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REVIEW ARTICLE

DIAGNOSTICS OF OPTIC DISC DRUSEN – MULTIMODAL IMAGING POSSIBILITIES

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Abstract: Optic nerve drusen (OND) are calcified deposits in the optic nerve head. Though often asymptomatic, they can compress small blood vessels, disrupting local blood flow and potentially damaging nerve fibers, which may lead to visual loss. Regular monitoring of the patients is recommended in which multimodal imaging helps.

Our study presents the diagnostic possibilities of multimodal imaging to illustrate pathology observed in OND and summarize clinical data about these methods.

Keywords: Optic Nerve Drusen, OND, multimodal imaging, fundus autofluorescence, FAF, optical coherence tomography, OCT, OCT Angiography, OCTA

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INTRODUCTION

Optic nerve drusen (OND)

Optic nerve drusen (optic disc drusen (ODD)) are yellow-white calcified, acellular deposits in front of the lamina cribrosa in the optic nerve head. These formations primarily consist of calcium, amino acids, nucleic acids, and mucopolysaccharides [12]. Most cases occur without systemic or ocular conditions. Sometimes they are associated with other pathologies, such as retinitis pigmentosa, Alagille syndrome, and pseudoxanthoma elasticum [9,12,24].

OND are present in approximately 0.3–2.4% of the general population and occurr bilaterally in about 75% of cases [12,26]. OND are more frequently observed in Caucasians and may have a genetic component. [3,15,23].

Patients with OND are typically asymptomatic. However, if symptoms do appear, visual field defects are the most common, affecting approximately 75% of individuals, with reported prevalence rates varying from 11.2% to 87% [28].

Multimodal imaging methods in OND

Superficial drusen can be directly observed, while deeper drusen may alter the optic nerve's shape, sometimes giving it a congested, swollen appearance [26]. OND, particularly when located deeper, can sometimes be mistaken for papilledema, which may lead to unnecessary testing for intracranial hypertension [1].

A range of imaging techniques used for accurate and reliable detection of OND include: visual field testing (VFT), color fundus photography, fundus autofluorescence (FAF), B-scan ultrasonography, optical coherence tomography (OCT), OCT angiography (OCTA), fluorescein angiography (FA), orbital computed tomography (CT) and electrophysiology.

With the increasing use of multimodal imaging techniques, diagnosing OND has become more accurate and streamlined. However, there is still no consensus on which of these methods are most reliable or should be included in a standardized approach for evaluating patients with suspected OND.

This review explores recent studies on the available diagnostic tools for OND and summarizes insights on best practices. We conducted a comprehensive review of OND diagnostic methods to support healthcare professionals in making proper diagnoses,

METHODS

Our study presents the diagnostic possibilities in OND to illustrate pathology in patients' visual field and in the optic nerve head (ONH) due to drusen presence in patients referred to the Ophthalmology Department of the Military Institute of Aviation Medicine in Warsaw, Poland.

Visual field testing (VFT)

OND can lead to visual field defects. VFT (perimetry) is often used to assess peripheral vision loss, and which results vary significantly based on the study methods used. On average, individuals with OND experience a gradual loss of 1.58% of their VF each year, regardless of other complications [10,18,33]. Malmqvist et al. observed a 27% reduction in the Goldmann perimetry in patients with OND, whereas the expected decrease due to aging in the control group (without OND) was only 12% [20].

VF loss in OND progresses gradually and the inferonasal and inferotemporal areas are most affected. Superficial drusen are more likely to lead to VF defects than buried OND. [1,18].

Lee reported that 48% of eyes with OND exhibited normal VF results, while 30% had an enlarged blind spot [17] (Figure 1A, B). Other frequent findings included arcuate defects and concentric narrowing, which were seen in 22% of cases [28]. What is more, pathologic conditions such as: anterior ischemic optic neuropathy (AION), central retinal artery occlusion (CRAO), central retinal vein occlusion (CRVO), choroidal neovascularization (CNV), and peripapillary, subretinal, retinal or vitreous hemorrhages have been suggested as cause of vision loss in patients with OND [1].

Color fundus photography and Fundus autofluorescence (FAF)

OND are usually located in front of the lamina cribrosa, as shown in postmortem studies, and only rarely extend behind it or toward the vitreous [14]. They can be located on the surface (superficial) or beneath the surface (buried). Buried OND often appear on color fundoscopic examination as a raised ONH with an irregular, scalloped edge but without covering the nearby peripapillary vessels. In contrast, superficial OND appear as distinct, hardened yellow deposits visible on the optic nerve surface (Figure 2A, B). What is more, swelling of the ONH can be detected [14,32].

FAF is a quick and safe imaging technique that can be used for patients with OND. It uses the natural fluorescence emitted by certain components of the drusen, allowing them to be visualized

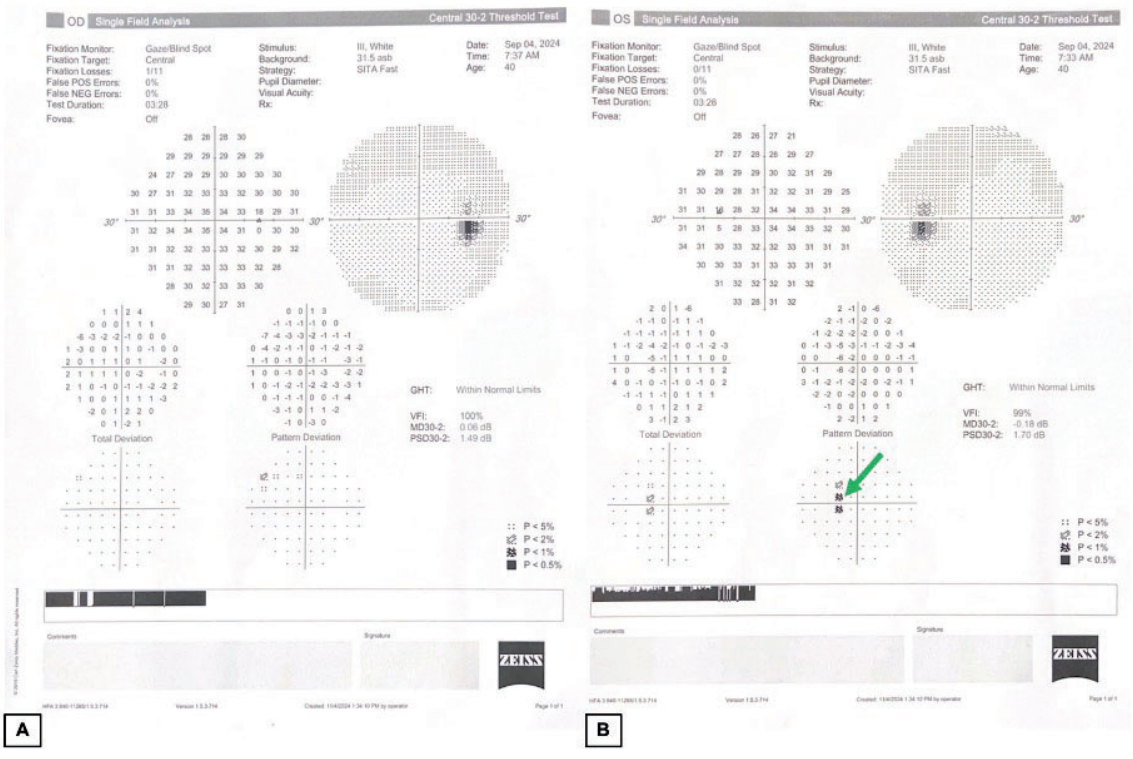

Fig. 1. VFT in patient with bilateral OND. (A) Right eye (RE) - result without abnormalities, (B) Left eye (LE) – enlarged blind spot is observed (green arrow).

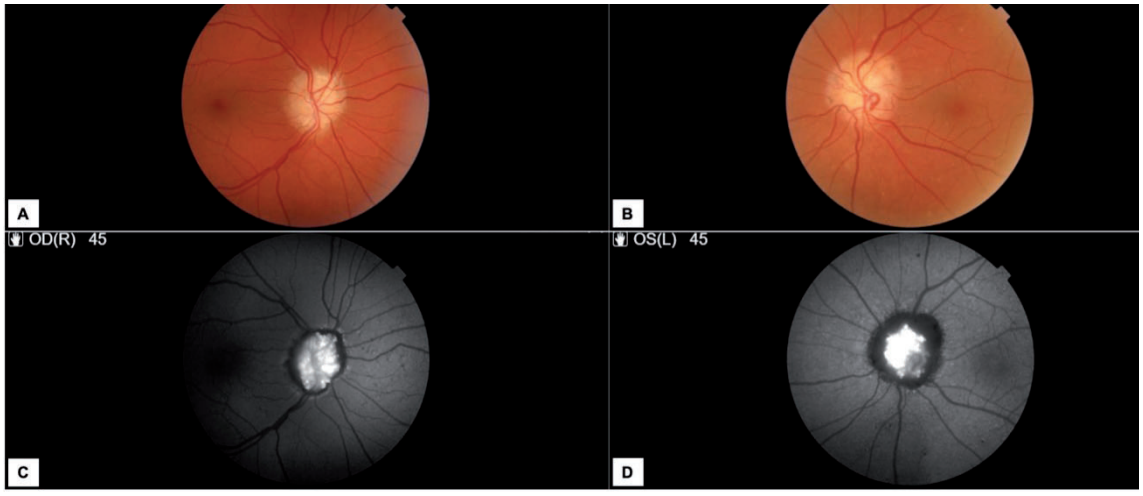

Fig. 2. Both eyes of the patient with OND. A and C – RE; B and D – LE (A, B) Color fundus images show blurred boundaries and slight swelling of the ONH. (C, D) FAF images reveal irregular, hyperautofluorescent, round structures with uneven borders, indicating drusen.

clearly. OND in FAF appear as distinct, hyperreflective spots on the ONH [13] (Figure 2C, D).

The exact sensitivity of FAF for detecting OND has not yet been established. Traber et al. found that it was effective in identifying drusen that were larger than 500 µm and clustered together [31].

The Optic Disc Drusen Studies Consortium advises including FAF as a supplementary tool for diagnosing OND [19].

B-scan ultrasonography

B-scan ultrasonography is supposed to be the gold standard for detecting OND, as it is reliable, fast, and identifies drusen as hyperechogenic structures with strong reflectivity and posterior acoustic shadowing (Figure 3). It is less effective at detecting buried drusen because these are often uncalcified [2,16]. B-scan ultrasonography can also detect additional calcium deposits that are not visible with ophthalmoscopy and allow differentiation of the OND from optic disc edema

(ODE). This method is known for providing greater accuracy than other methods, such as FAF and computed tomography (CT). B-scan ultrasonography as a non-expensive, easy method offers some insight into the posterior boundary and size of drusen. However, its resolution is relatively low, and that is why it provides limited information about the detailed structure of the retina [30].

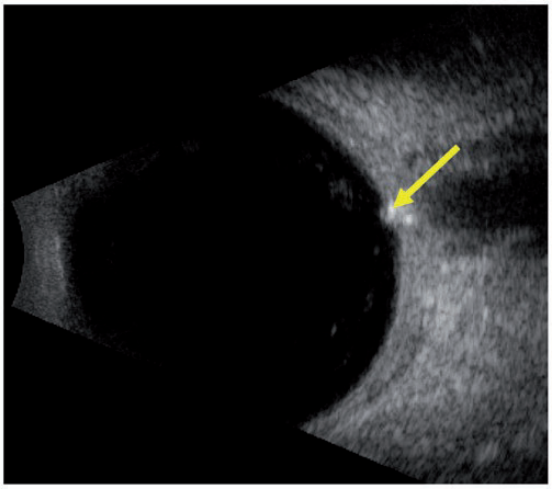

Fig. 3. B-scan ultrasonography in a patient with OND. A hyperechogenic round structure (yellow arrow) with posterior acoustic dark shadowing in the optic nerve of the right eye is observed.

Optical coherence tomography (OCT)

Spectral-domain OCT (SD-OCT) is a non-invasive imaging technique that uses light waves to create cross-sectional images of the retina. SD-OCT captures a complete scan almost instantly by using a broader spectrum of light. This technology allows for precise, detailed visualization of the retina's layers, making it essential for diagnosing and monitoring ocular conditions.

SD-OCT can provide more accurate images (compared to B-scan ultrasonography) of the optic nerve and is particularly useful in assessing the location and extent of the drusen. It may be useful in the differentiation of buried OND from ODE (the internal optic nerve contour is smooth in cases of ODE but irregular in cases of OND)[25].

According to Optic Disc Drusen Studies Consortium Recommendations, OND in OCT presents a low-signal central core surrounded by a hyperreflective border, most prominent superiorly [19] (Figure 4A). However, in SD-OCT the hyperreflective border is often incomplete, showing indistinct anterior edges and a lack of posterior signal, making it difficult to clearly define the full structure of the drusen [20,26]. Other studies have described OND with hyperreflective or both hypo- and hyperreflective internal reflectivity [17,31].

Previous OCT studies observed retinal nerve fiber layer (RNFL) thinning in patients with OND which was especially common in the inferonasal and nasal regions [33]. What is more, a thinning of ganglion cell complex (GCC) (corresponding to tinning in RNFL) in patients with OND was described by Casado et al. Therefore, the GCC has a useful additional value to the RNFL in this ocular condition [5] (Figure 4B, C).

While SD-OCT is a promising tool for OND detection, it has a major limitation – its resolution decreases with depth. This means that deeper drusen are often less clearly defined and can be difficult to differentiate. Enhanced depth OCT (EDI-OCT) achieves its highest sensitivity near the inner scleral layer, making it highly effective for visualizing buried OND. This technique works by shifting the coherence gate to focus on deeper tissue layers, providing clearer images of structures located deeper within the optic nerve head [30]. As stated in the recommendations of the Optic Disc Drusen Studies Consortium, if SD-OCT in EDI mode is unavailable, adjusting the eye position to obtain an inverted optic nerve head view can enhance visualization. Additionally, entering corneal curvature and refraction values into the system is recommended.

To identify, quantify, and classify ODD, a dense optic nerve head scan should be performed. This involves using EDI mode or an inverted scan, opting for high-resolution acquisition if possible, and centering a 15 × 10° scan area over the optic disc. The scan should include 97 sections spaced 30 µm apart, averaging at least 30 frames. Both horizontal and vertical scans should be conducted.

For assessing scleral canal size, a radial optic nerve head scan is advised. This should be done using EDI mode or an inverted scan, with a 20° 6-line radial scan centered on the optic disc.

To evaluate RNFL thickness, a peripapillary scan should be performed. In this case, EDI mode should be disabled, and a 12° peripapillary (circle) scan should be centered on the optic disc.

For excluding macular pathology, a macula scan should be carried out. This requires disabling EDI mode, centering a 20 × 20° scan area over the macula, using at least 25 sections spaced 240 µm apart, and averaging a minimum of 9 frames [19].

OCT angiography (OCTA)

OCT Angiography (OCTA allows to observe images of vessel density (VD) within the retina and ONH [1]. It is a promising technique in which as-

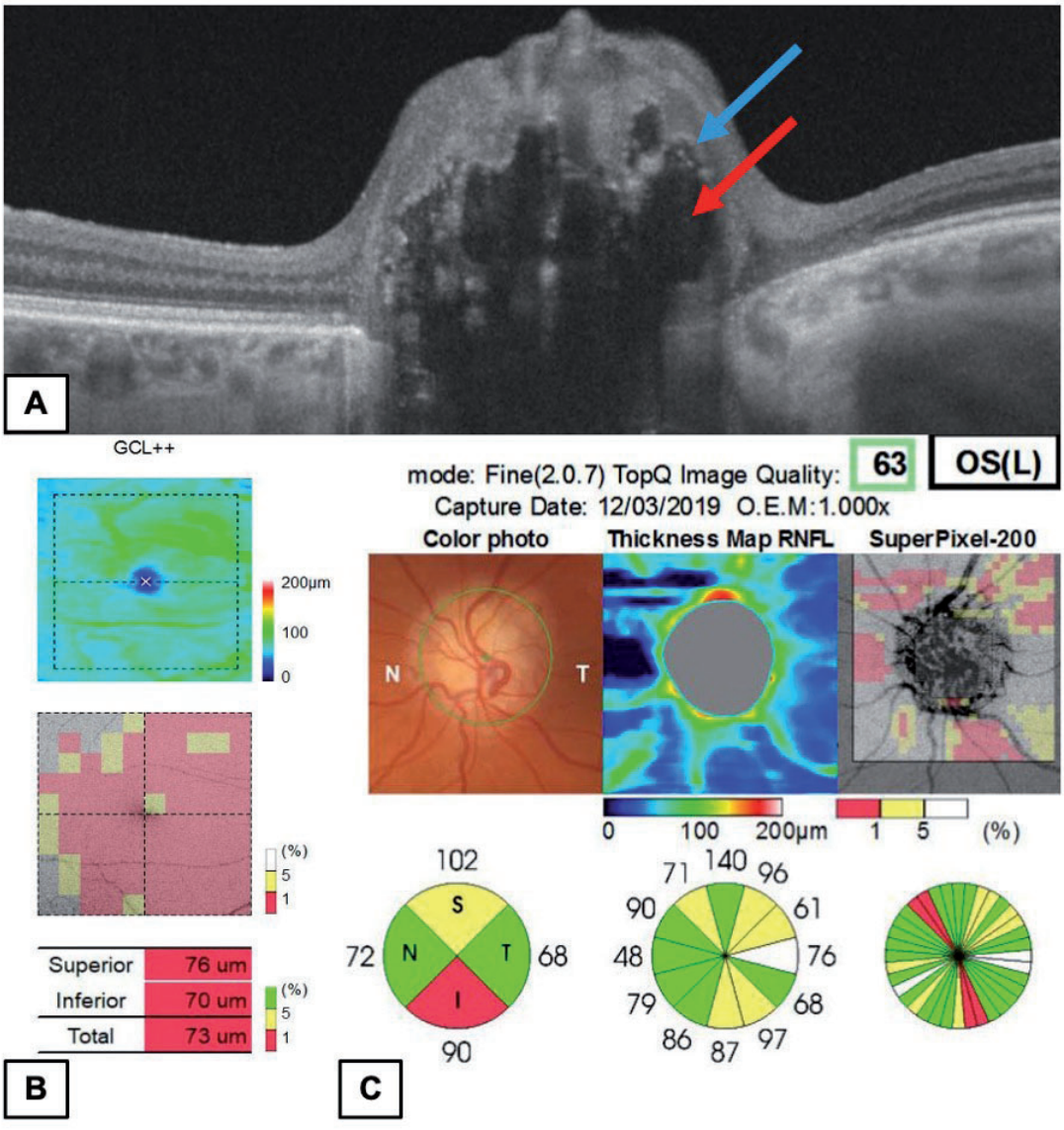

Fig. 4. OCT in a patient with OND (LE). (A) OCT B–scan – hyporeflective core (red arrow) and hyperreflective halo (blue arrow) around deposits visible in the ONH. (B) Decreased GCC is presented in superior and inferior parts of the macula. (C) Decreased RNFL is observed in superior and inferior quadrants due to drusen presence.

sessment of the vessels in the retina without dye injections is possible. The retinal vasculature can be described in layers, providing a detailed and comprehensive view of blood supply across different retinal structures [27].

It is already known that when OND accumulate, they can increasingly affect the optic nerve area and squeeze the tiny capillaries supplying blood. This crowding effect can disturb local circulation, sometimes leading to minor ischemic areas with reduced blood flow [4]. OCTA reveals these effects by showing reduced capillary density and areas of peripapillary dropout in patients with OND, which helps in evaluating the extent of vascular compromise [1] (Figure 5).

Recent studies described that patients with OND had lower radial peripapillary capillary plexus (RPC) VD values and higher choriocapillaris flow (CCF) area values [32]. Cennamo G. also noted that the flow index and VD were notably lower in patients with OND compared to control subjects. What was interesting, RNFL measurements did not show any significant differences between patients and controls. That is why Authors supposed the superior sensitivity of OCTA in detecting vascular changes associated with OND when compared to other diagnostic methods [6].

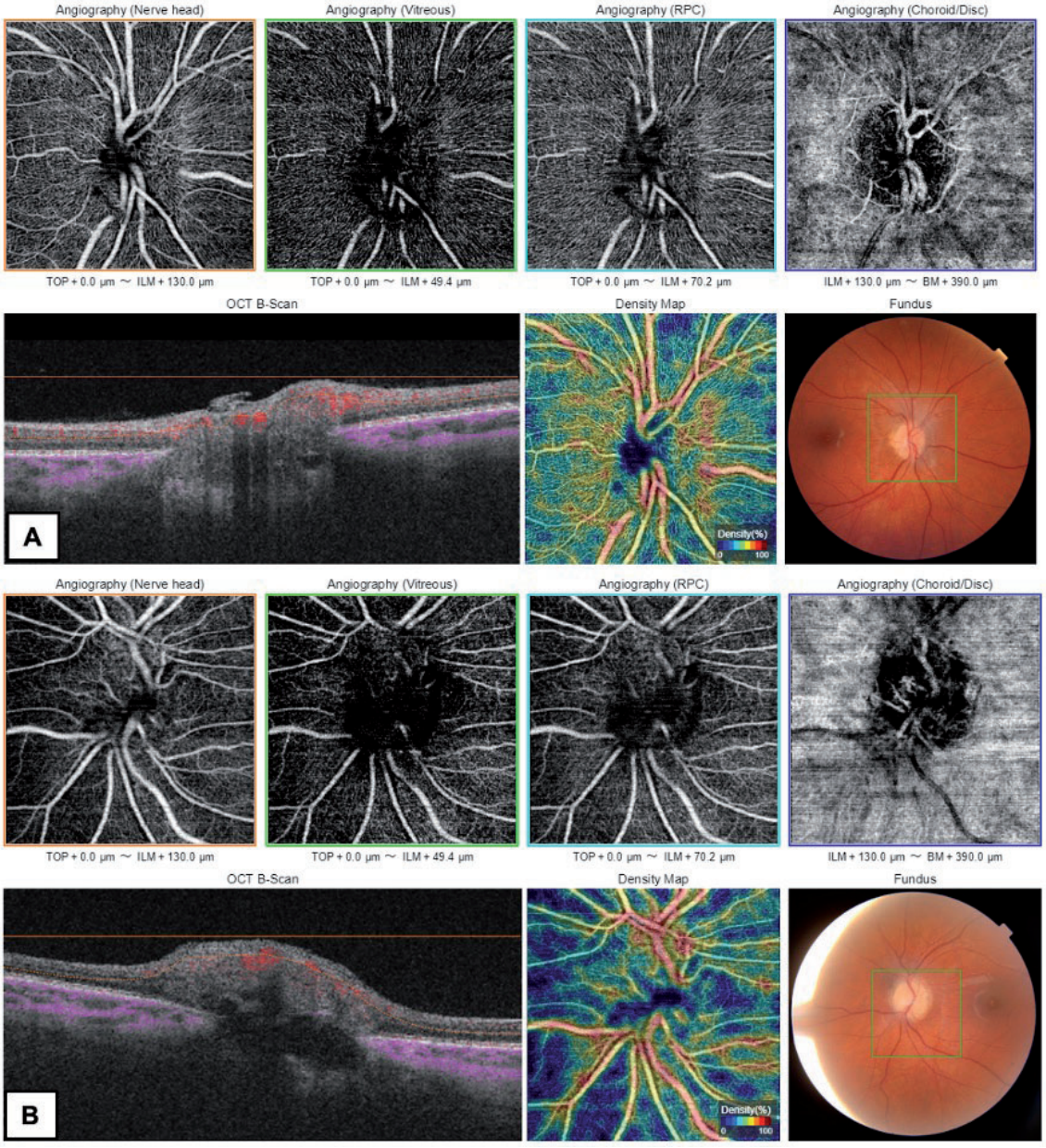

Fig. 5. OCTA in a patient with unilateral OND (in LE). (A) RE – without drusen, no disturbances in vessel density in the peripapillary region are observed (B) LE – decreased number of vessels visible in RPC and choriocapillaris level – a dark halo effect is observed, color vessel density map showed capillary dropout areas in blue color, which refers to ischemia in the peripapillary region.

Fluorescein angiography (FA)

Fluorescein angiography (FA) findings in eyes with OND typically include nodular staining of the ONH and delayed filling of the peripapillary choriocapillaris. Pineles and Arnold reported that nodular optic disc staining was present in 90% of cases with visible OND, compared to only 25% in cases with buried OND [21].

FA is valuable for distinguishing drusen from ODE, even when they are buried. ODE usually shows diffuse and early fluorescein leakage, while buried OND tends to exhibit late peripapillary staining, with 80% showing circumferential and 20% showing nodular patterns [11,21]. Chang et al. have emphasized that FA is the most reliable imaging technique for distinguishing between papilledema and pseudopapilledema. It is recommended by Authors in identification of the differences between these two conditions, aiding in the correct diagnosis and management of optic disc swelling [8].

Computed tomography (CT)

CT imaging has been used to detect OND, which appear as hyperdense spots on the scan. However, like B-scan ultrasonography, CT is only effective in identifying calcified OND. Additionally, with a spatial resolution of 1.5 mm, CT is not capable of detecting smaller drusen. For these reasons, CT imaging is not currently recommended for the diagnosis of OND [22].

Electrophysiology

Electrophysiological testing has shown abnormalities in eyes with OND, which are typically linked to the extent of RNFL damage [7]. Scholl et al. conducted pattern electroretinogram (PERG) testing on 24 eyes with OND and found that P50 amplitudes were reduced in 17% of the eyes. Additionally, a decrease or absence of the N95 component was observed in 79% of the eyes [29].

Full-field visual evoked potential (VEP) testing has also been applied to OND, but the results have been inconsistent. The P100 latency response was prolonged in 0% to 83% of OND eyes, depending on the study [7]. One limitation of full-field VEP testing is that it measures the overall sum of potentials generated by visual input, which means localized defects in the retina or optic nerve may not be detected, as they can be masked by the overall response [20].

DISCUSSION

Regular monitoring of early structural changes in ONH morphology through multimodal imaging diagnostic methods could offer valuable insights into the underlying mechanisms of vision loss in patients with OND. The disease usually progresses slowly, which is why follow-up ophthalmological examination in cases with OND is needed.

OCT-based measurements could be compared with functional tests sensitive enough to detect the initial signs of optic nerve dysfunction.

Patients with buried OND are less likely to show visual impairments compared to those with superficial OND, which can make it challenging to detect significant functional changes within a short follow-up period using older testing methods. Emerging imaging technologies, like OCT, offer a way to measure the size of optic disc drusen and assess the condition of surrounding retinal and optic disc structures. These tools hold promise for enhancing our understanding of the connections between OND, RNFL loss, and VF defects. They also enable ongoing monitoring of drusen over time, potentially shedding light on disease mechanisms.

CONCLUSIONS

Further studies using OCT could reveal risk factors linked to drusen-related visual field loss and contribute valuable prognostic information.

Development of advanced multimodal imaging techniques for assessing ONH vascularity in patients with OND, including OCTA, retinal function imaging, and oximetry, is necessary to better understand the vascular complications associated with OND.

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Study Design: Paulina Szabelska. Data Collection: Paulina Szabelska, Radosław Różycki, Joanna Gołębiewska. Manuscript Preparation: Paulina Szabelska, Joanna Gołębiewska. The Authors declare that there is no conflict of interest.

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