CASE REPORT

Optical Coherence Tomography-Angiography of Different Choroidal Neovascularization Subtypes in Wet Age-related Macular Degeneration

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INTRODUCTION

Age-related macular degeneration (AMD) is an acquired, multifactorial, degenerative disease characterized by progressive impairment of visual function. It affects the central part of the retina, the macula. AMD is a leading cause of irreversible loss of central vision in individuals over 55 years of age. The prevalence of AMD is expected to increase by 50% in 2020 due to increased life expectancy and aging population worldwide. Basically, AMD is divided into two groups – dry, also called non-neovascular, non-exudative form, and wet or neovascular, exudative form. The main phenotypic changes in dry AMD are extracellular deposits at the interface between retinal pigment epithelium (RPE) and Bruch membrane (BM), known as drusen. Choroidal neovascularization (CNV) is the hallmark of exudative AMD. CNV is composed of pathological new vessels combined with fibroblasts which originate from the choroid, penetrate BM and reach RPE and/or the subretinal space, forming a fibrovascular complex. The immature neovessels can lead to serous and/or hemorrhagic RPE and neurosensory retinal detachment, intra- and subretinal lipid accumulation, cystoid macular oedema, etc. with permanent loss of central visual acuity.

Fluorescein angiography (FA) is still considered the “gold standard” in diagnosing neovascular AMD. It allows functional and dynamic assessment of blood vessels in the retina and choriocapillaris. FA detects CNV due to leakage of dye from its abnormal vessels. According to Macular Photoco-
agulation Study, CNV is classified as classic, occult and mixed type. A major limitation of FA is its invasiveness. It requires intravenous injection of dye, which may cause discomfort, nausea, vomiting, rarely anaphylactic and anaphylactoid reactions.

Optical coherence tomography-angiography (OCT-A) is a relatively new, non-invasive diagnostic method. It is an upgrade to conventional optical coherence tomography (OCT) software and provides a high resolution 3D image with quantitative and qualitative structural information. In addition, OCT-A enables also functional assessment of blood vessels in the retina and choroid, without the need of an intravenous dye. Recently, OCT-A is widely used in the diagnosis of neovascular AMD. Based on the motion contrast in the different structural layers (superficial and deep vascular plexuses, avascular retina, choriocapillaris), OCT-A allows precise visualization of CNV – dimensions and morphology. According to the location, CNV is classified as type 1 CNV (under RPE), type 2 CNV (above PRE) and type 4 CNV (type 1 + type 2). Intraretinal neovascularization (retinal angiomatous proliferation) is described as type 3 CNV.

The purpose of this study was to report and analyze 3 cases with different CNV subtypes of wet AMD using OCT-A and FA. The study was approved by the Ethics Committee of Medical University of Plovdiv, Bulgaria, and conducted in accordance with the requirements of the Declaration of Helsinki. All 3 patients underwent a complete ophthalmologic examination, including best corrected visual acuity (BCVA, Snellen charts), slit-lamp biomicroscopy with fundus examination, tonometry, FA, OCT and OCT-A (Cirrus HD-OCT, Angioplex, Carl Zeiss Meditec, Dublin, CA). Written informed consent was obtained from all of them. Using OCT-A, scans with sizes 3 mm × 3 mm and 6 mm × 6 mm were obtained paying attention to the individual vascular plexuses. Qualitative assessments of FA and OCT-A findings were analyzed.

CASE REPORT

CASE 1

A 67-year-old woman reported worsening of vision in her right eye. BCVA was 0.09. She had a history of anti-vascular endothelium growth factor (anti-VEGF) therapy three times for neovascular AMD in the same eye. Color photography revealed drusen and pigmentary abnormalities as well as central retinal thickening suspected for CNV (Fig. 1A). FA showed areas of stippled hyperfluorescence with leakage of dye in the late frames of the angiography suspected to occult CNV (Figs 1B, 1C). OCT revealed fibrovascular CNV (Fig. 1D). Automated segmentation of the choriocapillaris on OCT-A detected abnormal blood flow originating from the choroid and located under RPE suspected for type 1 CNV (Figs 1E, 1F).

CASE 2

A 70-year-old woman presented with decreased and blurred vision in her left eye. BCVA was 0.1. She had no history of any known systemic and ocular diseases except initial lens opacification. Color photography revealed a hemorrhage and oedema in the central macula surrounded by hard exudates (Fig. 2A). FA showed early hyperfluorescence with well-defined membrane which progressively intensified throughout the study and leakage of dye in the late frames of the angiography that obscured the lesion margins suspected a classic CNV (Figs 2B, 2C). OCT revealed a hyper-reflective structure above the RPE with subretinal fluid, RPE detachment and ellipsoid zone atrophy (Fig. 2D). Automated segmentation of the outer retina on OCT-A detected abnormal blood flow above RPE in the normal avascular part of retina suspected for type 2 CNV (Figs 2E, 2F).

CASE 3

A 69-year-old man presented with a one-year history of significant worsening of his vision in the right eye. BCVA was 0.05. He had been diagnosed with AMD in both eyes five years before, without anti-VEGF therapy until now. Color photography revealed fibrotic changes affecting the macula and a big hemorrhage temporal to it, suspecting activity of the neovascular complex (Fig. 3A). FA showed areas of early hyperfluorescence that progressively intensified throughout the study with late leakage, pooling and staining of dye with blurring of the lesion boundaries as well as hypofluorescence due to the hemorrhage suspected mixed type of CNV (Figs 3B, 3C). OCT revealed a hyper-reflective structure above the RPE, intraretinal cystoid edema, serous and fibrovascular RPE detachments (Fig. 3D). Automated segmentation of the choriocapillaris and the outer retina on OCT-A detected abnormal blood flow originating from the choroid and located under the RPE as well as pathologic blood flow in the avascular retina suspected for mixed type of CNV (Figs 3E, 3F).
DISCUSSION

Neovascular AMD comprises only 10-15% of AMD patients but is responsible for more than 80% of blindness related to the disease. This unfavorable statistics requires regular screening, early diagnosis, and timely treatment of AMD. OCT-A has proved particularly convenient in the diagnosis of wet AMD, including follow-up after re/treatment. It allows visualization and assessment of retinal and choroid vasculature without the need of dye. Due to the noninvasiveness of this imaging method compared to FA, the disadvantages related to vascular leakage and staining are eliminated. Furthermore, FA is contraindicated in some circumstances because of some serious adverse effects. It is also a time consuming procedure. As a result of these drawbacks, FA is not used routinely in clinical practice.

A lot of studies compare OCT-A and FA in neovascular AMD reporting a high diagnostic accuracy between the two imaging modalities. A study by Gong et al. reported sensitivity and specificity of OCT-A for CNV detection of 86.5% and 67.6%, respectively. In comparison, de Carlo et al. estimated that the sensitivity and specificity of the method in 30 eyes with neovascular AMD were 50% and 91%, respectively. High sensitivity (89.2%) and specificity (93.3%) was also reported by Shaimov et al. in a study with 68 CNV patients (72 eyes). Using OCT-A quantitative assessments of the neovascular complex such as flow index, flow area and vascular

![Figure 1. Type 1/occult CNV.](image-url)
Figure 1. Type 1/occult CNV.
Optical coherence tomography-angiography, 6×6 mm scan (E) and 3×3 mm scan (F) (see text).

Figure 2. Type 2/classic CNV
Color photography (A), fluorescein angiography (B) (see text).
Figure 2. Type 2/classic CNV.
Fluorescein angiography (C), optical coherence tomography (D), optical coherence tomography-angiography, 6×6 mm scan (E) and 3×3 mm scan (F) (see text).
density can be registered as well.\textsuperscript{13}

In this study we report 3 patients with different CNV subtypes of neovascular AMD. There was 100\% concordance between OCT-A and FA in the examined cases. Nevertheless, type 1 CNV was more difficult to be detected by OCT-A (in comparison to type 2) due to signal reduction under the RPE. In such scenario, especially in cases with big RPE detachment, fluorescein angiography and/or indocyanine-green angiography is necessary to be performed. We demonstrate the inability of OCT-A to detect any pathological blood flow under a giant RPE detachment secondary to neovascular AMD (\textbf{Fig. 4}). Occult CNV was later confirmed by FA.

Other limitations of OCT-A are projection and moving artefacts, which make interpretation of the deeper structures more difficult. Any patient’s microsaccades will cause worsening of acquired image quality. Furthermore, the correct segmentation (automated and/or manual) of scans is essential for the visualization of different CNV subtypes avoiding misinterpretation.

\textbf{CONCLUSION}

This study demonstrated the utility of OCT-A in identifying different subtypes of CNV secondary to AMD. It is a promising noninvasive method which could be incorporated in the diagnostic routine and follow-up plan for patients with AMD. Because of software limitations, OCT-A cannot replace completely FA so far. Further studies are needed to as-

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\begin{minipage}{0.4\textwidth}
\includegraphics[width=\linewidth]{D.png}
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\caption{Type 4/mixed type CNV. Color photography (A), fluorescein angiography (B, C), optical coherence tomography (D) (see text).}
\end{figure}
Figure 3. Type 4/mixed type CNV.
Optical coherence tomography-angiography, 6×6 mm scan (E, F) (see text).

Figure 4. Giant RPE detachment secondary to occult CNV.
Color photography (A), fluorescein angiography (B) (see text).
Figure 4. Giant RPE detachment secondary to occult CNV. Fluorescein angiography (C), optical coherence tomography (D), optical coherence tomography-angiography, 6×6 mm scan (E) and 3×3 mm scan (F) (see text).
sess the role of OCT-A and develop our knowledge of this novel imaging modality.

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Оптическая когерентная томография-ангиография различных подтипов хориоидальной неоваскуляризации при влажной форме возрастной макулярной дегенерации

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Возрастная макулярная дегенерация является основной причиной необратимой потери зрения у людей старше 55 лет во всём мире. Условно она подразделяется на два подтипа – сухая форма (некровоаскулярная) и влажная форма (неоваскулярная). Возрастная неоваскулярная макулярная дегенерация затрагивает всего лишь 10-15% всех пациентов, но является причиной более 80% слепоты, связанной с заболеванием. Требуется ранняя диагностика и своевременное лечение. Флюоресцениновая ангиография в настоящее время является «золотым стандартом» для диагностики неоваскулярного типа. Однако, как инвазивная процедура, она может быть противопоказана при некоторых обстоятельствах и вызывать серьёзные побочные эффекты. Оптическая когерентная томография-ангиография является относительно новым, неинвазивным и быстрым методом визуализации, который приобретает популярность в диагностике возрастной макулярной дегенерации, особенно при неоваскулярной форме заболевания. Она предоставляет структурные и функциональные данные по кровеносным сосудам сетчатки и хориоидальным кровеносным сосудам без необходимости применения внутривенного окрашивания. В этом исследовании мы представляем и обсуждаем 3 случая различных типов хориоидальной неоваскуляризации, вторичной по отношению к возрастной неоваскулярной макулярной дегенерации. Все пациенты были обследованы с помощью флюоресцениновой ангиографии и оптической когерентной томографии-ангиографии. Результаты были проанализированы качественно.