Optical Coherence Tomography Angiography In Diagnosis Of Retinal Angiomatous Proliferation

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Abstract

Age-related macular degeneration (AMD) is the leading cause of irreversible severe visual loss in the United States and Europe in people over 50 years of age [1]. Retinal angiomatous proliferation (RAP) is a distinct subgroup of AMD characterized by the origination of new vessels from the retina or from the choroid with early formation of a retinal choroidal anastomosis [2]. The diagnosis of RAP is similar with the diagnosis of the AMD, but retinal pigment epithelial detachment, exudates and superficial hemorrhages are more common in RAP.

At present, different imaging modalities are used in the diagnosis of AMD. The imaging methods fluorescein angiography (FA) and spectral-domain optical coherence tomography (OCT) are widely used for diagnosis and follow-up of patients with this disease. Optical coherence tomography angiography (OCTA) is a recent noninvasive imaging tool capable of providing the retinal and choroidal vasculature information using split-spectrum amplitude-decorrelation angiography software without the need for dye injection.

We describe the case of a 63-year-old female with unilateral RAP, which was diagnosed and followed-up by using OCTA and treated successfully with intravitreal anti-VEGF injection.

In conclusion, we found that OCTA is a useful, safe, repeatable diagnostic tool for evaluating macular disorders.

Key words: Retinal angiomatous proliferation (RAP); Optical coherence tomography angiography (OCTA); ImageJ software

Introduction

Age-related macular degeneration (AMD) is the leading cause of blindness in older adults in developed countries [1]. Neovascular AMD is an advanced form of macular degeneration that historically has accounted for the majority of vision loss related to AMD [3].
Retinal angiomatous proliferation (RAP) is defined as a variant of neovascular AMD in which the retinal-choroidal neovascularization is characterized by intraretinal capillary proliferation or, if the origin of the process is in the choroid, then it is an early retinal-choroidal anastomoses without the presence of a neovascular membrane type 1. Although dry AMD represents the majority of all diagnosed cases, neovascular AMD associated with RAP is responsible for the majority of the severe vision loss and it can be very difficult to treat due to an unsatisfactory response to anti-vascular endothelial growth factor (VEGF) treatment. The diagnosis of RAP is similar with the AMD but exudate and superficial and multiple hemorrhages are more common [4-6].
Fluorescein angiography (FA) and indocyanine green angiography (ICGA) represent the gold standard techniques to study retinal and choroidal vasculature, but these imaging modalities are not able to show the deep microvascular capillary complex of neuroretina [7]. In addition, the risk of possible side effects, including vomiting, nausea, and, exceptionally, anaphylaxis, should be considered when performing these examinations [8]. Since the introduction of optical coherence tomography (OCT) to clinical practice, it has allowed for a better understanding of the anatomic changes occurring in several ocular pathologies because of its ability to provide high-resolution images of retinal and choroidal structures [9, 10]. Nevertheless, the visualization of microvascular structures including choriocapillaris remains challenging.
Optical coherence tomography angiography (OCT-A) is a novel, noninvasive method of visualizing the retinal and choroidal vasculature in a three-dimensional depth-resolved fashion without dye injection [11-13].

Compared with conventional structural OCT, OCTA displays erythrocyte movement over time by comparing multiple B-scans acquired exactly in the same location.

Case presentation

Sixty three year old female presented in the Ophthalmology Department of the Hospital Hradec Kralove in March 2016 with a 3 months history of vision loss in her right eye. The medical history of the patient revealed: a cataract surgery with a posterior chamber intraocular lens (IOL) in both eyes 4 years ago. She was also diagnosed with essential arterial hypertension 8 years ago. At the admission, her best corrected visual acuity (BCVA) was 0.1 (Decimal) in the right eye and 1.0 in the left eye. The finding in the anterior eye segment bilaterally corresponded to the age of the patient and posterior chamber IOL in both eyes. The indirect ophthalmoscopy examination revealed normal optic disc, a few macular hemorrhages situated in the inferior-temporal sector and macular edema in the right eye (Fig. 1). The finding at the fundus of the left eye was adequate to the patient's age. The fluorescein angiography in the right eye showed intraretinal neovascularization and late stages hyperfluorence due to leakage from neovascular tissue (Fig. 2). An OCT (Zeiss Cirrus 4000) and OCT-A (Zeiss AngioPlex) were performed to the patient before the inti-VEGF injection as shown below. Conventional structural OCT revealed sub- and intraretinal fluid in the right eye with central retinal thickness of 310 μm. (Fig. 3). The outer retinal OCT-angiogram (Fig 4A) showed high flow in a neovaskular network in outer layer of neuroretina (blue) in a pattern strikingly similar to the early phase of FA. The en face OCT angiogram of the choriocapillaris (Fig 4B) showed the area of neovaskular membrane (NM), which was measured by using of ImageJ software (developed by Wayne Rasband, National Institutes of Health, Bethesda, MD; available at http://rsb.info.nih.gov/ij/index.html; plug-in available at http://rsbweb.nih.gov/ij/plugins/multi-otsu-threshold.html).

An example of image processing is presented in Figure 5. For the purposes of this investigation, three levels, or "regions," are defined: background (Fig. 5B), diffuse leakage (non-hyperfluorescent leakage; Fig. 5C), and NM (hyperfluorescent leakage; Fig. 5D). The threshold within ImageJ is adjusted to include all pixels within the "Region 2" (NM) plugin output. The NV lesion was then loosely outlined by the user to avoid vessels and other non-lesion pixels (Fig. 5E). The Multi-Otsu thresholding technique effectively delineated the NV lesion from the surrounding retina in the experimental laser model, allowing for quantification of NV lesion areas. As seen in Figure 5B, the "background" threshold output contains only

the typical background fluorescence. The “diffuse leakage” (Fig. 5C) output contains the non-hyperfluorescent leakage around the NV lesion and from out-of-focus vessels. The “NV” output (Fig. 5D) includes the hyperfluorescent central region of the NV lesion.
The number of pixels within the lesion before treatement was 1141 (ImageJ software). After the investigations we decided to start the treatment consisting in one single intravitreal injection of aflibercept in the right eye. The follow-up visits were made at 2 days, 1 week, 4 weeks after the anti-VEGF injection. 1 week after injection the BCVA improved at about 0.3. In comparison with the improved BCVA the macular edema gradually resorbed and 1 months after the anti-VEGF injection the central retinal thickness was 233 μm (Fig 6). The outer retinal OCT angiogram (Fig 7) showed improvement of the state (disappearance of the blue color – fig. 7A). And OCT angiogram of the choriocapillaris (Fig 7B) revealed reduction of the area of NV (Fig 5F) and number of pixels within the lesion after treatement was 886 (ImageJ software). The fundus examination of the right eye showed reducing of the macular hemorrhages and macular edema (Fig 8).

Discussions

In 2001, Yannuzzi et al. described chorioretinal anastomosis as neovascular proliferation with origin in the retina and proposed the designation of RAP, which was also termed “type 3 neovascularization” [5]. The retinal circulation as well as choroidal circulation contributes to the vasogenic process. Owing to high vasogenic potential, RAP has a very poor functional prognosis without treatment, and it typically progresses to increasingly severe stages before ultimately developing a disciform scar [14]. With the advent of anti-VEGF drugs, the treatment of RAP has benefited profoundly, as have other types of neovascular AMD [15, 16]. Structural OCT has become an indispensable tool in the management of AMD. It allows the clinician to assess fluid exudation from CNV as manifested by intraretinal cysts, retinal thickening, and subretinal fluid accumulation. It identifies the alterations in normal retinal anatomy that are associated with visual potential. However, structural OCT images cannot identify the CNV structure itself. Although structural OCT can identify abnormal tissue above or below the RPE that might be CNV, positive identification is not possible because CNV tissue has similar reflectivity as drusenoid material, hemorrhage, RPE, and choroid [17].

Therefore, FA or ICGA is still needed in the initial diagnosis of neovascular AMD. Because FA and ICGA require intravenous dye injection, nausea and vomiting are common adverse reactions, and serious anaphylactic reactions are possible [18].

The novel technology of optical coherence tomography angiography makes it possible to visualize ocular circulation even to the capillary level without dye injection [19]. This technology has been described as a useful tool in the diagnosis or follow-up of various retinal or choroidal vascular pathologies, and has been used in diabetic retinopathy, chronic central serous chorioretinopathy and agerelated macular degeneration [19-23].

Due to its noninvasive nature, OCT-A has several compelling characteristics that make it a promising modality for clinical use. Optical coherence tomography angiography can be acquired in a few seconds, compared with several minutes for FA.

Furthermore, two features make OCT-A preferable to classic FA: a precise three-dimensional (3D) imaging and localization of the blood flow in different retinal layers. Moreover, OCT-A allows the examiner to vary the segmentation and to scroll through the different retinal layers in order to optimise the 3D localization of the AMD.

In the present case we demonstrate OCT-A findings in patient with RAP-lesion before and after anti-VEGF injection.

In addition, because contrast between retinal vessels and surrounding tissues is high, OCT-A lends itself to segmentation and quantification of the retinal microvasculature. Swept-source OCT technology uses longer-wavelength infrared light with less sensitivity roll-off with depth compared to conventional spectral-domain OCT. This allows a deeper penetration into tissue and better imaging through optical opacities. While this sensitivity benefit may be most apparent for choroidal vascular imaging, it also may be relevant to situations with retinal thickening, such as with macular edema.

Conclusions

This case report presents OCT angiography changes in patient with RAP-lesion before and after anti-VEGF injection. With this new imaging technique we were able to visualize the level of blood flow in the RAP. Simultaneous observations with standard OCT allowed exact localization of the RAP in the different retinal layers and assessment of levels of blood flow. Optical coherence tomography angiography provides additional dynamic information about the RAP, which is lacking on FA. It can therefore be seen as an alternative, noninvasive tool for evaluation of RAP, which enables a better understanding of their morphology and activity.

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Author contributions: All co-authors have read the final manuscript within their respective areas of expertise and participated sufficiently in the study to take responsibility for it and accept its conclusions.

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Conflict of interest statement: The authors state that there are no conflicts of interest regarding the publication of this article. None declared.

List of annexations

Figure 1. Macular hemorrhages and edema in the right eye before treatement.

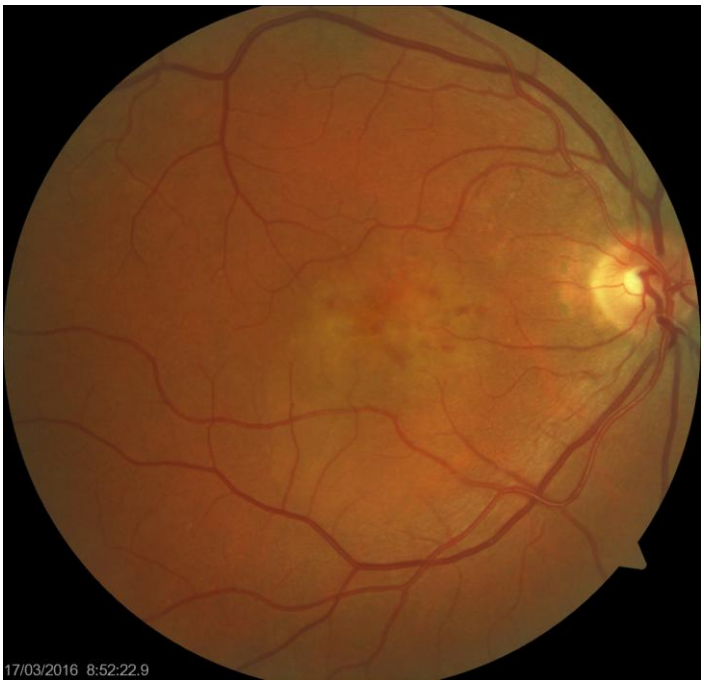


Figure 2. The fluorescein angiography: late stages leakage from neovascular tissue.

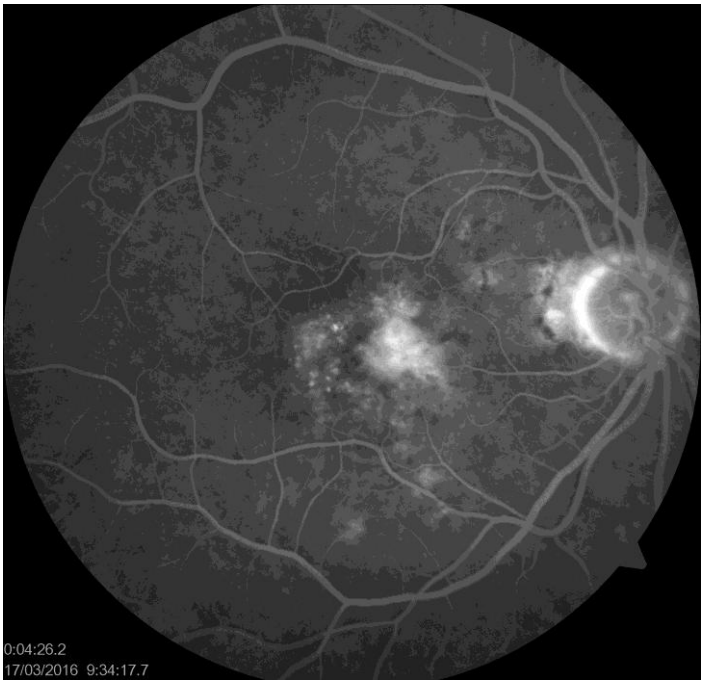


Figure 3. Conventional structural OCT: sub- and intraretinal fluid.

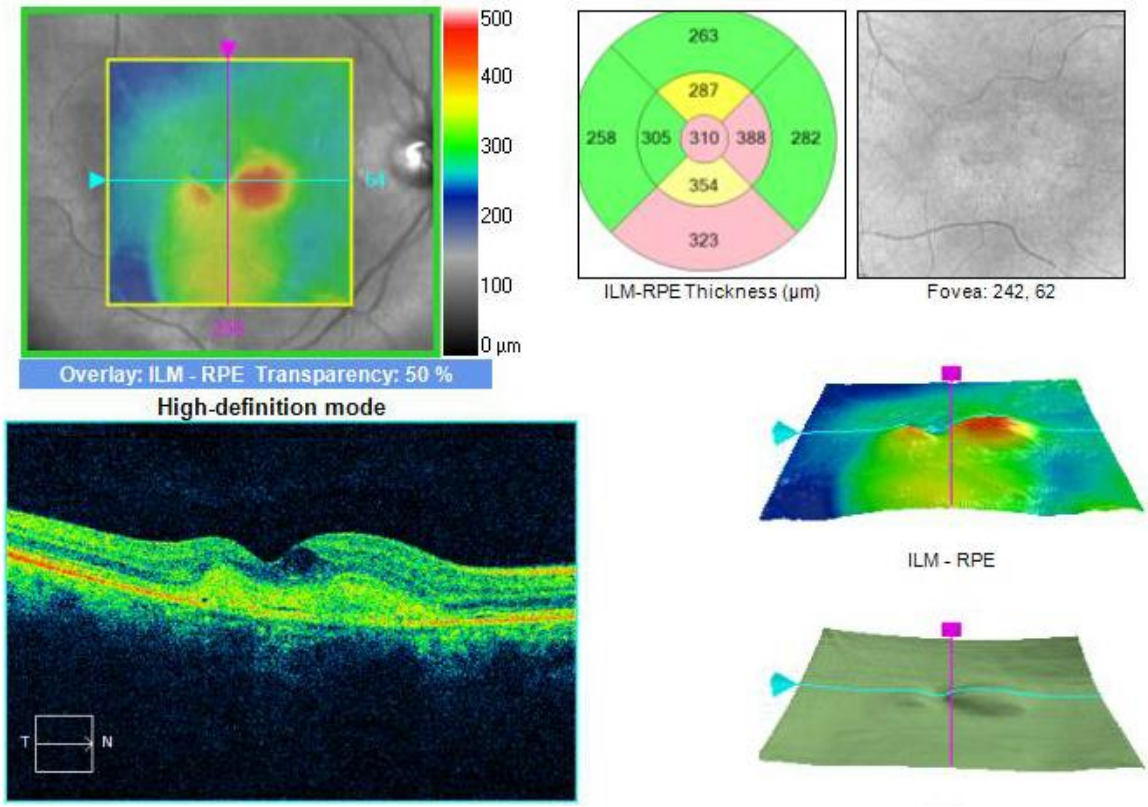


Figure 4. Retinal OCT-angiogram. **A**) high flow in a neovaskular network in outer layer of neuroretina (blue), **B**) area of neovaskular membrane on the layer of the choriocapillaris.

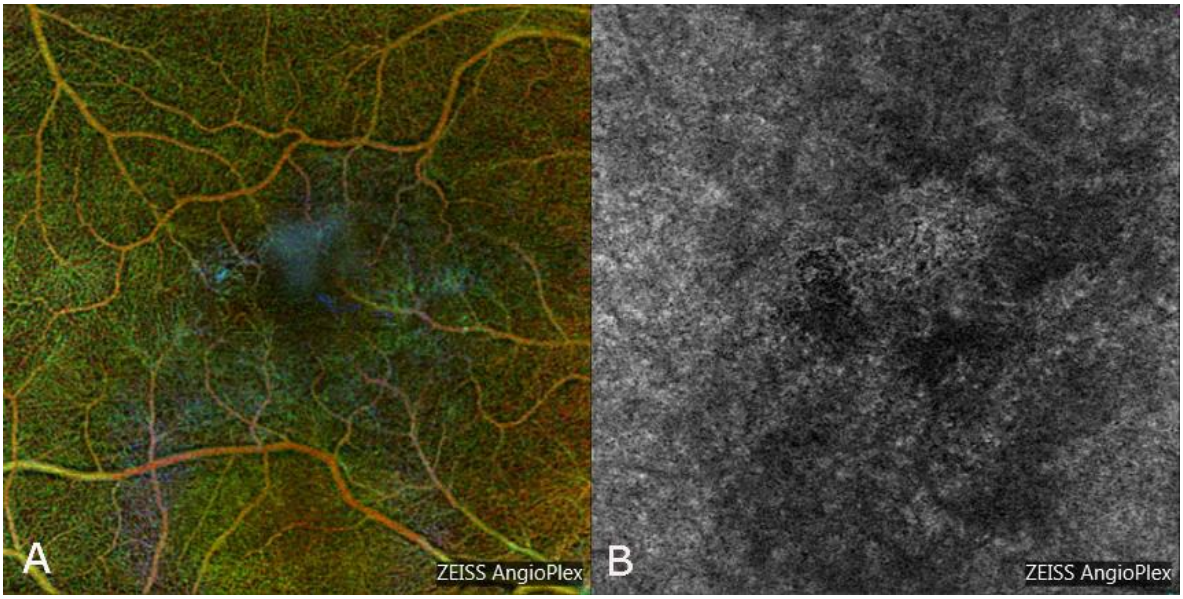


Figure 5. Lesion area quantification is performed using the "Multi-Otsu Threshold" plug-in for ImageJ. **A**) The original image is opened in ImageJ and three levels images are produced **B**) Region 0 (Background), **C**) Region 1 (Diffuse Leakage), and **D**) Region 2 (NV). With Region 2 selected, the threshold is adjusted to include all pixels within the image (shown as red in **E**). The lesion is outlined and the number of pixels within the lesion is measured. **F**) State after treatement.

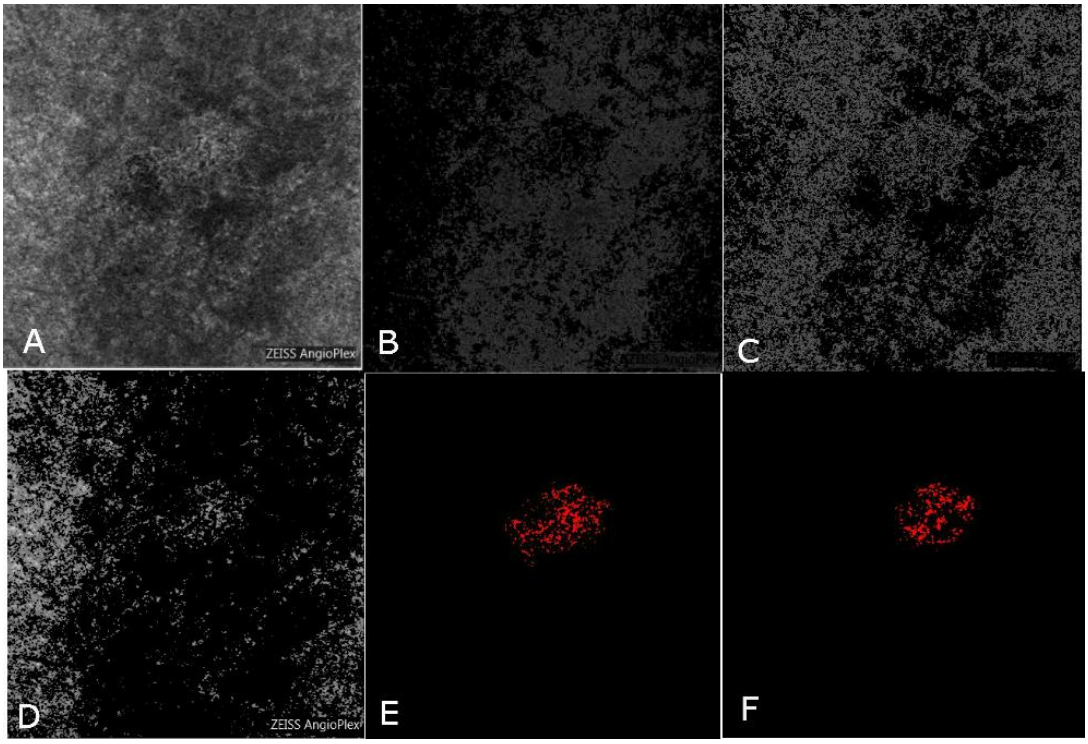


Figure 6. Reducing of the macular edema 1 months after the anti-VEGF injection.

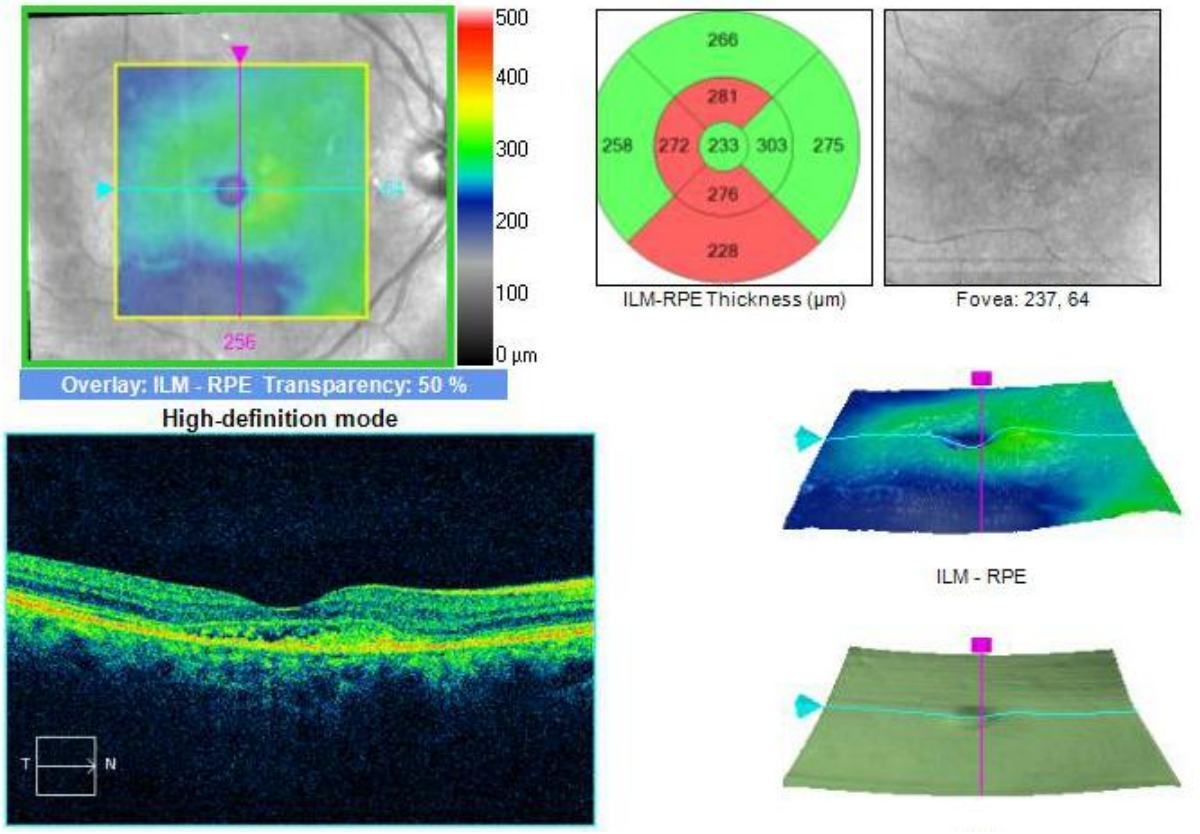


Figure 7. Retinal OCT-angiogram: state after the anti-VEGF injection. **A**) - disappearance of the blue color. B) reduction of the area of NV in the choriocapillaris layer.

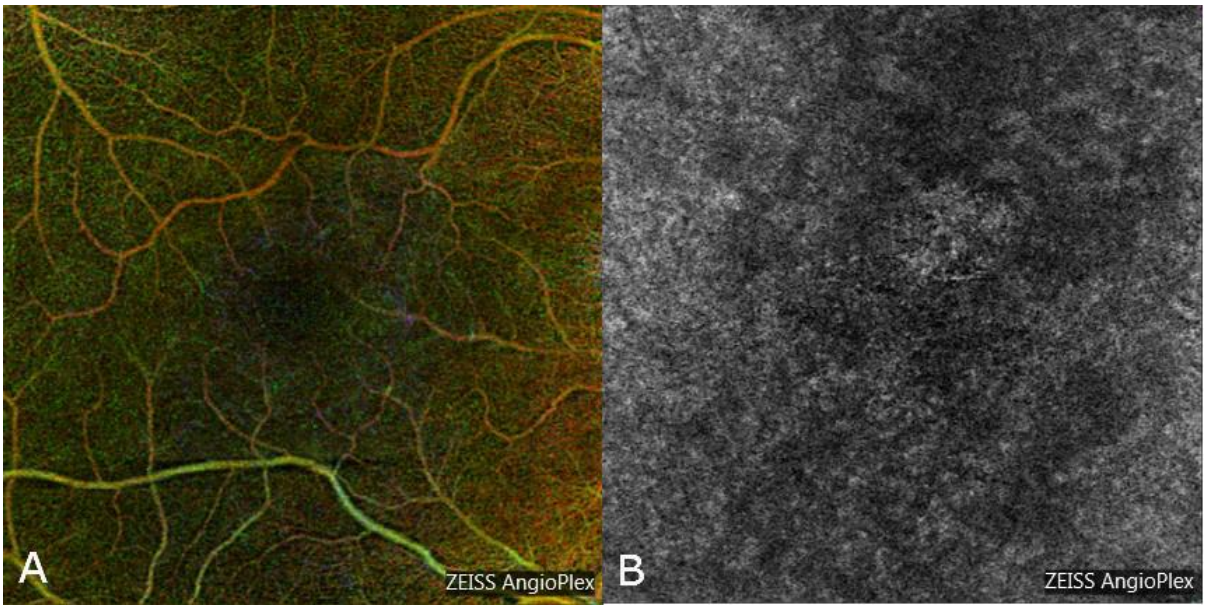
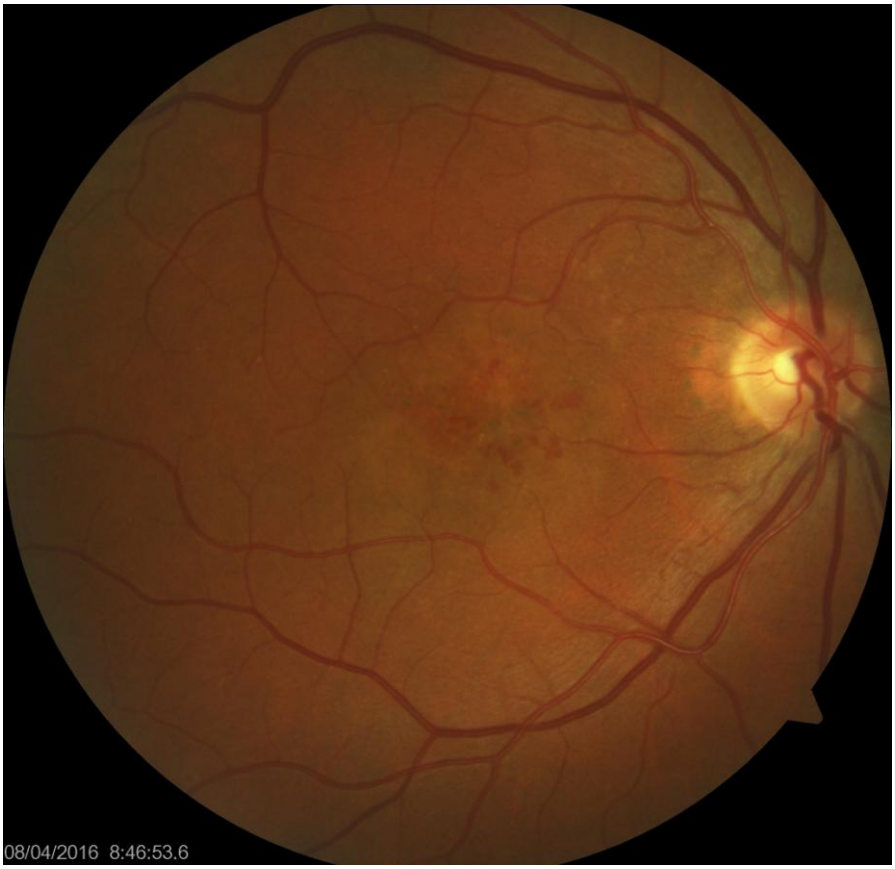


Figure 8. Reducing of the macular hemorrhages and macular edema 1 month after the anti-VEGF injection.



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