Effectiveness of Integrated Treatment Strategy for Diabetic Retinopathy in Patients with Diabetes Mellitus: A Case Report

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Abstract

Vascular pathologies are considered as severe complications of diabetes mellitus, which occur very frequently in patients. Namely, diabetic retinopathy, being one clinical form of diabetic angiopathy, may lead to distressing socioeconomic burden like decreasing visual acuity and blindness. In the literature, many treatment method have been described and used in many centres.

We present a case of 60-year-old diabetes sufferer, who underwent combined treatment strategy including panretinal laser coagulation, enzyme therapy, vitreoretinal surgery and intravitreal administration of an inhibitor of angiogenesis, which was highly effective in terms of restoring visual acuity with minimal periprocedural complications.

Keywords: *Diabetes mellitus, diabetic retinopathy, panretinal laser coagulation, vitreoretinal surgery, intravitreal administration of inhibitor of angiogenesis.*

Introduction

Diabetes mellitus is associated with vascular complications very frequently, which clinically presents with micro- and macrocircular disturbances. The basis of these disorders are hyperglycemia, metabolic disorders and insulin resistance due to the insulin deficiency and/or dysfunctions of its working mechanisms (Gurieva et al, 2019)[1].

Diabetic retinopathy (DR) is considered to be the fifth leading cause of visual impairment worldwide, and is a huge social and economic burden to the healthcare system[2]. Taking in account the escalating prevalence of DR in the world, WHO identified a variety of approaches to screening for the blindness prophylaxis, early diagnosis and treatment of the population in different conditions[4].

In the treatment of DR and diabetic maculopathy (DM), laser coagulation of the retina is remaining as the gold standard of the therapy due to its accessibility and long-lasting propitious effects after the treatment.[5]

Today, there are three main strategies in the treatment of patients with proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME): pharmacological (compensation of glycemia, control of blood pressure, metabolism correction)[6], laser and surgical (intravitreal administration (IVA) of anti-VEGF medicines and vitrectomy) (Fayzrakhmanov et al, 2017; Bhat et al, 2017; Figueira et al, 2018; Rong et al 2017)[7]. The combination of these treatment strategies often provides a more pronounced positive effect (Mitchell et al, 2011 and Nguyen et al, 2012)[8].

According to some researchers, anti-VEGF drugs are an important addition to the arsenal of treatment for PDR (Zhao et al, 2018)[9]. Efficiency and safety of local anti-VEGF therapy in DME was proved by a largeinternational multicenter studies undertaken in accordance with all rules of evidence based medicine (EBM) (Cheung et al, 2014 and Do et al, 2016)[10].

The complexity of the treatment of the PDR, in many cases, is defined by the absence of a unique opinion on the pathogenetic mechanisms of development of pathological processes in the posterior part of the eyeball, although for this issue is devoted a large number of studies (Yuldasheva, 2014).[11]

The purpose of the studywas to present a clinical case, demonstrating the efficiency of complex treatment of PDR and DME in a patient with second type diabetes mellitus.

Case Presentation: Patient S., was born in 1959, suffering from second type diabetes mellitus during 18 years. He admitted to the Clinical Ophthalmic Hospital of the Ministry of Health of the Republic of Uzbekistan in January 2015 with complaints of decreased vision, fog in front of both eyes. Vis OD = 0.04 sph - 3.0 D = 0.6-0.7. Vis OS = 0.05 sph - 4.0 D = Vis 0.8. The intraocular pressure of both eyes was normal. The front section is not changed. Local opacities of the lens. There are separate floating opacities, which is not fixed to the retina in the vitreous body.

In the fundus of eye: fibrovascular tissue along the temporal vascular arcades, neovascularization of the optic disc, cystic macular edema (up to 480 μm in height in the right eye, 420 μm in the left one). The level of glycemia ranges from 6.8 to 8.9 mmol/L. Microalbuminuria up to 0.086 g/l. Blood pressure was 130/80 mm.Hg. Diagnosis: Proliferative diabetic retinopathy, cystic macular edema, complicated with catarrh bilateral cataract. Second type diabetes mellitus, severe course, subcompensated stage.

In February 2015, to patient was performed panretinal laser photocoagulation in full volume (OD - 2350 coagulates, OS - 1693 coagulates). All stages of laser interventions went without complications. Visual acuity with correction OD - 0.2, OS - 0.7. On the left eye,we could manage to stabilize the pathologic process. In November of 2015, the patient admitted to our clinic with the presence of hemophthalmus in OD and a decrease in vision up to 0.06. Considering the freshness of the pathological process, the patient underwent resorption therapy with 0.5 ml Gemaza enzyme in combination with a solution of dexamethasone 0.5 in the same syringe. 5 parabulbar injection were performed. Wobenzym tablets were administrated orally (3 tablets three times per day), as systemic enzyme therapy. This drug is proved as absorbable agent in hemophthalmia. In the dynamics of observation, visual acuity improved to 0.2 with correction and it became possible to examine the eye fundus, where the growth of fibroglial tissue on the retina was observed ophthalmoscopically. At the control examination after 1 month in the right eye, the growth of the phenomenon of cystic macular edema and proliferation intensified with the development of traction retinal detachment. According to the results of OCT, the height of detachment of neuroepithelium in the macula increased to 759 microns on the right eye, epiretinal fibrosis proceeded in the central region. In February of 2016, patient was admitting with recurrent hemophthalmus and tractional retinaldetachment detected on the “B” scan, which were an indication for two-step vitreoretinal surgery on the right eye. The patient performed a subtotal vitrectomy 25 G with a temporary tamponade vitreal cavity perfluoroorganic compound substituting the silicon oil, removing epiretinal fibrosis and endolasercoagulation. During the postoperative period arterial hypertension was observed in the patient up to 180/100 mm Hg, which was cut off with medicines. Arterial blood pressure was steadily normalized by the use of ACE inhibitors at the level of 110/70 - 130/80 mm Hg. The glycemic range was between 5.7 and 7.2 mmol/L. Proteinuria up to 0.072 g/l. At the end of the surgical treatment, Vis OD = 0.1 n/corr. Vis OS = 0.05 sph - 4.0 D = 0.6. We detected a partial regression in fibrovascular proliferation. Three months later, on the right eye silicone oil was replaced with saline.

However, in May 2016, relapsed partial gemoftalms in the right eye first, and from July 2016 - in the left eye as well with decreased visual acuity to hand movement of a person, and 0.1, respectively. In the “B” scan,opacification was noted with the presence of cell suspension in the eye vitreous haze. Taking in account the previous experience that conservative therapy may not be effective due to the larger volume of hemorrhage in the vitreous body and the presence of neovascularization of disc of optic nerve, it was decided to intravitreal administration of an inhibitor of angiogenesis (IVAIA). From May to November 2016, patient had 4 injections of IVAIA on avitreal right eye, then from July to December 2016 4 injections were performed in the left eye. Injections were performed in the operating room under local anesthesia through the flat part of the ciliary body 27 G needle through tunnel access with dose of 1.25 mg. Postoperative examinations were carried out on the next day and after 7 days. During and after intravitreal injection of IVAIA we did not note any ophthalmic and somatic complications. During the treatment, active resorption of hemophthalmus, regression and obliteration of neovascularization, especially on the optic disc and in the vascular arcades, a decrease in fibrovascular proliferation, and a decrease in neuroepithelial edema in the macula were observed. As of March 2017, Vis OD = 0.1 sph - 3.5 D=0.3-0.4. Vis OS=0.08 sph - 3.75 D=0.5-0.6. Thickness of neuroepitheliumaccording to OCT OD

- 360 microns on OS - 257 microns. In October 2017, during the next subsequent examination noted the rapid progression of cataract in the right eye. Therefore, to the patient was performed facoemulsification of complicated cataract with IOL of Acrysof implantation on the right eye. The operation went without any complications. As of February 21, 2018. Vis OD = 0.3 sph - 1.5 D = 0.4-0.5. Vis OS = 0.1 sph - 4.5 D = 0.7-0.8. Objectively: OD - IOL in a capsule bag. In the lower parts of the vitreous cavity, fibrotic changes. Fundus of the eye: all parts of the retina adjoined, no fresh bleedings. Remains of glial tissue on the optic nerve disc and preretinal fibrosis in the lower segments are detected. Dystrophic changes in the macula, focal atrophy of the pigment epithelium. The thickness of the neuroepithelium on the OCT is 255 microns. OS - initial clouding of the lens. In ophthalmoscopy: optic disc is pale pink, borders are clear. In the course of the temporal vascular arcade, fibrovascular proliferation was reduced, there were no fresh hemorrhages. Architectonics of central part of macula is saved. The thickness of the neuroepithelium is 247 microns. The patient was under observation of an ophthalmologist at the place of residence, follow-up examinations are every three months, with the additional anti-angiogenic therapy if needed.

Discussion

In our opinion, this case report is very interesting for several reasons. During the entire period of observation, we used all method of treatment, ranging from conservative therapy with enzymes and hormones, further laser-coagulation of retina, vitrectomy with silicone oil tamponade, followed by its removal and intravitreal administration of an inhibitor of angiogenesis.

According to the standards of treatment of diabetic retinopathy, with complicated hemorrhagic changes, conservative enzyme therapy was proved and is effective in early treatment of the patient with partial hemophthalmia with relative visualization eye fundus.

The rest of the treatment method we used affect the level of VEGF-factor in the eye cavity: panretinal laser coagulation by blocking the production of neovascular factor in zones of poor perfusion, subtotal vitrectomy - by mechanically removed the VEGF from the cavity vitreous body, the introduction of an angiogenesis inhibitor by binding its molecules to a specific antigen. However, combined use of several anti-VEGF techniques demonstrates high efficacy in cases of advanced PDR.

In this clinical case, our IVA anti- VEGF technique once in every first 6 weeks (1 time in 1.5 months) 4 times, and then 1 time in 2-3 months for 2 years was enough effective. Intravitreal administering of VEGF inhibitors in standard dosage, not only inhibit the progression of neovascularization, epiretinal gliosis and cystoid macular edema development, but also ensured the preservation of the productive central vision. Our studies prove that stopping the processes of proliferation and neovascularization on timely prolonged, massive intravitreal administration of angiogenesis inhibitors is fully proved. Taking into account that with increasing duration of diabetes mellitus, pathophysiological processes in the retina cannot be improved independently, refractory edema of the macular zone does not spontaneously resolved, especially patients with the background of increasing arterial blood pressure are not guaranteed from relapse of hemophthalmus. So, we recommend to conduct IVAIA throughout the whole life for patients with indications.

Our 5-year observation period for patients with PDR who received intravitreal angiogenesis inhibitors showed that most of them managed to achieve improved functional results during the entire observation period and with a minimum number of IA injections after 3 years. During the observation period, no systemic adverse events were observed in the patient. Exceptions group consisted of patients who had undergone acute cerebrovascular accident or myocardial infaction during the last 6 months.

In the literature the potential risk of systemic side effects of intravitreal administration of VEGF-factor inhibitors are clearly described, namely - arterial hypertension, proteinuria, gastrointestinal bleeding, impaired wound healing process, which is particularly unfavorable in diabetic patients.

Conclusion

The case study shows that combined use of several anti-VEGF techniques guaranteesthe effectiveness of treatment for advanced proliferative diabetic retinopathy, complicated with DME and recurrent hemophthalmus. In planning vitrectomy after applying the anti- VEGF drugs, it is reachable to decrease fibrovascular tissue hemorrhages, therefore there is less intraoperative bleedingand, in many cases, it is fully avoidable this kind of complications.

Patient Consent: Written informed consent was obtained from the patientfor publication of this case report and any accompanying information related to this study. A copy of the written consent is available for review by the authors of the paper.

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