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VON HIPPEL–LINDAU DISEASE WITH CONCOMITANT HODGKIN'S DISEASE AND CONGENITAL HYPERTROPHY OF THE RETINAL PIGMENT EPITHELIUM

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✧ The article presents a rare case of combination of von Hippel–Lindau disease and Hodgkin's disease. The disease began with neurological symptoms with gradual progression over the next 3 years. The diagnosis of von Hippel–Lindau disease was made after MRI of brain and spinal cord, abdominal MICTs, and detection of brain stem and spinal cord tumors, multiple pancreatic cysts. We performed resection trepanation of the posterior cranial fossa and microsurgical total removal of hemangioblastoma of the medulla oblongata. After 1.5 years the patient is diagnosed with Hodgkin's disease and several courses of chemotherapy are carried out, reaching full remission, confirmed by PET with CT. 14 months later, the patient consulted an ophthalmologist due to visual impairment and floating opacities in her left eye. The ophthalmologic examination for the first time revealed multiple bilateral retinal hemangiomas and vitreal hemorrhages from tractional retinal tears caused by posterior hyaloid detachment and unrelated to hemangiomas in the left eye. The barrier laser coagulation of the left eye retinal tears was performed, and the observation tactics was adopted.

✧ ***Keywords:*** von Hippel–Lindau disease; Hodgkin's disease; congenital hypertrophy of the RPE.

БОЛЕЗНЬ ГИППЕЛЯ – ЛИНДАУ В СОЧЕТАНИИ С ЛИМФОМОЙ ХОДЖКИНА И ВРОЖДЁННОЙ ГИПЕРТРОФИЕЙ РЕТИНАЛЬНОГО ПИГМЕНТНОГО ЭПИТЕЛИЯ

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✧ В статье представлен редкий случай сочетания болезни Гиппеля – Линдау с лимфомой Ходжкина. Болезнь началась с неврологических симптомов с постепенным прогрессированием в течение последующих 3 лет. Диагноз болезни Гиппеля – Линдау был выставлен после магнитно-резонансной томографии головного и спинного мозга, мультиспиральной компьютерной томографии брюшной полости и выявления опухолей ствола мозга и спинного мозга, множественных кист поджелудочной железы. Выполнена резекционная трепанация задней черепной ямки, микрохирургическое тотальное удаление гемангиобластомы продолговатого мозга. Через 1,5 года у пациентки диагностировали лимфому Ходжкина и провели несколько курсов химиотерапии, достигая полной ремиссии, подтверждённой позитронно-эмиссионной томографией совмещенной с компьютерной томографией. Спустя 14 мес. пациентка обратилась к офтальмологу в связи с ухудшением зрения и плавающими помутнениями в левом глазу. При офтальмологическом обследовании у неё впервые выявляют множественные билатеральные гемангиомы сетчатки и гемофтальм из тракционных разрывов сетчатки, случившийся в результате отслойки задней гиалоидной мембраны и не связанный с гемангиомами на левом глазу. Выполнена барьерная лазерная коагуляция разрывов сетчатки левого глаза и принята тактика наблюдения.

✧ ***Ключевые слова:*** болезнь Гиппеля – Линдау; лимфома Ходжкина; врождённая гипертрофия ретинального пигментного эпителия.

INTRODUCTION

The von Hippel–Lindau disease is an autosomal dominant hereditary disease predisposed for the development of a wide range of lesions such as retinal, cerebellar, spinal, and medullary hemangioblastomas, renal cell carcinomas, and pheochromocytomas. Renal, pancreatic, and epididymal cysts (spermatoceles) are the most common manifestations of the disease. The combination of von Hippel–Lindau disease and lymphomas, in particular Hodgkin's disease, is described in individual cases [1, 2].

CLINICAL CASE

Female patient B., 20 years old, visited the Traumatology Department of the Diagnostic Center No. 7 (ophthalmic) on December 12, 2019, with complaints of sudden visual impairment and floating opacity in the visual field of the left eye that occurred 3 days before. The ophthalmic history revealed mild myopia since adolescence. The patient wears glasses since school age without ophthalmic supervision. Past medical history revealed the von Hippel–Lindau disease diagnosed in 2017. The disease onset was 6 years ago (2014), manifested with nausea and vomiting. A diagnosis of chronic gastroduodenitis was set, and the patient remained under gastroenterological supervision. Episodes of numbness in the lower extremities were noted since October 2015. Since August 2016, asthenia, dizziness, choking during food intake, and sudden weight loss (by 14 kg for 5 months) were noted. In January 2017, she was hospitalized in the City Children's Hospital No. 2 due to the deterioration of the condition; tumors of the brain stem and spinal cord at the level of C2–C3 and Th2–Th12 were detected by magnetic resonance imaging. Multispiral computed tomography of the abdominal cavity of January 13, 2017 revealed signs of multiple cystiform lesions of the pancreas.

On January 25, 2017, resection trepanation of the posterior cranial fossa and microsurgical total removal of the medulla oblongata tumor were performed at the V.A. Almazov National Medical Research Center. Histological examination revealed grade I hemangioblastoma.

In October 2018, the patient noticed a nodule on the right side of the neck; referred by a general practitioner, she was hospitalized in the Botkin Infectious Diseases Hospital. Histological analysis revealed Hodgkin's disease (classical) and nodular sclerosis (NS2). She was then referred for treatment to the N.N. Petrov Research Institute of Oncology where she received 2 chemotherapy courses of prednisone, vincristine, doxorubicin, and etoposide (OEPA) and 2 chemotherapy courses of prednisone, dacarbazine, vincristine, and cyclophosphamide. In March 2019, positron emission tomography combined with computed tomography revealed complete remission.

On examination in the Diagnostic Center No. 7 (ophthalmic) on December 12, 2019, visual acuity without correction of her right eye (RE) was 0.1, with correction (sph –2.5 D) it was 0.8, and visual acuity without correction of her left eye (LE) was 0.1, with correction (sph –2.75 D) it was 0.6. Pneumotonometry revealed IOP of her RE 17.0 mm Hg and IOP of her LE of 11.5 mm Hg. In both eyes, adnexa were normal, eye movements were preserved, and anterior segment was unaltered.

Eye fundus

The vitreous body was transparent in the RE, and there were no pathologic changes in the macula. There was an oblique insertion of the optic nerve head (ONH). From the ONH, the considerably and unevenly dilated inferior nasal branch went to angiomatous nodes of different caliber in the inferior nasal quadrant (Figure 1). The largest peripheral node was covered with a fibrous capsule with vitreoretinal tension (Figure 2).

In the LE, there were floating elements of hemorrhage in the vitreous body and a detachment of the posterior hyaloid membrane. In the macula, no pathologic condition was found. There was a peripheral retinal tear with an overlying operculum in the superior temporal quadrant (at the 1 o'clock position) (Figure 3). In the inferior temporal quadrant, there was a 2 ONH diameter-sized flat pigment focus with depigmented lacunae (congenital hypertrophy of the retinal pigment epithelium) and a strip of preretinal hemorrhage near it (Figure 4). There was a small retinal flap tear at the extreme periphery (at the 6 o'clock position). In the nasal quadrant, there was a group of angiomatous nodules of different calibers (1–5 ONH diameters) with dilated afferent vessels extending from the ONH, similar to that in the right eye (Figure 5). In both eyes, no characteristic of lymphogranulomatosis foci were found.

B-scan revealed that the posterior hyaloid membrane in both eyes was detached and partially adherent to the retina in the periphery. In the inferior nasal quadrants, there were areas of vitreoretinal interaction with traction (the retina was elevated by traction). In the nasal quadrant of the RE, there was a small protruding focus; the protrusion was up to 1.18 mm, and the basis of the lesion was 4.11 mm. In the nasal section of the LE fundus, there was a preretinal condensation in the vitreous cavity, and the

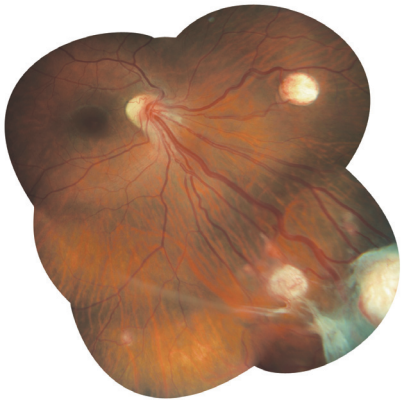

Fig. 1. RE. Angiomatosis nodules with dilated afferent and efferent blood vessels extending from the optic disc

Рис. 1. OD. Ангиоматозные узлы с расширенными питающими и дренирующими сосудами, тянущимися от диска зрительного нерва

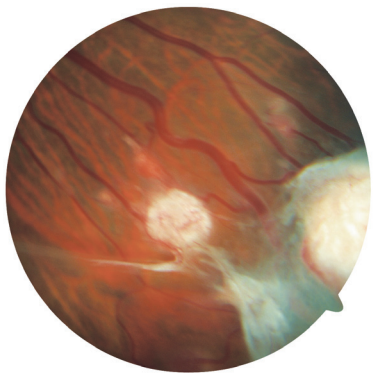

Fig. 2. RE. Glial proliferation on the surface of hemangiomas

Рис. 2. OD. Глиальная пролиферация на поверхности гемангиом

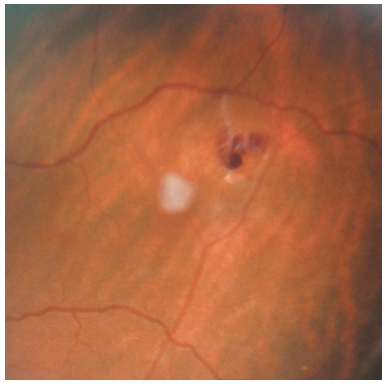

Fig. 3. LE. Peripheral retinal tear with an overlying operculum

Рис. 3. OS. Тракционный разрыв сетчатки с крышечкой

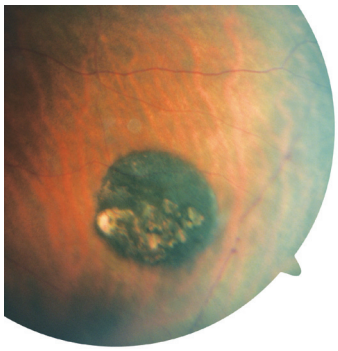

Fig. 4. LE. Congenital hypertrophy of the RPE

Рис. 4. OS. Врождённая гипертрофия ретинального пигментного эпителия

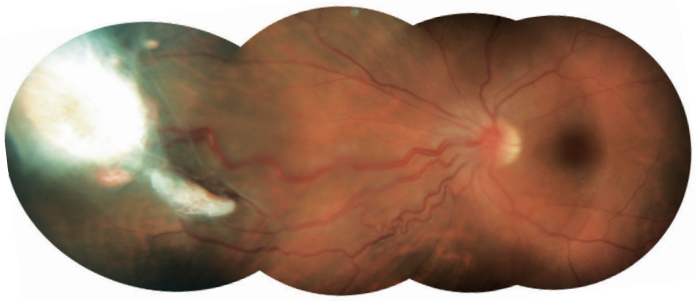

Fig. 5. LE. Angiomatosis nodules with dilated afferent and efferent blood vessels extending from the optic disc

Рис. 5. OS. Ангиоматозные узлы с расширенными питающими и дренирующими сосудами, тянущимися от диска зрительного нерва

local prominence of the inner contour of the eyeball. Optical coherence tomography of macula revealed no pathology in both eyes.

Diagnosis

The von Hippel–Lindau disease, multiple retinal hemangiomas in both eyes, mild complex myopic astigmatism were diagnosed. In the LE, acute symptomatic detachment of the posterior hyaloid membrane, multiple peripheral retinal tears, vitreous hemorrhage, congenital hypertrophy of the retinal pigment epithelium were detected. The concomitant diagnosis was Hodgkin's disease in remission.

On December 13, 2019, barrier laser photocoagulation of peripheral retinal tears at 1 o'clock and 6 o'clock positions of the LE was performed using a ZEISS, VISULAS 523s laser with impact duration of 0.13 s, spot diameter of 300 μm, impact number of 210, and power of 180–200 mW.

At the control examination on January 29, 2020, the patient reported no complaints. Visual acuity without correction of the RE was 0.1, with correction (sph −2.5 D cyl −1.0 D) it was 0.9. Visual acuity without correction of the LE was 0.1, with correction (sph −2.75 D cyl −1.25 D) it was 0.8. Intraocular pressure measured with ICare tonometer was 14.5 mm Hg in the RE and 14.3 mm Hg in the LE. There were no changes in the RE condition. In the LE, the anterior segment was unaltered, the vitreous body was transparent, tractional peripheral tears were surrounded by a barrier of pigmented laser spots, the retina was attached, there were no new

tears, preretinal hemorrhage resolved, and angiomatous nodes had no changes.

Further treatment approach to retinal angiomas takes into account concomitant diseases, high visual acuity, severity of nodules, lack of leakage, and high risk of complications during any surgical procedure. It was decided to perform only a follow-up.

CONCLUSION

The von Hippel–Lindau disease requires an interdisciplinary approach in monitoring and treatment of patients. Treatment of retinal hemangioblastomas aims at preventing exudative complications and retinal detachment. Careful monitoring of retinal changes using wide-angle photography is required to document lesions and changes caused by disease progression.

Currently, various methods are used to treat retinal hemangiomas in von Hippel–Lindau disease (laser, vitreoretinal surgery, radiation therapy, and antiangiogenic therapy). The choice of treatment depends on the size and location of hemangiomas and on existing complications. Currently, laser coagulation is the leading treatment method that can effectively destroy angiomas of up to 3 mm in size. Antiangiogenic therapy can stop the progression of small retinal lesions and reduce retinal exudation and edema in some cases [4]. Vitreoretinal surgery is used for severe exudative changes with a threat of development or already developed traction or exudative retinal detachment.

The best results were revealed by early detection of angiomas and laser coagulation of angiomatous nodes.

In this clinical case, the combination of severe concomitant pathology raises the question of choosing the treatment approach for retinal hemangioblastomas taking into account the general condition while maintaining high visual functions, and the absence of retinal exudation and lesion of the macular zone. Assessment of the dynamics of the angiomatosis development was impossible due to the short follow-up period and the lack of objective information on the condition of the fundus over the past 3 years.

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