MODERN ASPECTS OF MULTIMODALITY APPROACH TO THE DIAGNOSIS OF IDIOPATHIC EPIRETINAL MEMBRANE

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Idiopathic epiretinal membrane (iERM) is the most common abnormality of the vitreoretinal interface. This condition often stays asymptomatic for a long time. At present, the diagnostic "gold standard" for iERM is spectral-domain optical coherence tomography (SDOCT) and biomicroscopy. However, other diagnostic approaches to ocular fundus pathologies have emerged recently, including multispectral imaging in the MultiColor mode used to estimate tissue proliferation, En Face OCT-angiography that can precisely locate retinal lesions, and microperimetry instrumental in assessing retinal sensitivity and the impact of tissue proliferation. In this work we evaluate the effectiveness of the multimodal approach to iERM diagnosis. We examined 46 patients (46 eyes; mean age was 65.3 ± 11.2 years) with different stages of iERM, pseudophakia and incipient cataract. The multimodal approach allowed us to better discriminate between disease stages and to identify 15 patients with stage 0 iERM, 19 patients with stage 1, and 12 — with stage 2. We were also able to generate a map of the vitreoretinal interface for 2 patients with stage 2 iERM that facilitated the choice of treatment and allowed planning a sparing surgical intervention. Based on our clinical experience and study findings, we conclude that the multimodality approach should be promoted in the clinical setting.

Keywords: multimodality imaging, epiretinal membrane, optical coherence tomography, OCTA En Face, microperimetry, MultiColor

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СОВРЕМЕННЫЕ АСПЕКТЫ МУЛЬТИМОДАЛЬНОЙ ДИАГНОСТИКИ ИДИОПАТИЧЕСКОЙ ЭПИРЕТИНАЛЬНОЙ МЕМБРАНЫ

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Идиопатическая эпиретинальная мембрана (иЭРМ) — наиболее распространенная патология витреоретинального интерфейса. Для этой патологии характерно бессимптомное течение на протяжении достаточно длительного времени. «Золотым стандартом» ее диагностики является исследование с помощью спектральной оптической когерентной томографии (СОКТ) и офтальмобиомикроскопия. Однако к настоящему времени разработаны и другие подходы к выявлению патологий глазного дна, обладающие важными достоинствами: мультиспектральное исследование в режиме MultiColor (оценка распространенности пролиферативного процесса), ОКТ-ангиография в режиме En Face (точная локализация повреждений ретинальных слоев), компьютерная микропериметрия (оценка качества зрения и влияния на него пролиферативного процесса). В исследовании оценивалась эффективность мультимодального подхода в диагностике иЭРМ. Обследовали 46 пациентов (46 глаз; средний возраст — 65,3 ± 11,2 года) с иЭРМ различных стадий, артифакией и начальной катарактой. По результатам обследования у 15 пациентов установили иЭРМ стадии 0, у 19 — стадии 1, у 12 — стадии 2. Применение мультимодального подхода позволило точнее дифференцировать стадии заболевания, а в группе пациентов с иЭРМ стадии 2 также в 2 случаях — разработать карту витреоретинального интерфейса для выбора тактики лечения и плана малотравматичного для сетчатки хирургического вмешательства. Основываясь на собственном клиническом опыте и результатах исследования, мы полагаем, что мультимодальный подход перспективен для более широкого распространения в клинической практике офтальмологов.

Ключевые слова: мультимодальная диагностика, эпиретинальная мембрана, оптическая когерентная томография, En Face ОКТА, микропериметрия, MultiColor

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Idiopathic epiretinal membrane (iERM) is a thin translucent fibrocellular tissue in the center of retina that is capable of contraction leading to distortion of retinal interface surface [1]. This pathology progresses slowly: most often, iERM remains anatomically stable for a long time and its symptoms do not manifest themselves [2]. According to Feng et al. [3], in 25.7 % of cases iERM regresses and in 38.8 % of cases it becomes stable. However, other researchers [4, 5] state that 28.6 %

of iERM cases result in progression to the contractile phase, proliferation on the retina surface that may cause complications like macular edema and macular rupture [6].

Back in 1976, Gass developed an ERM classification; later, Klein modified it based on the color pictures of the fundus [7]:

– stage 0: the membrane is translucent, there is no deformation on the surface of the retina (maculopathy);

– stage 1: uneven wrinkling of retina's inner surface (macular cellophane);

– stage 2: dense membrane on the surface of the retina, general shrinkage of the macula throughout its depth, possibly - macular edema, small hemorrhages, a cotton-like exudate (macular pucker).

This classification is still used in epiretinal fibrosis diagnostics.

To reveal fundus pathologies, including iERM, practitioners routinely make use of ophthalmoscopy, B-mode ultrasound imaging and spectral optical coherence tomography (SOCT) [8]. B-mode ultrasound imaging is the most common non-invasive diagnostics technique applied to fundus, with iERM it does not provide sufficient amount of data. The most effective approach is SOCT. It highlights ERM as a hyper-reflective band adjacent and/or soldered to the inner surface of the retina. In some cases, there are point joints between ERM and retina surface [2]. Besides, SOCT reveals foveolar profile, an important diagnostic indicator. At the beginning, the profile is usually unchanged, but as the pathology progresses, it can be deformed (smoothed out) or disappear altogether [9]. Non-invasiveness, painlessness and quickness make this examination method comfortable for the patient, and its simplicity and technical features -- suitable for screening [10]. Nevertheless, the "golden standard" does not draw a complete picture of structural changes happening in the vitreoretinal interface, as well as that of the pathological process dynamics, its spread and localization and concomitant vision disorders.

Confocal scanning systems allow a more detailed analysis of all layers of the retina and vitreoretinal interface. Basics of ophthalmochromoscopy [11] fostered the development of multispectral laser scanning of the retina (MultiColor), which allows estimating the degree of proliferation on the retinal interface surface intra vitam. The method implies adding 3 images using monochromatic filters: blue (BR; 488 nm), green (GR; 515 nm) and infrared (IR; 820 nm). With MultiColor, surface of the examined membrane and folds thereon appear yellow-green, the intensity of the color depends on elevation of ERM relative to the retina. Blue and green filters allow getting a detailed view of the retina's inner surface and vitreoretinal interface. Combined, they allow finding boundaries of the membrane, folded area and traction component, if any [12]. Multispectral examination is a good complement to SOCT. To increase the effectiveness of screening, these methods can be applied together [9].

Another promising technology is OCT-angiography (OCTA) [13], which allows assessing the state of retinal vasculature and frontal surface of vitreomacular interface (En Face mode) without intravenous administration of contrast agents [14]. The En Face mode of OCTA ensures precise localization of damages in certain retinal layers based on their axial location on SOCT cross-sectional scans and allows converting OCT images to other models of fundus visualization while retinal vessels serve as reference points [13].

Technical capabilities of the new methods enabled improvement of Gass classification for the En Face mode [9]:

– stage 0: foveolar profile remains unchanged on the cross-sectional OCT scan; central retinal thickness is normal; En Face mode reveals single diffuse foci of fibrosis on the retina's surface.

– stage 1: cross-sectional OCT scan shows increased central retinal thickness; the foveolar profile changes insignificantly; En Face mode reveals a "patch" with a small number of radial folds.

– stage 2: cross-sectional OCT scan shows increased central retinal thickness; the foveolar profile disappears; En Face mode reveals a solid "patch" with radial folds.

When examining a vitreoretinal interface with En Face OCTA, practitioners should pay particular attention to changes in the posterior hyaloid membrane (PHM) and ERM as the relate to the pathological process development. When focused on PHM, the retina's surface appears "cloudy" or "foggy". In cases of detachment of PHM or ERM, local separated parts appear as "retinal windows", which is a diagnostic indicator the surgeon should take into account when removing an ERM. Sometimes, the inner limiting membrane ruptures in places; then, En Face imaging reveals naked zones of the retinal nerve layer visualized as "craters" [9].

Best corrected visual acuity (BCVA) may not provide the data quality needed to correctly evaluate vision disorders related to various fundus pathologies. If that is the case, there is an alternative, computer-assisted microperimetry, a noninvasive method that allows estimating light sensitivity of the macular area and localization and stability of the point of gaze [15].

The analysis of pros and cons of the existing iERM diagnosis methods tells that getting a complete picture of morphofunctional changes associated with this pathology takes a multimodal approach. This study aimed to evaluate such a multimodal approach that includes ophthalmoscopy, multispectral examination, microperimetry, SOCT and En Face OCTA as they are applied in combination to diagnose stages of iERM.

METHODS

46 patients (46 eyes) took part in the study; they had iERM at varying stages. The inclusion criteria were pseudophakia and early cataract. The average age of participants was 65.3 ± 11.2 years (18 women and 27 men). The exclusion criteria were: mature cataract, glaucoma, diabetic retinopathy, fundus dystrophy regardless of its genesis, occlusion of retinal vessels, registered eye trauma, chronic and acute inflammatory eyeball diseases.

The standard ophthalmologic examination was complemented with SOCT, multispectral examination (MultiColor mode, various filters), microperimetry and En Face OCTA. The following instrumentation and devices were used: Spectralis HRA-OST, Spectralis OCT-2 module, frequency of 85,000 Hz with TruTrack Active Eye Tracking (Heidelberg Engineering, Germany); MAIA version 2.4.0 (CenterVue, Italy). SSDA algorithm was applied to OCTA (Angio Retina mode). The scanning was performed in the macular zone, gaze fixed centrally, size of the macular cube — 10 × 10°, number of scans — 512, distance of 6 μm (Macular Map mode). If the patient's gaze wandered, scanning was repeated until the images obtained were free from artifacts caused by eye movement.

SOCT data allowed evaluation of the degree of structural disturbances in vitreoretinal interface, overall central retinal thickness and foveolar profile. En Face OCTA images were used to assess frontal profile of the vitreoretinal interface, including internal limiting membrane and ERM within the macular zone.

Microperimetry allowed assessing photosensitivity of retina's central zone. The examination was performed in the

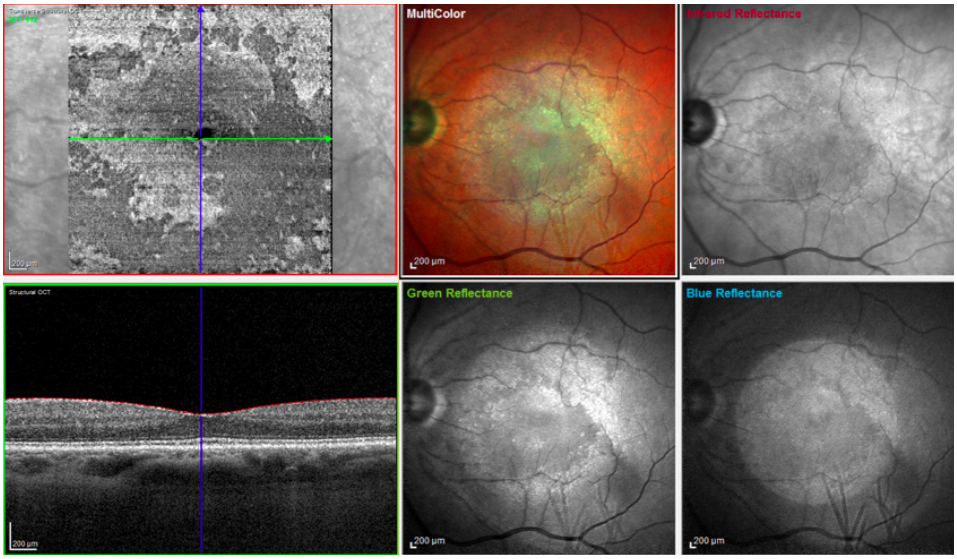

Fig. 1. Example of multimodal diagnostics results, iERM, stage 0. Membrane area and boundaries are almost invisible, no wrinkles/folds on the retina, no traction component, sporadical diffuse fibrosis foci

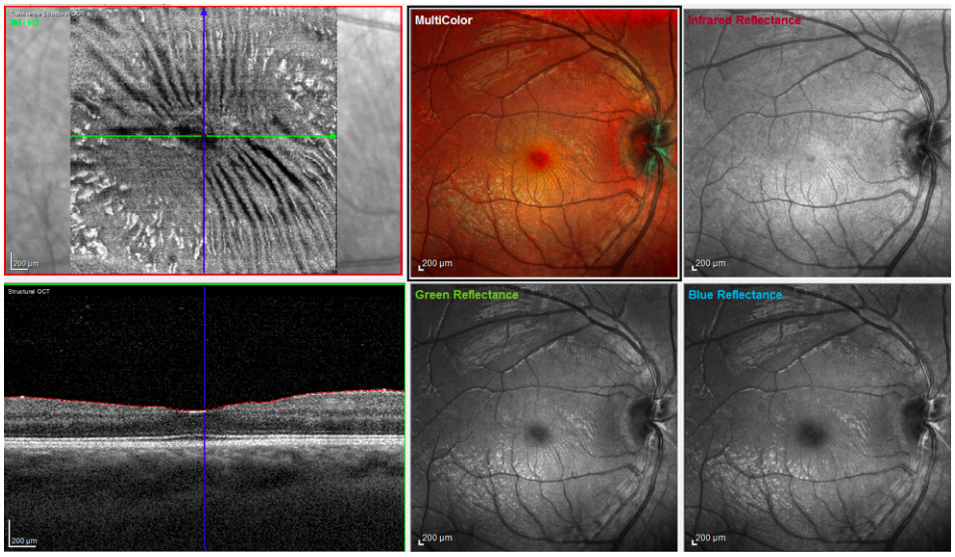

Fig. 2. Example of multimodal diagnostics results, iERM, stage 1. Membrane area and boundaries are well defined, sporadical wrinkles/folds on the retina, unpronounced traction, visible star patterns on the retina and patches

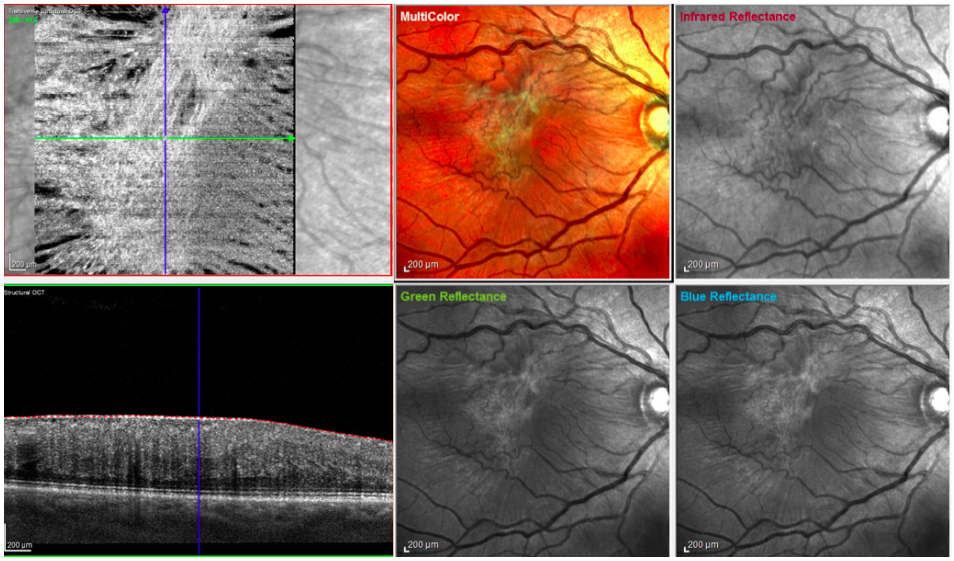

Fig. 3. Example of multimodal diagnostics results, iERM, stage 2. Membrane area and boundaries are clear, pronounced wrinkles/folds on the retina, pronounced traction, increased retinal thickness

macular zone, gaze fixed centrally, Expert exam mode [method 4–2], 10° grid (37 points). The results of the examination were superimposed on a picture of fundus shot with a built-in fundus camera. In case the patient registered more than 30 % of dots in the area of the blind spot, the test was deemed unreliable and was repeated to obtain reliable data.

RESULTS

Based on the results of the multimodal examination, the Gass classification and its modified version, we divided the patients into 3 groups: 15 patients (15 eyes) in the first group, all with initial manifestations of epiretinal fibrosis (stage 0); 19 patients (19 eyes) in the second group, with changes to vitreomacular interface more pronounced (stage 1); 12 patients (12 eyes) to the third group, with marked changes in the macular zone (stage 2).

Multispectral (MultiColor) examination of the first group showed weak yellow-green foci from ERM surface, localized in the center zone; the membrane's total area and boundaries could not be differentiated, there were no folds nor traction (Fig. 1). SOCT showed no changes to the foveolar profile, and the central retinal thickness was normal (average of 276.8 ± 24.4 nm). En Face images revealed single diffuse foci of fibrosis on the surface of retina of all patients. The average photosensitivity of retina in the macular zone was 26.2 ± 1.4 dB.

Multispectral (MultiColor) examination of the second group showed pronounced yellow-green reflection from ERM surface, localized in the center and helping to see the membrane's total area and boundaries; there also were some folds and weak traction (Fig. 2). SOCT showed minor changes to the foveolar profile (smoothening) and increased retinal thickness to the average of 303.1 ± 42.2 nm. En Face OCTA visualized "retinal stellata" and "patches" with individual radial folds in all patients. The average photosensitivity of retina in the macular zone was 25.1 ± 2.4 dB.

Multispectral (MultiColor) examination of the third group showed clearly pronounced yellow-green reflection, ERM area and boundaries clearly visible; traction was well-expressed and folds diffused (Fig. 3). COCT revealed gross structural changes to the retina, lack of foveolar profile, increase of the central retinal thickness to the average of 427.0 ± 85.4 nm. En Face images showed diffuse retinal folds in the central zone, all patients. The average photosensitivity of retina in the macular zone was 22.2 ± 2.2 dB. In 2 cases out of 12, a partial ERM detachment was observed: En Face OCTA showed "retinal windows". Thus, we were able to draw up the vitreoretinal interface topography scheme while taking into account the zones where ERM was farthest from the retina. Further on, we developed a map of vitreoretinal interface that allowed planning treatment and surgical removal of ERM with minimal trauma to the retina.

DISCUSSION

For many years, the "golden standard" in diagnosing epiretinal fibrosis was ophthalmoscopy and SOCT. However, new, non-invasive confocal microscopy diagnostic methods gave ophthalmologists more details on the development of proliferation at various stages of the disease.

Multispectral examination in combination with SOCT and En Face OCT allows diagnosing and assessing changes to iERM at different stages. What is more, the data describe not just cross sections but entire areas of the membrane. En Face OCT provides a deeper insight into the morphofunctional changes in the vitreoretinal interface. This method is not a routine one yet, but it can find wide use in diagnosing fundus pathologies.

The type and extent of symptoms a patient develops largely depend on the thickness of the pathological membrane, on retina deformation it causes, on its location and the presence/absence of macular edema or macular rupture. In the absence of complications, visual acuity can remain at a sufficiently high level, therefore BCVA does not allow correct assessment of proliferation dynamics. Here, microperimetry can help, since this method ensures control over the threshold of central retina photosensitivity and localization and stability of the point of gaze.

Combination of the "golden standard" and new, non-invasive diagnostic technology is a promising approach to uncovering iERM, drafting treatment tactics and observing dynamics.

CONCLUSIONS

Based on our own practical experience and the data obtained through the study, we can state that each of the diagnostic methods used separately does not yield a complete picture of morphofunctional changes peculiar to epiretinal fibrosis. Multimodal approach opens new opportunities before for the practitioner and provides more detailed data on the structure of vitreoretinal interface in iERM at various stages of its development; allows assessing dynamics of pathology not only by cross-sectional spectral OCT scans but also by area imaging enabled by MultiColor or En Face OCTA methods; helps determining the effect proliferation produces on the quality of vision using the microperimetry data. Such information allows better planning of treatment tactics, including scope and nature of surgical intervention.

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