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Specific Clinical Manifestations of Proliferative Diabetic Retinopathy in Young Patients and Assessment of Technical Challenges of Endovitreal Surgery and its Outcomes

Yan B. Lebedev[1], Oleg V. Kolenko [1,2,3], Alexander Yu. Khudyakov[1], Evgenii L. Sorokin[1,3]

[1] The S. Fyodorov Eye Microsurgery Federal State Institution, the Khabarovsk branch, Khabarovsk, Russia;

[2] Postgraduate Institute for Public Health Workers, Khabarovsk, Russia;

[3] Far-Eastern State Medical University, Khabarovsk, Russia

ABSTRACT

BACKGROUND: The number of young patients with type 1 diabetes mellitus is steadily increasing in all countries of the world. Technical features of performing vitrectomy for proliferative diabetic retinopathy in patients with type 1 diabetes mellitus have not been sufficiently studied. The need for their study is very urgent, since the number of such patients is constantly increasing, the information obtained will help to avoid intra- and postoperative complications that may arise during vitrectomy.

AIM: The work aimed to study the morphological and functional features of proliferative diabetic retinopathy in young patients with type 1 diabetes mellitus and to assess the technical challenges of endovitreal surgery and its outcomes.

METHODS: The study included unselected young patients with proliferative diabetic retinopathy and type 1 diabetes mellitus who were indicated for vitreoretinal surgery. A total of 32 patients (55 eyes) aged 18 to 46 years were selected; best corrected visual acuity with light projection was up to 0.3. A three-port pars plana endovitreal procedure was performed in all patients.

RESULTS: A total of 48 eyes had dense fused posterior hyaloid and internal limiting membranes and affected vessel hemorrhages tending toward re-occur when they were separated. Flat fusions of the preretinal membranes, retinal vessels, and retina were observed in 25 eyes. These characteristics prolonged endovitreal surgery. All procedures were completed with silicone oil tamponade. On day 1, 40 eyes had small preretinal hemorrhages at the posterior pole. Large preretinal hemorrhages developed in 15 eyes. One month after silicone oil removal, best corrected visual acuity in 36 eyes increased to 0.2–0.8.

CONCLUSION: Significant technical challenges of vitrectomy were noted in all patients and were caused by a severe damage to the vitreomacular interface. One month after silicone oil removal, proliferative diabetic retinopathy was stabilized in 96% of the eyes.

Keywords: proliferative diabetic retinopathy in young patients; endovitreal surgery; technical challenges; complications.

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Особенности клинических проявлений пролиферативных стадий диабетической ретинопатии у молодых пациентов, оценка технических трудностей выполнения эндовитреальной хирургии и её исходов

Я.Б. Лебедев[1], О.В. Коленко[1,2,3], А.Ю. Худяков[1], Е.Л. Сорокин[1,3]

[1] Хабаровский филиал Национального медицинского исследовательского центра «Межотраслевой научно-технический комплекс «Микрохирургия глаза» им. акад. С.Н. Фёдорова», Хабаровск, Россия;
[2] Институт повышения квалификации специалистов здравоохранения, Хабаровск, Россия;
[3] Дальневосточный государственный медицинский университет, Хабаровск, Россия

АННОТАЦИЯ

Обоснование. Число молодых пациентов с сахарным диабетом 1-го типа неуклонно растёт во всех странах мира. Технические особенности выполнения витрэктомии при пролиферативной диабетической ретинопатии у пациентов с сахарным диабетом 1-го типа изучены недостаточно. Необходимость их исследования очень актуальна, поскольку число таких пациентов постоянно увеличивается, то полученные сведения позволят избегать интра- и постоперационных осложнений, способных возникнуть при выполнении витрэктомии.

Цель — изучение морфофункциональных особенностей пролиферативной диабетической ретинопатии у молодых пациентов с сахарным диабетом 1-го типа, оценка технических трудностей эндовитреальной хирургии, её исходов.

Материалы и методы. Проведена сплошная выборка всех молодых пациентов с пролиферативными стадиями диабетической ретинопатии при сахарном диабете 1-го типа, кому была показана витреоретинальная хирургия. Было отобрано 32 пациента (55 глаз) от 18 до 46 лет: максимально корригированная острота зрения от неправильной проекции до 0,3. Всем пациентам выполняли трёхпортовое эндовитреальное вмешательство через плоскую часть цилиарного тела.

Результаты. В 48 глазах имелось плотное сращение задней гиалоидной мембраны с внутренней пограничной мембраной, кровотечение из пересечённых сосудов, при их отделении — склонность к рецидивированию кровотечения. В 25 глазах — плоскостные сращения преретинальных мембран, ретинальных сосудов и сетчатки. Всё это повышало длительность эндовитреального вмешательства. Все операции завершились силиконовой тампонадой. В 1-е сутки на 40 глазах имелись небольшие преретинальные кровоизлияния в заднем полюсе. На 15 глазах возникли массивные преретинальные кровоизлияния. Спустя месяц после удаления силикона максимально корригированная острота зрения на 36 глазах повысилась до 0,2–0,8.

Заключение. Имелись значительные технические трудности выполнения витрэктомии у всех пациентов из-за тяжёлого состояния витреомакулярного интерфейса. Стабилизация клинического течения пролиферативной диабетической ретинопатии спустя месяц после удаления силикона была достигнута в 96% глаз.

Ключевые слова: пролиферативная диабетическая ретинопатия у молодых пациентов; эндовитреальная хирургия; технические трудности; осложнения.

Как цитировать

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BACKGROUND

Statistical data show that the number of young patients with type 1 diabetes mellitus (T1DM) is steadily increasing worldwide. In 2021, there were 2,607,712 children and adolescents under 19 years with DM worldwide. The annual increase in new cases in this age group is up to 96,000 children and adolescents under 15 years and over 132,000 adolescents and young people aged 15–20 years [1]. According to the Russian Diabetes Mellitus Federal Register, in 2021, the total number of children, adolescents, and young people under 18 years with T1DM increased to 42,951 compared with 29,690 in 2016 [2]. The incidence of T1DM in young people is constantly increasing. The official expected increase is about 3% per year, although it may vary depending on a geographical region [3].

The most common and severe vascular complication of T1 DM is diabetic retinopathy (DR). Duration of T1DM of up to 5, from 5 to 10, and over 15 years results in DR in 9%–17%, 44%–80%, and 87%–99% of cases, respectively [4–6]. Proliferative DR is the most severe stage, causing irreversible blindness and visual impairment [7–11]. Compared with proliferative diabetic retinopathy (PDR) in elderly patients with type 2 DM, the DR clinical course in T1DM is characterized by the rapid development and progression of retinal neovascularization [12]. PDR in T1DM develops early in adolescence and has an aggressive course. Without adequate control and prompt preventive panretinal photocoagulation, PDR poses a risk of irreversible blindness after 10–15 years of DM [4, 6, 13].

Dhillon et al. [14] report that PDR develops in 14-year-old adolescents after 7.7 years of DM (0.6%–13.7%). Notably, glycated hemoglobin (HbA1c) level averages 8.6% (5.6%–13.1%). However, if the mean HbA1c increases to 9.1% (7.2%–14%), this period is reduced to 5 years. Higher HbA1c levels and a longer DM duration are significant risk factors for the DR development and progression [15].

Published data describe features of the post-vitrectomy period in young patients with PDR. Usui et al. [16] report visual impairment in 22% of young patients after vitrectomy for PDR. The authors attribute this to irreversible changes in the retina and optic nerve, neovascular glaucoma, and several other common factors. Liao et al. [17] agree with this opinion and note that the incidence of post-vitrectomy complications in young patients with PDR is higher than in elderly patients. In their opinion, this may be explained by the longer duration of DM and poorer glycemic control.

In recent years, vitreoretinal surgery (VRS) has become widely used in clinical practice and significantly expanded surgical treatment options for PDR. Diagnostic capabilities of in-life vitreoretinal visualization have also expanded. Technical aspects of vitrectomy for PDR in young patients with early onset of DM have not been described in the available published sources. There are some data on VRS outcomes in young patients with DM [18].

Ricca et al. [19] evaluated the functional outcomes of vitrectomy in young patients with PDR secondary to T1DM, but the study only assessed if visual functions complied with the US minimum standard for car drivers. Technical intraoperative challenges of vitrectomy and specific features of the early postoperative period remain unstudied.

As technical aspects of vitrectomy and its anatomical and functional outcomes in patients with PDR secondary to T1DM are poorly understood, we considered it significant to research this issue in our clinical practice. In our opinion, it is highly relevant, as the number of patients is steadily increasing, and the information obtained will allow preventing possible intra- and postoperative complications of vitrectomy.

The study aimed to analyze the morphological and functional features of PDR in young patients with T1DM and to assess the technical challenges of endovitreal surgery and its outcomes.

METHODS

The study included unselected young patients with PDR and T1DM who were eligible for VRS. Inclusion criteria were DM onset in childhood or adolescence and severe or advanced PDR. Non-inclusion criteria were HbA1c above 10 mmol/L and/or fasting blood glucose above 12 mmol/L. We referred these patients to an endocrinologist at their place of residence for glycemic control, and surgery was planned when they reached acceptable glycemic levels.

Using these criteria, 32 patients (55 eyes) were selected; the age ranged from 18 to 46 years. There were 13 men and 19 women. The age of T1DM onset ranged from 1 to 25 years, with the mean age of 9.5 years. The DM duration ranged from 7 to 30 years. Pre-operatively, all patients achieved relative DM control.

The recommended pre-op blood glucose level was below 10.0 mmol/L [20]. However, given the severity and rapid progression of intraocular proliferative changes, we planned surgery in 4 patients with fasting blood glucose of 9.0–12.0 mmol/L. In these cases, pre-op therapeutic measures were taken to normalize it. For fasting hyperglycemia of 9–12 mmol/L, we increased the dose of long-acting insulin by 4–6 U/day, and the doses of prandial insulin were adjusted based on the glycemic control [21].

The PDR presence and severity were assessed using the ETDRS clinical classification (1991). Based on this classification, severe PDR was diagnosed in 24 eyes.

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It was manifested by glial scarring with areas of retinal neovascularization and proliferation, mainly along the vascular arcades. Of these, glial scarring and peripapillary neovascularization affected the optic disc (OD) in 12 eyes, involved the OD and vascular arcades in 9 eyes, and extended from the OD and vascular arcades to the area between the arcades in 3 eyes (see Fig. 1).

A total of 31 eyes had advanced PDR. It manifested as severe vitreoretinal proliferation causing traction retinal detachment in the macular area. The foveal area was affected in 17 eyes (see Fig. 2). Traction retinal detachment involved one macular quadrant in 10 eyes, 2 quadrants in 5 eyes, 3 quadrants in 1 eye, and 4 quadrants (the entire macular area) in 1 eye (Kroll, 1987).

All 55 eyes had concomitant vitreous hemorrhage (see Fig. 3). It lasted from 2 weeks up to 2 years, with a mean duration of 6 months. It was total vitreous hemorrhage in 13 eyes and manifested as suspended RBC in the vitreous cavity and preretinal and vitreal hemorrhages in 42 eyes.

Panretinal photocoagulation was performed in 18 patients (29 eyes) 1–18 months pre-operatively. As all enrolled patients had a proliferative stage of DR, intravitreal angiogenesis inhibitors were not administered before surgery. All patients had concomitant moderate or severe diabetic nephropathy, 11 patients had stage 1 or 2 chronic kidney disease (CKD), 4 patients had stage 3 CKD, of which 1 patient received parenteral dialysis and 3 patients received hemodialysis. Surgeries in these patients were planned between hemodialysis sessions to reduce the risk or prevent hemorrhagic and other complications of anesthesia and surgery associated with circulating anticoagulants. The preoperative examination included ophthalmoscopy using Schepens' binocular indirect ophthalmoscope with a 20 D lens; macular biomicroscopy using a noncontact lens, widefield lens (in case of adequate transparency of ocular media); B-scan ultrasound of the vitreous cavity (Aviso B-scanner, France, 50 Hz probe). If ocular media were transparent, optical coherence tomography of the macula (Cirrus HD-OCT, Germany) was performed. The anatomical characteristics of the vitreoretinal interface (internal limiting membrane [ILM] and posterior hyaloid membrane [PHM]) were evaluated. Macular thickness and volume, posterior vitreous detachment, degree of vitreoretinal traction and traction retinal detachment were determined. Baseline best corrected visual acuity (BCVA) was low and ranged from perception without light projection to 0.3.

All patients underwent minimally invasive vitreoretinal surgery (VRS). A standard three-port pars plana technique was used. The Constellation® Vision System (Alcon, USA) with 25G and 27G instruments was used. The 27G beveled tip and position of the vitrectomy cutter window closer to the retina allowed using fewer instruments. The vitrectomy cutter was used as both a delamination spatula, which smaller diameter allowed penetrating dense membranes to separate them, and scissors to cut and remove them. This technique shows particular benefit when used for bimanual surgery with additional illumination provided by a chandelier.

For prompt access and improved visualization of intraocular abnormal structures, the cloudy, altered vitreous was first removed. If necessary, Pfokalin® (ophthalmic vitreous substitute, Betamed LLC, Russia) was used. During surgery, we focused on determining areas of formation and spread of vitreous strands, membranes, their location, and prevalence of retinal neovascularization

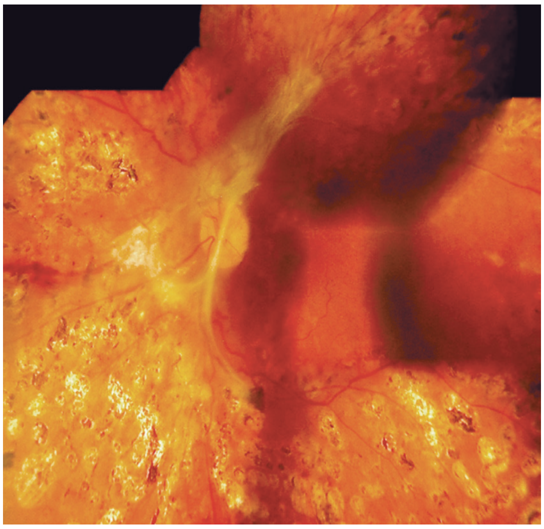

Fig. 1. Patient A, 28 years old. OS: Glial scarring of the optic disc and arcades, traction retinal detachment, and vitreous hemorrhage. Duration of type 1 diabetes mellitus is 19 years. HbA1C 8.5%.

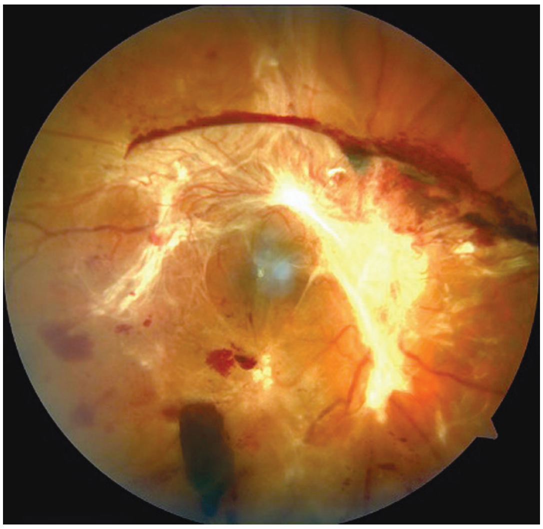

Fig. 2. Patient B, 27 years old. OD preoperatively: Severe fibrovascular membrane, affecting the optic disc and vascular arcades; traction macular detachment in all quadrants. Duration of type 1 diabetes mellitus is 17 years. HbA1C 10%, moderate nephropathy.

areas. We assessed technical challenges of the following VRS stages: removal of the altered vitreous, intravitreal blood clots, and fibrovascular membranes, hemostasis, manipulations with the detached retina, and laser coagulation.

RESULTS

During VRS, we noted several serious baseline morphological characteristics of the vitreomacular interface. For example, almost all the patients (48 eyes) had dense fused PHM and ILM. This challenged their mechanical separation and posed a risk of intraoperative hemorrhages. Attempts to mechanically separate the PHM from the retina may often lead to retinal defects and hemorrhages. Therefore, we had to pre-cut the PHM first using vitreous scissors and forceps and, if necessary, a bimanual technique. When the fibrovascular tissue was isolated and an adequate PHM area was peeled, a vitrectomy cutter was used to completely remove it. The vitrectomy cutter was used for a stepwise and layer-by-layer removal of abnormal structures — proliferative fibrovascular strands freed from traction and underlying tissues. In addition, the residual vitreous to be removed was characterized by high density, which reduced the vitrectomy cutter performance. Sometimes it even had to be replaced with a new one.

These specific features required gentle removal of the altered vitreous filled with blood in layers prior to visualization of the PHM and retina. Only this approach allowed minimizing the risk of retinal damage. Additionally, the vitrectomy cutter position and tip direction had to be constantly monitored. In particular, it was necessary to carefully and consistently separate the PHM mechanically by delaminating it using the vitrectomy cutter, scissors, and forceps and then cutting it with scissors.

There were also technical challenges of intraoperative hemostasis, which prolonged surgery. For example, bleeding often occurred from the cut vessels supplying the fibrovascular membrane, when dense membranes fused with the retina were separated. Endodiathermy of the newly formed vessels was performed to stop bleeding. To minimize the risk of retinal injury, the newly formed vessels were coagulated on the remaining proliferative tissue. This technique is universal for surgical treatment of proliferative changes in type 2 DM (T2DM) and in other post-thrombotic proliferative retinopathies.

Notably, intraoperative hemorrhages tended to reoccur in these patients despite intraoperative hemostasis achieved using endodiathermy. This resulted in preretinal blood clots of various size and volume. They had to be mechanically removed using forceps and vitrectomy cutter; however, then the blood clots in the vessels were compromised, and hemorrhages often re-occurred.

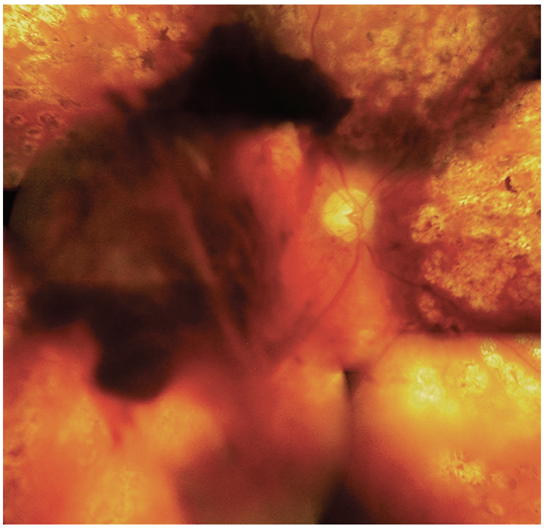

Fig. 3. Patient C, 30 years old. OD: Vitreous hemorrhage, glial scarring, and traction retinal detachment. Duration of type 1 diabetes mellitus is 20 years. HbA1C 9%, nephropathy.

Therefore, this procedure had to be repeated multiple times.

The procedure required time-consuming manipulations to reduce microscopic retinal damage. Besides, a typical symptom in this patient group is high-density glial membranes taking longer to remove. They were detected in 25 eyes (14 patients).

Additionally, another trend was identified. Many patients had continuous flat fusions of the preretinal membranes, retinal vessels, and retina (25 eyes). Notably, there was almost no space between the preretinal fibrovascular membrane and retina compared with membranes in elderly patients with PDR secondary to T2DM. Inter-tissue empty space facilitates manipulations, as they allow the vitreous instrument to safely penetrate the preretinal membrane and gently separate it from the retina and other adherent tissues, for example, vascular arcades. Dense fusion of the fibrovascular membrane and retina in the studied patients significantly complicated peeling, cutting of the strands, and removal of the preretinal membrane, PHM, and other proliferative structures.

All these complicating aspects prolonged VRS, and its duration ranged from 45 to 180 minutes. Given the high risk of intraoperative hemorrhagic complications, much focus was on monitoring blood pressure in patients using special equipment.

When removing dense preretinal membranes, retinal damage was prevented in most cases; however, iatrogenic breaks occurred in 5 cases (see Fig. 4, *a*). Iatrogenic breaks of the adjacent retina were treated using laser coagulation. For breaks of the detached retina or retinal detachment around the break, Pfokalin® or a gas-air tamponade was used to adhere the retina before laser coagulation. All procedures were completed with 5700 cSt silicone oil tamponade (see Fig. 4, *b*).

We believe that silicone oil tamponade was preferable to gas–air tamponade or pneumatic retinopexy, as it has several benefits. Silicone oil is viscous, transparent, and completely fills the vitreous chamber, therefore hemorrhages are preretinal and local. In addition, silicone oil mechanically presses the clot against the retina, preventing the leaked blood from dispersing into the vitreous cavity. Interfacial surface tension of silicone oil of 45 din/cm is sufficient to block existing retinal breaks. Moreover, silicone oil is chemically inert and has a bacteriostatic effect, which is a positive factor in PDR treatment [22].

On postoperative day 1, ophthalmoscopy revealed small preretinal hemorrhages in the area of vascular arcades, optic disc, and peripapillary in 40 eyes. As the macular area was intact, visual acuity in these eyes increased by 0.05–0.4, on average by 0.25, as measured using the Sivtsev chart (see Fig. 4, *c*). Large preretinal hemorrhages were observed in 15 eyes in the early postoperative period. As a rule, they occurred on postoperative day 1 and were detected at the first postoperative examination. These patients had noticeable preretinal blood clots in the area of the vascular arcades and optic disc with macular involvement. They were the reason for no positive visual changes. Visual acuity decreased below baseline, up to no spatial, vision in 4 eyes, as the hemorrhage shaded the macular and foveal areas.

After 7–10 days, as the preretinal hemorrhages in these patients were resolving, blood plasma migrated to the anterior chamber, forming total hyphema in 4 eyes. In 2 cases, we attempted to surgically wash out hyphema through a corneal paracentesis until the anterior chamber aqueous humor was transparent. But the next day, erythrocytes migrated back to the anterior chamber. This induced an IOP increase up to 32–38 mmHg within 1–10 days in 11 eyes. Hypotensive therapy decreased IOP to the upper limit of normal of 25–26 mmHg in 7 eyes.

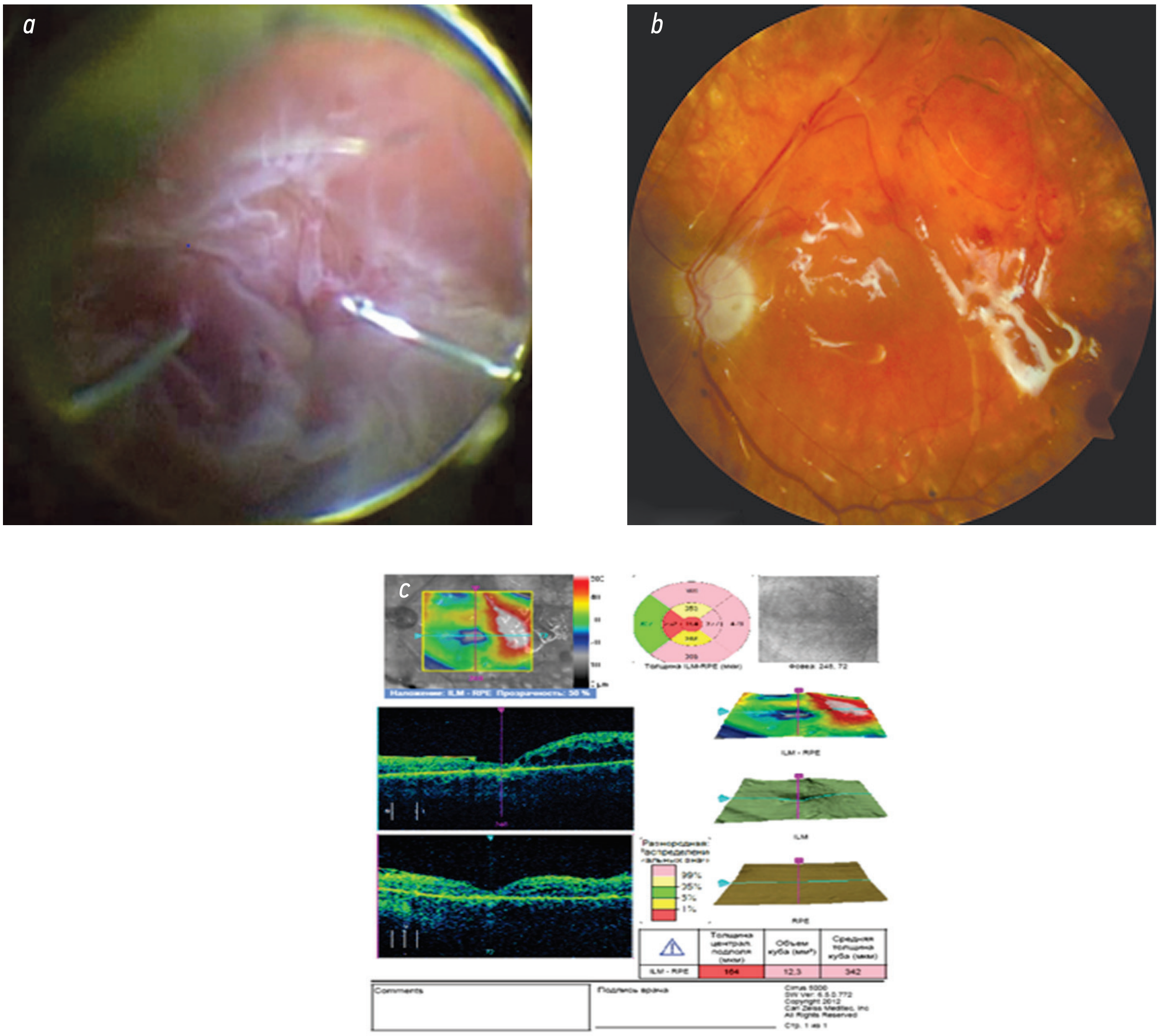

Fig. 4. Patient D, 38 years old. OS: *a*, intraoperative closed funnel-shaped retinal detachment, significant preretinal membrane; *b*, postoperative day 3, silicone oil tamponade, the retina is adherent in all quadrants; *c*, postoperative day 3, diffuse macular edema based on optical coherence tomography data. Duration of type 1 diabetes mellitus is 24 years. HbA1c 12%.

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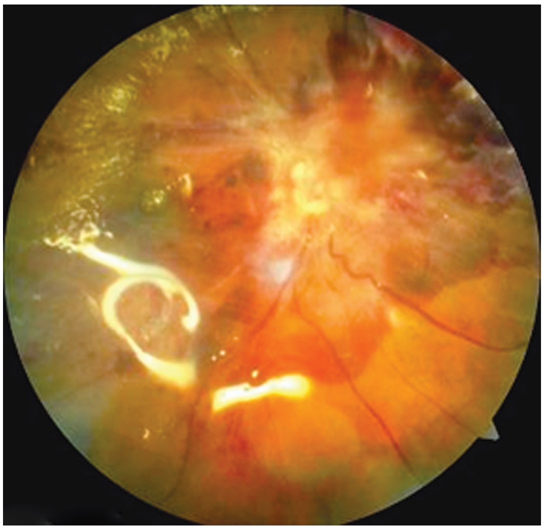

Fig. 5. Patient E, 27 years old. OD: repeated silicone oil tamponade. Day 3 after surgery for large postoperative hemorrhage and ocular hypertension. The retina is adherent. Subretinal and premacular hemorrhage is observed in the early postoperative period. Duration of type 1 diabetes mellitus is 17 years. HbA1C 10%, moderate nephropathy.

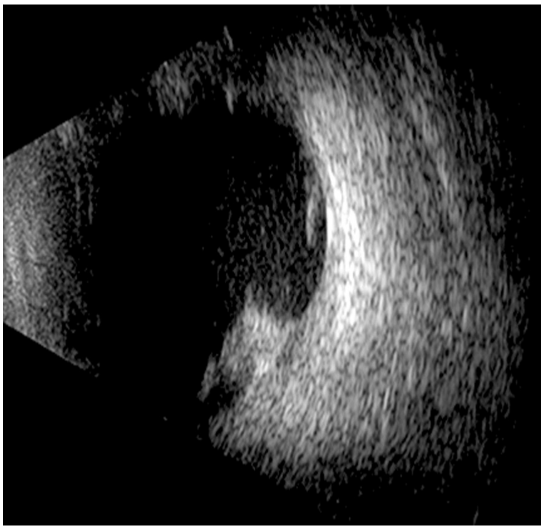

Fig. 6. Patient F, 38 years old. Remaining proliferative tissue and preretinal blood clots in the center and periphery based on B-scan of the OD vitreous cavity after silicone oil removal.

IOP decreased but remained high (30–32 mmHg) in 4 patients (4 eyes) while on therapy. These patients were followed-up on an in- and outpatient basis, daily or every other day.

Silicone oil was removed within 3–7 days in 4 eyes with hyphema and hypotensive therapy failure. After that, the blood clots were removed in layers using a vitreous cutter (see Fig. 5).

When removing large preretinal hemorrhages, we attempted to preserve a flat part of the preretinal clot for the blood clots on retinal vessels to remain intact. We also did it to minimize the mechanical impact on the retina, to prevent iatrogenic retinal break along the edge of the tightly adherent blood clot (see Fig. 6).

The patients received standard postoperative treatment. On day 3 after discharge, they were prescribed dexamethasone and antiseptic eye drops for 4 weeks. The postoperative reaction was resolved at week 4 after discharge in all cases. Prior to silicone oil removal, all patients underwent panretinal photocoagulation.

Silicone oil was removed after 2–4 months, on average after 2.2 months. On day 1 after silicone oil removal, suspended erythrocytes were observed in 10 eyes; treatment resolved them within 2–21 days, on average within 7 days in 9 patients. Vitreous hemorrhage persisted for 30 days in one patient; therefore, we performed re-intervention, washed out the vitreous chamber, and removed blood clots from the vitreous basement with silicone oil tamponade.

BCVA in 36 eyes increased significantly to 0.2–0.8 one month after silicone oil removal. Although 10 eyes had no positive changes in BCVA, we considered them surgical success. BCVA decreased after ocular hypertension in 7 eyes.

Iris neovascularization did not progress in 53 eyes, supporting adequate treatment strategy. Three months after silicone oil removal, 2 eyes developed rubeosis iridis and neovascular glaucoma with spatial vision loss, which required transscleral diode laser cyclophotocoagulation.

DISCUSSION

PDR is one of the most serious conditions requiring surgical treatment because of its severe and irreversible outcomes. In our study, we found that its course is most rapid in young patients with early onset of T1DM, and puberty is the trigger. Recent advancements in VRS have made treatment of these patients more promising. Favorable outcomes in PDR stabilization and prevention of its severe complications have been reported [7, 23, 24].

Our study revealed several features of the vitreomacular interface in young patients with PDR and technical challenges of vitrectomy caused by anatomical and morphological characteristics of the vitreoretinal interface structures in these patients. They were the following: no PHM detachment, tight fusion of preretinal membranes with newly formed vessels and retina, and formation of massive preretinal hemorrhages in the early postoperative period. These hemorrhages are characterized by high density and tight adhesion to the retina. Increased bleeding is explained by abnormal rheological and biochemical blood parameters in young patients caused by concomitant nephropathy and chronic pyelonephritis (20 patients, 28 eyes).

Based on our observations, the clinical course of PDR in young patients with T1DM is characterized by rapid intraocular changes (within 2–3 months). Traction retinal detachment usually occurs in the center and is often accompanied by vitreous hemorrhage. PDR in these patients is often secondary to diabetic nephropathy or chronic inflammatory kidney disease, which may significantly complicate both the intra- and postoperative periods. The mentioned challenges of vitreoretinal surgery for PDR should be considered in young patients with T1DM to minimize intra- and postoperative complications.

CONCLUSION

Significant technical challenges of vitrectomy were observed in all patients with PDR secondary to T1DM. They were manifested by severe baseline alterations of the vitreomacular interface, including tight fusion of PHM with ILM in 87% of patients, which posed a technical challenge to separate it mechanically; high density of the altered vitreous, which reduced the vitrectomy cutter performance; glial membranes tightly fused with retinal vessels and retinal tissue in 45% of eyes, challenging their safe separation from the retinal structures.

Technical challenges of intraoperative hemostasis included bleeding from newly formed vessels, which undoubtedly prolongs the surgical procedure and may increase the risk of postoperative complications. Therefore, surgeons should attempt to optimize the procedure time, which is possible by using modern technologies and instruments such as vitreous cutters with a cut rate of 20,000 and small gauge instruments.

Large preretinal hemorrhages affecting the vascular arcades, optic disc, and macula occurred in the early postoperative period and tended to increase IOP.

In our experience, silicon oil tamponade is a stabilizing factor in the postoperative period, as it prevents blood clots from dispersing into the vitreous cavity and creates optimal conditions for panretinal photocoagulation.

One month after the silicone oil removal, PDR was stabilized in 96% of the eyes.

ADDITIONAL INFO

Author contributions: Ya.B. Lebedev: investigation, formal analysis, writing—original draft, conceptualization; A.Yu. Khudyakov: conceptualization; E.L. Sorokin: substantial contribution to conceptualization, writing—review & editing, final approval of the manuscript. All the authors approved the final version of the manuscript for publication and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Statement of originality: No previously obtained or published material was used in this article.

Data availability statement: All data generated during this study are available in this article.

Generative AI: No generative artificial intelligence technologies were used to prepare this article.

Provenance and peer-review. This paper was submitted unsolicited and reviewed following the standard procedure. The peer review process involved two external reviewers, a member of the editorial board, and the in-house scientific editor.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Я.Б. Лебедев — сбор и обработка материала, написание текста, дизайн и концепция; А.Ю. Худяков — концепция и дизайн исследования; Е.Л. Сорокин — существенный вклад в концепцию и дизайн работы, редактирование, окончательное утверждение версии, подлежащей публикации. Авторы одобрили версию для публикации, а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой ее части.

Этическая экспертиза. Одобрение этического комитета на проведение исследования не получали. Причина — заключение этического комитета на применение стандартных методов лечения не требуется, так как оно необходимо при каких-либо изменениях в способах лечения. Авторы получили письменное согласие пациентов на публикацию медицинских данных и фотографий.

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения.

Доступ к данным. Все данные, полученные в настоящем исследовании, доступны в статье.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали два внешних рецензента, член редакционной коллегии и научный редактор издания.

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AUTHORS' INFO

***Yan B. Lebedev,** MD; address: 211 Tikhookeanskaya st., Khabarovsk, 680033, Russia; ORCID: 0000-0001-7563-6757; eLibrary SPIN: 5952-2909; e-mail: naukakhvmntk@mail.ru

Oleg V. Kolenko, MD, Dr. Sci. (Medicine); ORCID: 0000-0001-7501-5571; eLibrary SPIN: 5775-5480;

ОБ АВТОРАХ

***Лебедев Ян Борисович;** адрес: Россия, 680033, Хабаровск, ул. Тихоокеанская, д. 211; ORCID: 0000-0001-7563-6757; eLibrary SPIN: 5952-2909; e-mail: naukakhvmntk@mail.ru

Коленко Олег Владимирович, д-р мед. наук; ORCID: 0000-0001-7501-5571; eLibrary SPIN: 5775-5480;

* Corresponding author / Автор, ответственный за переписку

Alexander Yu. Khudyakov, MD;
ORCID: 0000-0001-8027-9192;
eLibrary SPIN: 5642-5155;
e-mail: naukakhvmntk@mail.ru

Evgenii L. Sorokin, MD, Dr. Sci. (Medicine), Professor;
ORCID: 0000-0002-2028-1140;
eLibrary SPIN: 4516-1429;
e-mail: naukakhvmntk@mail.ru

Худяков Александр Юрьевич;
ORCID: 0000-0001-8027-9192;
eLibrary SPIN: 5642-5155;
e-mail: naukakhvmntk@mail.ru

Сорокин Евгений Леонидович, д-р мед. наук, профессор;
ORCID: 0000-0002-2028-1140;
eLibrary SPIN: 4516-1429;
e-mail: naukakhvmntk@mail.ru