boundaries for the DVC.

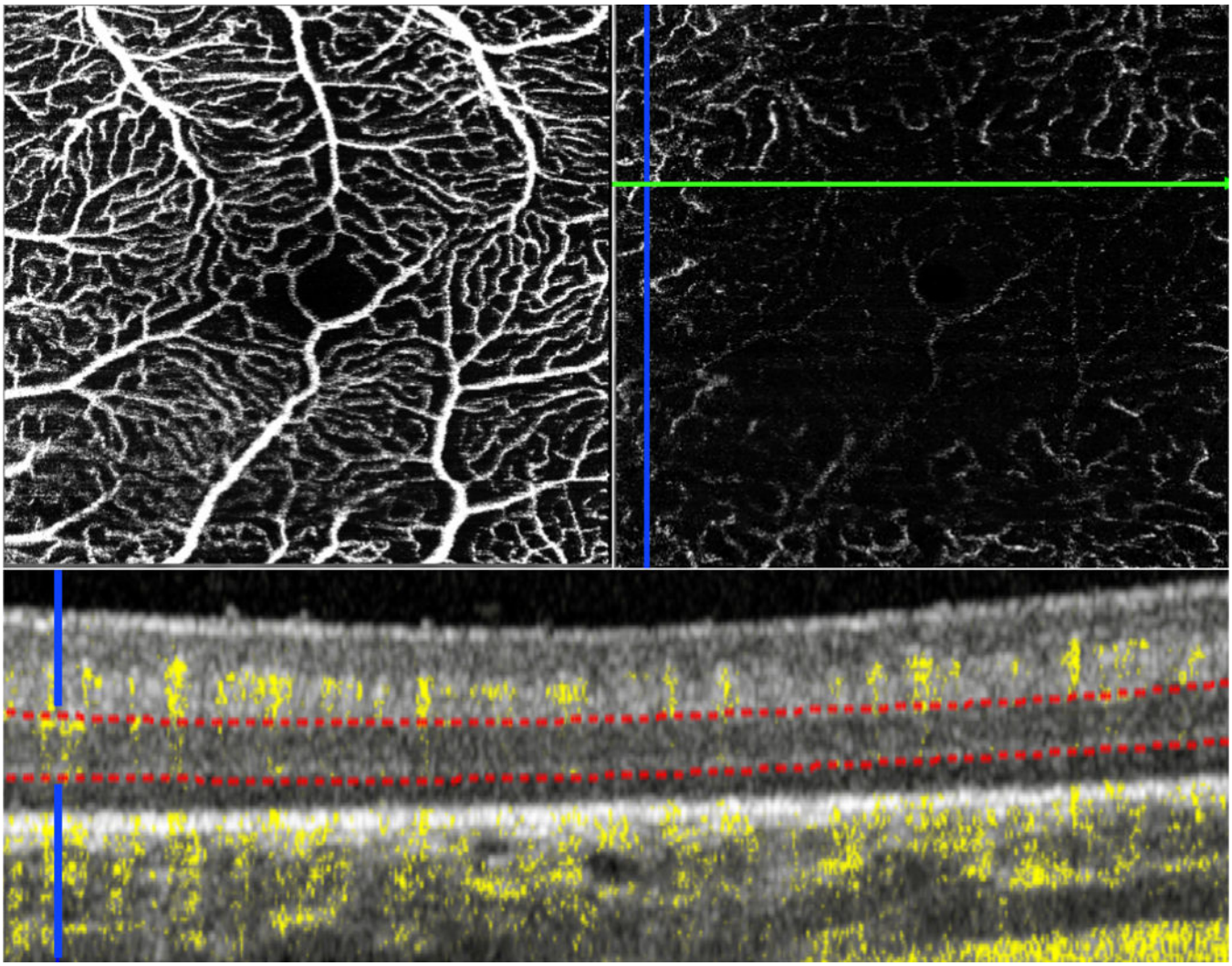

Figure 2.

The macula of the left eye of an infant with ROP imaged at 40 weeks postmenstrual age showed a small foveal avascular zone on the en face OCT-A image of the SVC (A) and lack of central macular flow in the DVC (B). A cross-sectional B-scan in the superior perifoveal region (green line on the en face OCT-A image) showed flow signal at the level of DVC only in the peripheral perifoveal region (blue crosshair and upper 1/4 of the DVC in B), and otherwise absence of flow signal in the inner nuclear layer. Red dotted lines indicate the boundaries used to generate the OCT-A image of the DVC. Note the location of the superficial vasculature is deeper than observed in mature retinas; orange brackets highlight the relatively avascular ganglion cell layer.