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Hyperreflective dots in optical coherence tomography

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HIGHLIGHTS

OCT is a non-invasive imaging method of posterior segment of the eye. Hyperreflective dots observed in OCT scans can be a useful biomarker in diagnostics and course of treatment in retinal diseases.

ABSTRACT

Optical coherence tomography is a non-invasive and repeatable imaging method of posterior segment of the eye used in medical practice. Hyperreflective dots visible in OCT scans have been reported in various retinal diseases such as age-related macular degeneration, diabetic macular edema, retinal vein occlusion and central serous chorioretinopathy. In the future, HRDs may become a useful biomarker in making treatment decision and monitoring ocular conditions among the patients with mentioned diseases.

Key words: hyperreflective dots, HRDs, optical coherence tomography, AMD, diabetic retinopathy, retinal vein occlusion

INTRODUCTION

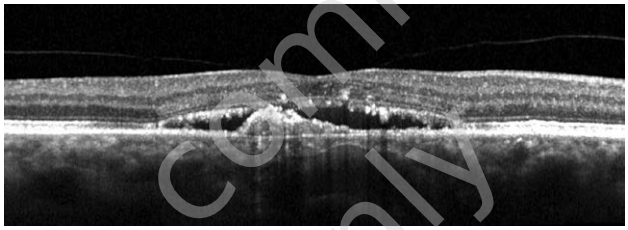
Optical coherence tomography (OCT) is a non-invasive and repeatable imaging method of posterior segment of the eye used in medical practice. It provides real-time, in vivo visualization of the histological structure of the eye tissues [1]. It is useful tool in diagnosis and follow-up of ocular abnormalities involving the macula. It provides detailed information for the evaluation of drusen, intraretinal and subretinal fluid, detachment of retina pigment epithelium and hyperreflective dots (HRDs) [2]. Hyperreflective dots in OCT were firstly demonstrated and termed by Coscas et al. as a punctiform, small hyperreflective lesions of approximately 20–40 μm diameter scattered through retinal layers [3, 4].

HRDs have been reported in various retinal diseases such as age-related macular degeneration (AMD), diabetic macular edema (DME), retinal vein occlusion (RVO), central serous chorioretinopathy (CSCR), uveitis and macular telangiectasia [2].

Histopathology of HRDs is unknown, however there are some hypotheses about its structure in OCT [4]. Authors suggested that they are accumulations of pigment such as lipofuscin granules, lipid deposits because of breakdown of the blood-retinal barrier or microglia cells and macrophages [2].

FIGURE 1

OCT scan-B of the right eye showing intraretinal fluid. RPE detachment and hyperreflective dots in patient with AMD.



AGE-RELATED MACULAR DEGENERATION

AMD is a leading case of central vision impairment in patients over the age of 55 years worldwide. Medical experts differentiated two main groups of the disease: non-exudative and exudative form based on the presence of the macular neovascularization [4]. Exudative form of AMD is characterized by neovascularization and following occurrence of subretinal or intraretinal fluid in retinal layers. Neovascular AMD accounts for 10–20% of total AMD patients, however it is responsible for 90% of severe visual loss among this group. Current treatment for neovascular AMD are intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF). Researchers identified retinal biomarkers in OCT associated with visual acuity (VA) useful to predict and evaluate treatment response [4].

The researchers hypothesized about the structure of HRDs in AMD. Curcio et al. in their study assumed that they could be composed of two different cells population activated migrating RPE and lipid-filled microglia cells moving from inner to outer retina [5].

Altay et al. reported that hyperreflective signs more likely represent macrophages and microglia that are the immune cells located in the retina involved in the pathogenesis of AMD. This finding is supported by the observation of HRDs in other retinal diseases with neuroinflammatory components, such as diabetic maculopathy. Moreover, their study results revealed HRDs in OCT scans in early AMD forms as a main risk factor of progression to severe forms such as geographic atrophy [6].

Similar results were made by Heußen et al. who mentioned hyperreflective signs as the initial symptom of type 3 macular degeneration (type 3 of MNV) [7].

Coscas et al. have analyzed the prognostic value of HRDs in 100 eyes with neovascular AMD [8]. Their study has shown the correlation between poor VA and occurrence of HRDs in OCT scans after anti-VEGF therapy. Moreover, authors have shown persistence of high number of this biomarker in non-responder patients and quickly decreasing number of HRDs after treatment in responding ones. Furthermore, Turgut et al. in their study included patients with nAMD and HRDs presence in OCT. The results have shown that all included subjects were at active phase of the disease and the biomarker was presented in outer retinal layers [2].

The results of international studies indicate that occurrence of HRDs in OCT might be a significant biomarker useful in monitoring and making treatment decisions in patients with neovascular AMD.

FIGURE 2

OCT scan-B of the right eye showing intraretinal fluid, RPE detachment and hyperreflective dots in patient with AMD before anti-VEGF injections.

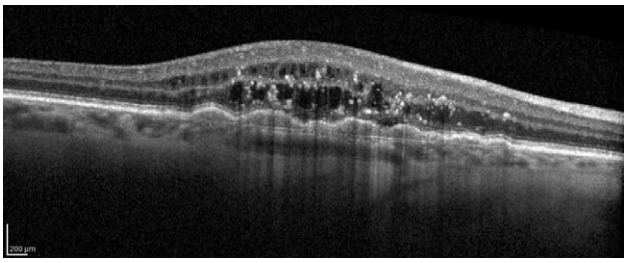
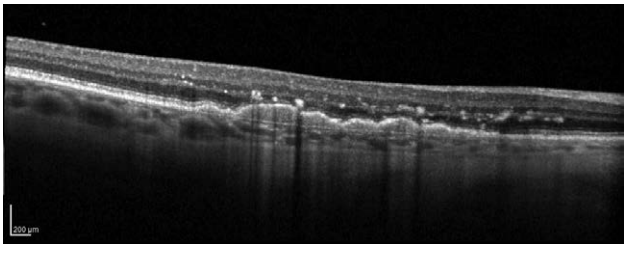


FIGURE 3

OCT scan-B of the same patient after anti-VEGF treatment. It shows reduction of retinal fluid and decreased number of HRDs.



DIABETIC RETINOPATHY

Diabetic retinopathy (DR) is a chronic progressive retinal vascular disease and one of the most common complications of diabetes mellitus. The duration of diabetes is significantly associated with its development and severity. The major cause of the vision loss in individuals of working ages is diabetic macular edema (DME). It is characterized by the swelling of the central retina, which can be detected as increased retinal thickness using OCT [9–11].

The latest studies confirm that HRDs can be observed in DME. They can be organized in a contiguous ring along the inner wall of cystoid spaces on the macular OCT and be named as the pearl necklace sign. This indication may be commonly seen in DME patients who require intravitreal treatment. Ajay et al. mentioned that HRDs can accompany large fluid spaces and be a precursor of hard exudates in majority of cases of DME. They said that the presence of HRDs does not affect VA prognosis or the response to intravitreal treatment (except where it is located under the fovea) [12].

Huang et al. conducted a systemic review concerning the role of HRDs as a predictor of the treatment results in patients with DME. There are several hypotheses of HRDs including precursors of hard exudates, the migration of RPE cells and the activation of microglia cells. A hyperglycemia environment in the retina can stimulate the accumulation of inflammatory mediators which induce the activation of microglia cells and the increase in the appearance of HRD [9–11].

Hwang et al. investigated the association between the number of HRDs on spectral-domain optical coherence tomography (SD-OCT) according to treatment response to intravitreal bevacizumab (IVB) injections or intravitreal dexamethasone implants in eyes with DME. The main finding of this study was that the number of HRDs in bevacizumab non-responders was significantly higher than that in responders. In contrast, the number of total HRDs, inner retinal HRDs, and outer retinal HRDs were significantly higher in dexamethasone responders than the eyes that did not respond to dexamethasone implants [10].

Wong et al. conducted the study to compare the HRDs count of normal and diabetic subjects and to determine the correlation between HbA_{1c} level and HRDs count and to determine the HbA_{1c} cut-off level for the appearance of HRD in diabetic patients. Comparisons indicated that the mean HRDs count for the normal group was significantly different to the diabetic without retinopathy group and the mean number of HRDs for the mild-to-moderate non-responder group was significantly higher than in the diabetic without retinopathy. The study has shown the optimal cut-off point for the appearance of HRDs is the HbA_{1c} level of 5.4%, because it has 89.20% of sensitivity and 96.60% of specificity [11].

In conclusion, increased number of HRDs is correlated with the increase in HbA_{1c} levels and indicates the severity of disease. Future investigations are needed to confirm a role of HRDs as a predictive indicator of treatment response in patients with DME. Results in the treatment of DME are often unsatisfactory and because of that, it is important to develop biomarkers that can help to predict the outcome to get treatment optimization for individual patients [9–11].

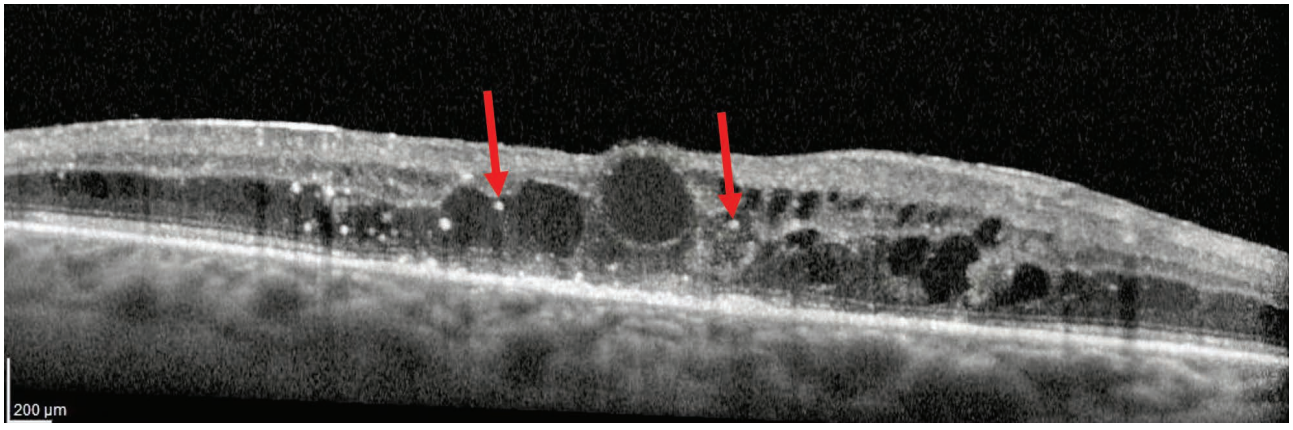
RETINAL VEIN OCCLUSION

Retinal vein occlusion (RVO) is identified as a retinal vascular disorder with engorgement and dilatation of the retinal veins. As a consequence of these changes, we have seen hemorrhages and edema in the retina. Retinal ischemia including cotton wool spots, retinal exudates and macular edema can be also observed in RVO [13]. There are two types of RVO: branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) [14].

That hyperreflective signs can be visible in RVO, as well in other ocular conditions [13, 15–17]. Ogino et al. described the presence of HRDs in all retinal layers [16]. They illustrated that HRDs were attached to the external limiting membrane

FIGURE 4

OCT scan-B of the right eye showing intraretinal fluid in patient with diabetes. The arrows indicate hyperreflective dots.



(ELM) in most of the eyes with serous retinal detachment. Authors also indicated that HRDs in retinal areas might explain the leakage of blood components. Hyperreflective dots on SD--OCT, mainly in the outer layers could suggest inflammatory reaction, and may be a marker of disease activity [17].

In one study SD-OCT delineated hyperreflective foci in 74% (54 eyes) with RVO. The hyperreflective foci attaching on the external limiting membrane (ELM) were observed more frequently in BRVO than in CRVO (53.3% vs. 11.1%). The study says that extravasated blood constituents might diffuse into the vitreous cavity in CRVO and can be indicated instead of the deposition of foci on the ELM [16].

Numerous of studies have shown that the presence of HRDs was associated with final best corrected visual acuity (BCVA) after anti-VEGF treatment [18]. Another study says that presence and number of HRDs could be predictive of visual outcomes after bevacizumab administration for the treatment of macular edema in patients with BRVO. Baseline HRDs in the outer retinal layers on SD-OCT might predict the final photoreceptor status and poor BCVA, although ME improved after treatment in BRVO [19]. Chatziralli et al. also reported that the number of HRDs and its foveal location related to the final BCVA in patients with ME due to BRVO and it could be a potential biomarker of poor final visual outcome [18].

OTHER DISEASES

The current literature offers a few publications about hyperreflective spots visualized in OCT scans in other retinal diseases.

Central serous chorioretinopathy (CSCR) is common retinopathy among young patients, typically males between the ages of 20 and 50 years old. It causes vision loss due to serous retinal detachment in the macular area with the occurrence of subretinal fluid.

Hanumunthadu et al. analyzed association between hyperreflective signs in the choroid and visual acuity and OCT parameters among subjects with CSCR. They included 32 eyes with acute and 29 with chronic CSCR. The results have shown the negative correlation between presence of HRDs and patient's age as well as subfoveal choroidal thickness both in acute and chronic forms of the disease. Moreover, in chronic CSCR hyperreflective signs are associated with macular thickness and height of neurosensory detachment [20].

Focal choroidal excavation (FCE) is an excavation of the choroid and can be recognized with OCT. There are two types of FCE: conforming and non-conforming and its depending on whether there is a separation between the neural retina and the retinal pigment epithelium [21].

Hashimoto et al. documented a patient with HRDs who had FCE. They suggested that the RPE and Bruch's membrane impairment, following chorioretinal inflammation, may play a role in the pathogenesis of FCE and HRDs can be also observed in this ocular condition [22].

Furthermore, HRDs findings were described in other diseases. Fong et al. in their study mentioned small intraretinal hyperreflective dots in 3 eyes with patients diagnosed with Vogt-Koyanagi-Harada disease [23].

CONCLUSIONS

Based on the available published research, hyperreflective dots visualized by optical coherence tomography are a promising biomarker in retinal diseases that may be used as a predictor of treatment outcome and prognosis of the disease. Further studies are needed to confirm this assumption.

Figures: from the author's own materials.

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