



Clinical manifestations and classification of lesions of the macular area in diabetes.

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ABSTRACT

To date, modern ophthalmology has not developed a single standard in approaches to the classification of DME. It is generally accepted that diabetic macular edema, as one of the manifestations of DR, can develop as ischemia and/or macular retinal edema. In DME, retinal edema always develops a second time, due to impaired capillary permeability in the macular area (lesion of the internal hemato-retinal barrier), followed by secondary damage to the retinal pigment epithelium (internal RRP) [199]. Damage to the inner and outer barriers leads to the accumulation of fluid in the macula. The consequence of these disorders is the appearance of complaints of patients about blurred central vision, the occurrence of metamorphopsia is less typical. Patients may complain about the appearance of a pinkish tint in the image, increased sensitivity to light, and there may be a cyclic decrease in visual acuity at certain times of the day (more often in the morning) [52, 87, 204, 216].

Keywords:

It should be especially noted that the severity of morphological changes in the retina does not always correlate with the depth of visual function decline.

In this regard, the issue of classification of lesions of the macular region in diabetes mellitus seems to be relevant. The American Academy of Ophthalmology has proposed a four-level clinical classification of diabetic maculopathy (Table 1) [2].

This classification has not found wide clinical application, since it is reduced to ascertaining the presence of thickening (edema) of the retina and hard exudates, as well as the removal of these signs from the center of the macular region. Meanwhile, the predominantly focal type of DME responds well to laser treatment and has a good

prognosis for vision at the initial stages of the disease, while the diffuse nature of retinal edema responds poorly to laser coagulation and usually requires repeated intravitreal administration of glucocorticoids or angiogenesis inhibitors.

Improving knowledge about the pathogenesis of the disease, introducing new research methods into clinical practice, inevitably affects the principles and approaches to classification. Their development is characterized by the desire of the authors to link the clinical manifestations of the disease with its pathogenesis and prognosis in order to preserve the patient's visual functions

after treatment. One example of such an approach is Yu.A. Ivanishko's classification developed in the interests of laser surgery. (2001), which suggests the allocation of the following forms of DME: 1 - "dry"; 2 - transudative; 3- cystic; 4 - hemorrhagic; 5 - macular proliferation; 6 - macular hole; 7 - ectopic fovea; 8 - ischemic (subatrophy of the fovea) [26].

Initial DME involving the center of the macula is usually accompanied by the disappearance or deformation of the foveolar reflex. Visual acuity usually does not change, which explains the frequent absence of visual complaints in patients. With more pronounced edema, patients note the instability of vision, which fluctuates during the day within 1-2 lines or more. In the case of long-term existence of DME, a violation of normal metabolism and ischemia of the retina lead to an increase in its degenerative changes. Clinically, this is manifested by cyst formation in the edematous retina and a more pronounced visual impairment, up to 0.1-0.2 due to the fusion of cysts in the center of the macula [142]. Subsequent degenerative changes in the retina usually lead to a decrease in visual acuity to 0.04-0.07, less often to small hundredths [57].

Along with cyst formation, long-term DME is characterized by the appearance and slow progression of atrophic changes in PE, which continues after the complete disappearance of retinal edema, regardless of laser treatment. Sometimes this process is accompanied by the development of focal PE hyperplasia [169]. On fluorescein angiography, small areas of flat retinal edema in the arterial phase are not visible. In case of severe edema or retinal detachment, chorioidea luminescence may be blurred (relative block of choroidal luminescence). In the late phases of FAG, dye accumulation (moderate to pronounced, depending on the intensity of transudation) is noted in the retinal edema areas. In the presence of large cysts in the retina, accumulation of dye in the form of a "flower" is observed [20].

The most convenient and widely used in clinical diagnosis and subsequent treatment is the classification of DME according to its location in the macula [136]. According to this classification, there are focal and diffuse macular edema:

1) focal macular edema arises from decompensated microaneurysms or microvascular anomalies [69]. Its long-term existence is characterized by the deposition of solid exudates within the edema zone, in the case of the dominant retinal edema - in the form of a ring (circinates). Clusters of microaneurysms and large hemorrhages within the edematous retina indicate severe retinal hypoxia. Focal DME may be local or multifocal. On biomicroscopy, a ring-shaped reflex is usually well distinguished around the area of focal retinal edema. When examining with a slit, local thickening of the light section of the edematous retina is noted. Patients with focal edema complain of blurred vision, image distortion, difficulty in reading due to loss of certain letters. If the fovea is not affected, there are no visual complaints and these patients are detected incidentally during a preventive examination. In the focal type of DME, visual acuity ranges from 0.1 to 1.0 and is usually characterized by its high values [56]. According to the authors, in 63% of patients it is within 0.4-0.7, and if the fovea area is not affected, it is 1.0 in 10% of cases [85];

diffuse macular edema is a more severe variant of hematoretinal barrier disorder with diffuse fluid seepage from the capillary bed. In this form of DM, visual acuity can be high at the first signs of retinal edema and decrease to 0.01 with its prolonged existence. According to some data, in 70% of patients with this form it usually ranges from 0.1-0.3 [15, 111]. Biomicroscopy reveals an extensive zone of retinal thickening, without clear boundaries and often extending to the vascular arcades. In the diffuse type of DME, cystic changes in the macular area are quite often detected [64];

The mixed type of DME is manifested by a combination of the diffuse component of retinal edema with the presence of solid exudates,

which can form massive TE deposits in the center of the macula or a ring of circinates around a long-standing area of retinal edema; The ischemic type of DME is characterized by a predominance of focal retinal nonperfusion. With extensive retinal nonperfusion in the posterior pole and in the macula, there may be no retinal edema. Such cases are more accurately defined terminologically as an ischemic type of diabetic maculopathy rather than diabetic macular edema.

Clinically significant macular edema is the initial stage of DME for which laser treatment is indicated. According to the ETDRS, this stage is defined as the presence or combination of the following signs [84]:

Retinal thickening within 500 μm in the center of the macula;

The presence of solid exudates in the center or at a distance of 500 μm from the center of the macula, combined with thickening of the adjacent part of the retina;

presence of retinal thickening with a diameter greater than d.m.s., within 1 d.m.s.

from the anatomical center of the macula.

The concept of "CMR" has found wide application in ophthalmological practice to determine the indications for the initiation of laser treatment [75], but does not reflect the severity and does not allow predicting the results of laser interventions in more severe manifestations of DME. In 2004, Ismailov A.S. and Balashevich L.I. published a new classification of DME based on the 3-year prognosis for the patients' vision after laser treatment (Table 2) [10, 28].

This classification is based only on those clinical features that affect the prognosis for preserving a patient's ability to read. In addition, in creating this classification, the authors took into account the experience of

The results of the effectiveness of treatment of patients with different forms of DME, which makes it possible to predict the success of laser intervention.

To define the initial stage of DME (DMO-1), we used the ETDRS concept of CMD [104] as the generally accepted standard of indications for laser photocoagulation. However, focal macular edema with preserved high visual function of the patient (Vis0.5) was implied. The initial form of DME lends itself well to laser treatment, which provides long-term preservation of the patient's ability to read.

Moderate diabetic maculopathy (DME-2) was defined by the authors as focal macular edema, but with significantly greater visual impairment (Vis<0.5). Moderate DME, according to the authors of the classification, also lends itself well to laser photocoagulation, in most cases it is possible to achieve DME regression, which has a favorable effect on the patient's central visual prospects. However, the prognosis for reading is more often poor.

Diffuse and mixed types, as well as the focal type of retinal edema with neuroepithelial detachment or deposition of solid exudates in the center of the macula are classified as severe DME (DME-3), since they are characterized by a poor prognosis for reading and anatomical results of laser coagulation.

To date, optical coherence tomography (OCT) is considered the most informative method for interpreting DME severity and choosing treatment tactics of a patient, which enables to accurately assess changes in its structure and retinal edema dynamics [118]. The experience of using and interpreting OCT data allowed revealing a number of important regularities in the development of different variants of DME [60]. It is shown that edema can be symmetric or involve only one of the macular sectors. It usually begins as a focal lesion and often progresses to a diffuse form. In a number of cases there is thickening of the paramacular while the center of the foveola remains normal. Prolonged retinal edema leading to Müller cell necrosis is accompanied by the formation of cystic cavities located mainly in the outer part of the retina (Henle fibers and outer retinal layer), and sometimes in the inner retinal layer. In the

late stages of macular edema several centrally located cysts are detected, which merge with each other, forming large hyporeflexive cavities, leading to significant thickening of the macula [154].

The first OCT classification of DME was presented by Otani T. et al. (1999) on the basis of morphological changes in the retina and included: spongy edema, cystic edema and serous retinal detachment [177]. The accumulation of practical OCT experience led to the formation of a complex classification of DME. The most interesting and comprehensive in this respect is the classification proposed by Koleva-Georgieva D. (2009), which is based on the author's own experience and previously published data [139]. This classification takes into account quantitative and qualitative assessment parameters in OCT, including retinal thickness, its morphology, retinal topography, macular traction, the state of macular photoreceptor cells:

Changes in retinal thickness:

No macular edema - normal macular morphology, its thickness does not reach the level of subclinical DMO.

Early subclinical macular edema - no clinically detectable retinal thickening on ophthalmoscopy, with OCT assessment of retinal thickness demonstrating an excess of normal.

Expressed macular edema - retinal thickening and morphological signs of edema.

Morphology of retina:

Simple non-cystic macular edema - increased retinal thickness, decreased intraretinal reflectivity, irregular layer structure, flattening of the central fossa in the absence of cystic structures (spaces).

Cystic macular edema - the above criteria are associated with the presence of well-defined cystic spaces:

a) mild cystic edema - cystic space with a horizontal diameter of $<300\ \mu\text{m}$;

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b) moderate cystic macular edema - cystic space with a horizontal diameter of 300-600 microns;

c) severe cystic macular edema - cystic space with a horizontal diameter of $\geq 600\ \mu\text{m}$, or the presence of large confluent cavities with the appearance of retinoschisis.

Serous retinal detachment - in the presence of any of the above signs, in combination with retinal detachment

(hyporeflex fields under the exfoliated neurosensory retina or above the hyperreflective PE line).

Topography of changes in the retina:

Unexpressed macular edema.

KZMO according to the ETDRS criteria and the results of the evaluation according to the OCT map.

Presence and severity of macula traction - incomplete vitreoretinal junction and/or epiretinal membrane:

Absence of signs of macula traction - the presence of a complete connection of the retina with the vitreous body (with ophthalmoscopy, the Weiss ring is determined), the absence of an epiretinal membrane [139].

Macular traction in question - incomplete vitreoretinal connection with perifoveolar or peripapillary adhesion of the epiretinal membrane without visible deviations and distortions of the reticular contour at the points of adhesion.

Pronounced macular traction - incomplete vitreoretinal connection with perifoveolar adhesion or focal epiretinal membrane with visible distortion of the reticular contour at the points of adhesion.

The integrity of the layers of the retina (by the state of the border between the inner and outer segments of photoreceptor cells, corresponding to the position of the outer boundary membrane):

The border between the outer and inner segments of photoreceptor cells and the outer limiting membrane are intact.

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Violation of the integrity of the outer limiting membrane and segments of photoreceptor cells.

The proposed classification not only facilitates the verification and determination of the severity of macular edema, but also takes into account the nature of the vitreoretinal junction even in the absence of clinical signs, and also optimizes the choice of tactics for treating patients with DME [115].

In 2009 Gatsu M.V. and Balashevich L.I. a new clinical classification of diabetic maculopathies has been proposed. With its help, maculopathies are divided into "wet" (edematous), "dry" and mixed forms [17]. "Wet" forms are divided into "edema with and without traction." Edema without traction is recommended to be subdivided into "flat" (thickening of the macula center on average up to $220 \pm 28 \mu\text{m}$ and an increase in volume up to $8.0 \pm 0.8 \text{ mm}^3$) and "high" (thickening of the macula center on average up to $383 \pm 103 \mu\text{m}$ and volume values of 6 mm zone up to $9.3 \pm 1.5 \text{ mm}^3$).

Each classification of DME has certain advantages, however, there is still no generally accepted classification of retinal changes in the macula in diabetes, suitable for use in specialized ophthalmological centers with modern laser equipment and vitreoretinal surgical technologies.

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