Vascular remodeling of choroidal neovascularization after anti-VEGF therapy visualized on optical coherence tomography angiography

Alexandra Miere, MD (1), Pauline Butori, MD (1), Salomon Yves Cohen, MD, PhD (1), Oudy Semoun, MD (1), Vittorio Capuano, MD (1), Camille Jung, MD, PhD (2), Eric H. Souied, MD, PhD (1),(2)

(1) Retina Créteil, University Paris Est Créteil, Créteil, France
(2) Clinical Research Center GRC Macula and Biological Ressources Center, Centre Hospitalier Intercommunal de Créteil, Créteil, France.

Purpose: To qualitatively and quantitatively describe the long term changes in choroidal neovascularization (CNV) flow pattern after anti-vascular endothelial growth factor (anti-VEGF) therapy, by means of optical coherence tomography angiography (OCTA).

Methods: Consecutive patients with neovascular age-related macular degeneration (AMD) underwent multimodal imaging, including OCTA at baseline and at last visit. High flow networks in the choriocapillaris segmentation of OCTA were qualitatively and quantitatively analyzed at baseline and at follow up, in order to characterize vascular flow changes after anti-VEGF treatment and to correlate these changes with final exudation signs on SD-OCT.

Results: Seventeen eyes were included. Mean follow-up was of 11.7 +/- 3.3 months. Baseline images showed: 6 medusa pattern (35.3%), 4 seafan pattern (23.5%) and 7 indistinct network patterns (41.2%). Mean CNV area at baseline was 1.58 +/- 1.72 mm2. Final OCTA images revealed a decrease in CNV total area of 21.6%. In 6/17 eyes the baseline neovascular pattern was unchanged; these cases were associated with exudation at the final SD-OCT examination (p=0.034) and a decrease in CNV area of 34.1 %. Conversely, in 11/17 eyes (64.7 %), the initial pattern had changed to a pruned vascular tree pattern, with variable exudative status on SD-OCT at the final visit and a decrease in total CNV area of 0.07%.

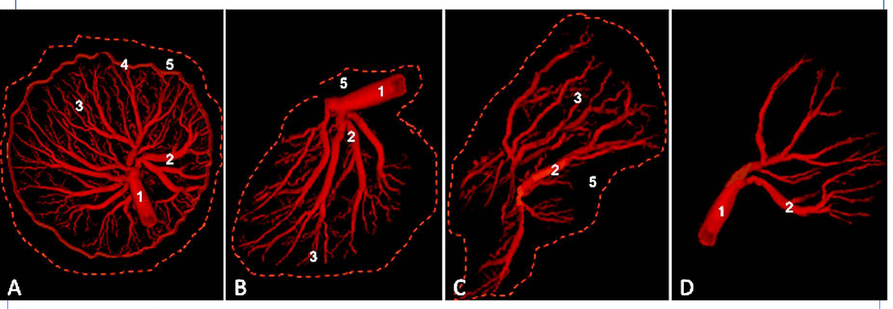

Figure 1. Illustrative drawing showing different CNV patterns in OCTA. A. “Medusa” pattern, consisting of a central feeder vessel (1), centrifugal vascular trunks (2), tiny capillaries (3), and a circular peripheral anastomosis (4). A surrounding dark halo (5) can be observed. B. “Seafan” pattern, consisting of an eccentric feeder vessel (1), main vascular trunks (2), tiny capillary ramifications (3), and an optional dark halo (5). C. “indistinct network” pattern was characterized by the visualization of only main vascular trunks (2) and thin branches (3) but with no detectable feeder vessel; a dark halo and/or a circumferential peripheral anastomosis may be observed (5). D. “pruned vascular tree” pattern is defined by a variable visualization of feeder vessel (1), with persistence of main vascular trunks (2) but no thin ramifications.

Table 1. Comparison between treatment-naïve and previously treated eyes. Note that out of the 9 treatment-naïve eyes included in this study, 8 (88.88%) belonged to the “changing pattern” group at final follow up visit. Out of 8 previously treated eyes at study inclusion, only 3 (37.5%) had changed patterns after anti-VEGF treatment.

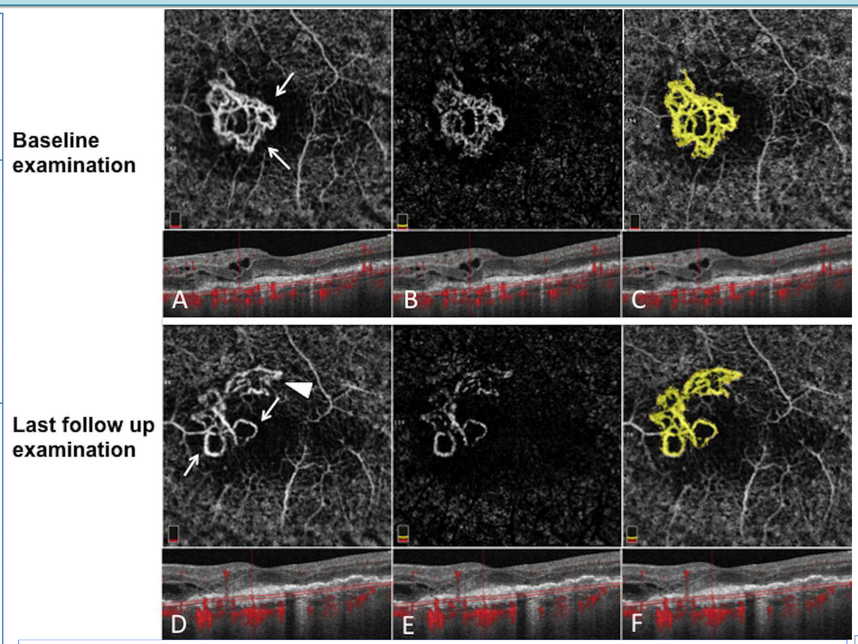

Figure 2. Changes in CNV morphology from immature to mature pattern with persistence of exudative signs. OCTA flow image of the choriocapillaris segmentationand corresponding B scans of an 86-year-old woman with an active Type 2 CNV at initial visit and 6 months later. The patient underwent 3 ranibizumab injections before baseline OCTA imaging and 3 other ranibizumab injections during the 6-month follow-up. A. Reveals a high-flow network with a circumferential peripheral anastomosis (white arrows) and tiny capillary ramifications but no visualization of a feeder vessel suggestive for the “indistinct network” pattern. B. Corresponds to image (A) with projection artifact removal. C. Mean area at baseline averaged 0.58 mm^2. Lower row (D, E, F) represents the final follow-up visit OCTA flow images and corresponding B scans of the choriocapillaris segmentation. D and E. (with artifact removal) show the regression of tiny ramifications and persistance of the main vascular trunks with margin loops (white arrows). The enlarged caliber of the vessels is suggestive for arteriogenesis. Nonetheless, sprouting of new vessels can be observed in the superior part of the lesion (white arrowhead). E. Mean area at follow-up was 0.65 mm^2, whereas at the baseline visit, mean area was 0.58 mm^2. Note that, while the mean area increased by 12.54%, vessel area diminished by only 4% (0.42 mm^2 at baseline vs. 0.40 mm^2 at the final visit).

TREATMENT NAIVE EYES (n=9)			
CHANGING PATTERN (8/9 ; 88.88%)		*CONSTANT PATERN (1/9 ; 11.11%)*	
Total area	Vessel area	Total area	Vessel area
↓21.34%	↓23.47%	↑15%	↑2.3%
PREVIOUSLY TREATED EYES (n=8)			
CHANGING PATTERN (3/8 ; 37.5%)		*CONSTANT PATTERN (5/8 ; 62.5%)*	
Total area	Vessel area	Total area	Vessel area
↑17.5%	↑1.33%	↓9.23%	↓10%

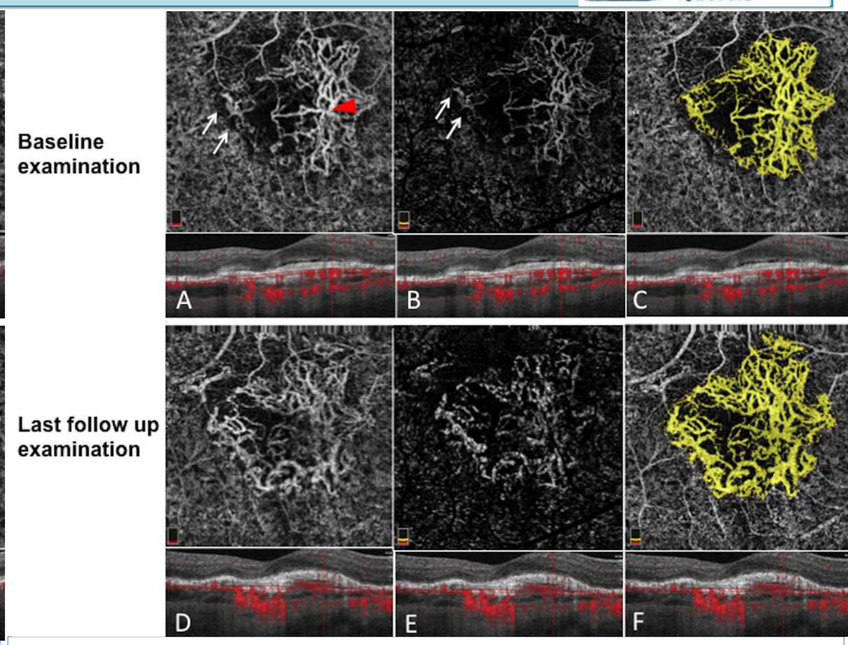

Figure 3. Constant active pattern over time despite recurrent anti-VEGF treatment, associated with a persistent exudative activity in SD-OCT. OCTA flow image of the choriocapillaris segmentation and corresponding B scans of an 83-year-old woman with a Type 2 CNV, previously treated by 9 anti-VEGF intravitreal injections at initial visit and 15 months later. The patient underwent four anti-VEGF injections between both examinations. On (A), a central feeder vessel is visible (red arrow), together with a circular peripheral anastomosis, thin branches within and adjacent (white arrows) to the high-flow network, and a surrounding dark halo are present in the choriocapillaris segmentation. B. corresponds to image (A) with projection artifact removal. Note that the adjacent thin branches (white arrows), corresponding to capillary sprouting, are slightly less visible. C. Mean area at baseline averaged 2.21 mm^2. Lower row (D, E, F) represents the final follow-up visit OCTA flow images and corresponding B scans of the choriocapillaris segmentation. D and E. (with artifact removal) show the persistence of thin branches and enlarged vascular trunks. E. Reveals the manual delineation and automatic measurement of the neovascular membrane. Mean area at final follow-up visit was 2.87 mm^2. Note that while the mean area increased by 23%, vessel area increased by only 29% (1.18 mm^2 at baseline vs. 1.66 mm^2 at the final visit).

Conclusion: The initial CNV pattern observed frequently switched toward a mature pattern after anti-VEGF therapy. OCTA may help to accurately evaluate treatment response and to recognize the patterns usually associated with recurrent exudative activity.

References:
1. Kuehlewein L, Bansal M, Lenis TL, et al. Optical coherence tomography angiography of type 1 neovascularization in age-related macular degeneration. Am J Ophthalmol. 2015;160:739-748.
2. El Ameen A, Cohen SY, Semoun O, et al. Type 2 neovascularization secondary to age-related macular degeneration imaged by optical coherence tomography angiography. Retina 2015;35:2212-2218.
3. Miere A, Semoun O, Cohen SY, et al. Optical coherence tomography angiography features of subretinal fibrosis in age-related macular degeneration. Retina 2015;35:2275-2284.
4. Coscas GJ, Lupidi M, Coscas F, et al. Optical coherence tomography angiography versus traditional multimodal imaging in assessing the activity of exudative age-related macular degeneration : a new diagnostic challenge. Retina 2015;35:2219-2228.
5. Muakkassa NW, Chin AT, de Carlo T, et al. Characterizing the effect of anti-vascular endothelial growth factor therapy on treatment-naive choroidal neovascularization using optical coherence tomography angiography. Retina 2015;35:2252-2259.