Clinical cases

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Surgical management of macular edema associated with von Hippel-Lindau disease: a case report

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high-frequency electric welding of biological tissues, von Hippel-Lindau disease, vitrectomy, retinal hemangioblastoma, macular edema, retina

We report a case of surgical management of macular edema associated with von Hippel-Lindau (VHL) disease. The patient received vitrectomy with angioma endoresection using high-frequency welding of biological tissues. Follow-up findings included complete resorption of hard exudates, improvement in the macular profile and partial restoration of vision. A review of the treatment outcome for this case confirms the efficacy of vitrectomy with endoresection of retinal hemangioblastoma in the management of macular edema associated with VHL disease. Timely diagnostic evaluation and adequate postoperative follow-up are essential for the best treatment outcome.

Introduction

Von Hippel-Lindau (VHL) disease is an autosomal dominant syndrome which occurs secondary to germline mutations in the VHL tumor suppressor gene, located on chromosome 3. It is characterized by benign vascular and cystic tumors that develop in various organ systems of the body, most commonly in the retina, cerebellum, spinal cord, kidney, adrenal gland, and pancreas [1-2]. The disease is commonly found in individuals aged 20 to 30 years. Major ocular findings in VHL disease are retinal angioma (also known as retinal hemangioblastoma [RHB] or retinal capillary hemangioma), dilated feeder vessels and subretinal exudation [3].

Various treatment options have been used to treat patients with RHB associated with VHL disease, including observation alone, laser photocoagulation, photodynamic therapy, cryotherapy, and radiotherapy and vitreoretinal surgery. The effectiveness and applicability of these options depend on tumor location and size and the presence of subretinal fluid, exudates and signs of traction [4-8]. Macular edema, a serious complication of RHB, can develop due to abnormal vascular permeability [9].

Although vitrectomy is an effective treatment option for VHL syndrome, a disadvantage of this option is the high risk of intraoperative hemorrhage from feeder vessels during tumor resection. A high risk of hemorrhagic complications in the treatment of VHL syndrome has been reported, despite the use of diathermy and laser coagulation, high infusion pressure values, and feeder vessel ligation [10-12]. Our previous experimental and clinical studies have demonstrated that the use of high-frequency electric welding (HFEW) of biological tissues during endoresection of RHB allowed us to avoid hemorrhage of the vessels supplying the tumor [13-15].

Case description

A 34-year-old male patient presented to the Department of Vitreoretinal Microsurgery, SI “The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine” after he had been diagnosed with VHL syndrome, localized exudative retinal detachment and macular edema oculus dexter (OD), and received unsuccessful anti-vascular endothelial growth factor (VEGF) treatment for the RHB and edema, at a treatment facility near his place of residence.

At the time of presentation, physical examination found no parenchymal or brain lesions. Additionally, the best-corrected visual acuity (BCVA) in the affected eye was 20/100, and the intraocular pressure (IOP) was within the normal range. There was ophthalmoscopic evidence of a 2-disc diameter neoplasm in the nasal retina. There were dilated and tortuous tumor feeder artery and draining vein, a secondary localized retinal detachment, and macular edema with massive subretinal exudation (Figs. 1A and B).

The patient underwent fluorescein angiography (FA), optic coherence tomography (OCT) and ocular ultrasonography (US). Arteriovenous phase FA showed hyperfluorescence of the lesion, and accumulation of fluorescein dye with visualization of feeder vessels. Late phase FA showed the accumulation of fluid in the macula (Fig. 1C). There was OCT evidence of macular edema, with a central retinal thickness of 340 µm (Fig. 1D).

US revealed fibrotic changes in the vitreous. A localized 10.44-mm retinal detachment was found at 3 o’clock from the optic disc and appeared acoustically dense on ul-

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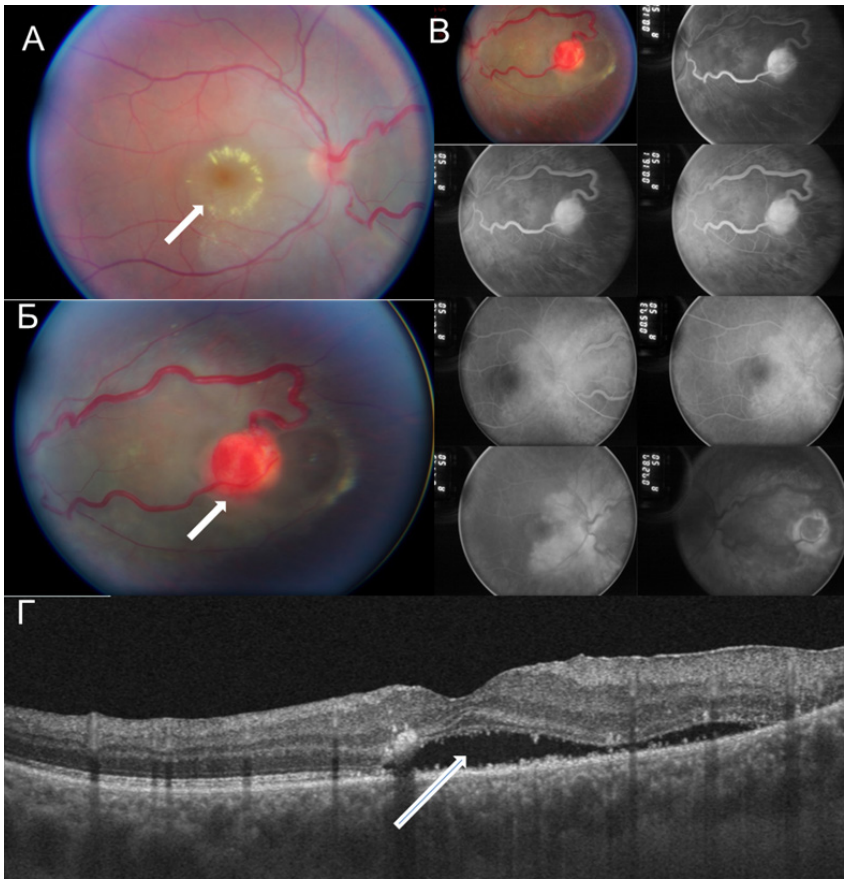

Fig. 1. Images of the right eye at baseline. A, B: Color fundus photographs. Note macular hard exudates (A; arrow) and retinal hemangioblastoma with feeder vessels (B; arrow) in the nasal retina. C: Fluorescein angiogram. Note hyperfluorescence of the tumor, dye staining of feed vessels and late macular leakage. D: Optic coherence tomography image. Note macular edema (arrow). Retinal thickness is 340 μm.

trasonography. The height of retinal detachment was up to 2 mm. At 6 mm from the optic disc, ultrasonography depicted the 1.54-mm thick mural substrate measuring 3.4 x 3.5 mm and with moderate acoustic density (Fig. 2).

Taking in account that the patient was unresponsive to multiple intravitreal anti-VEGF injections and had a secondary retinal detachment, he was proposed to have vitrectomy with endoresection of RHB. Informed consent was obtained prior to the procedure. The patient was completely informed of what the procedure involved and

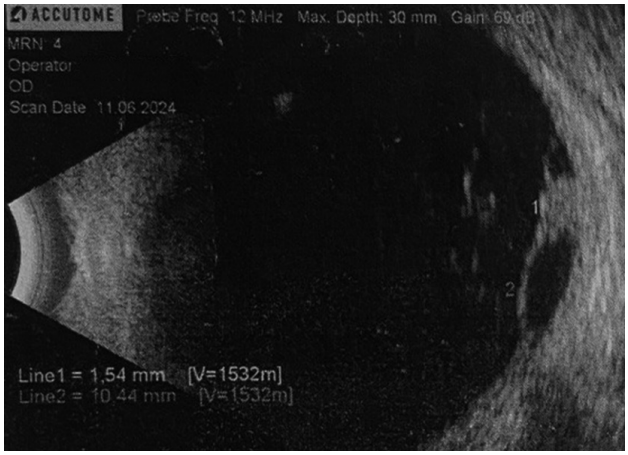

Fig. 2. Ultrasonogram of the posterior segment of the right eye. Note the mural substrate with moderate acoustic density (1) and localized retinal detachment (2)

possible complications. A three-port subtotal pars plana vitrectomy was performed with a 25-gauge instrument. An upgraded high-frequency current generator EK-300M1 with a proprietary 23-gauge welding probe was used to perform HFEW of the feeder vessels and the retina around the tumor and achieve homeostasis [14]. The variables of HFEW were 24-30-V voltage, up to 0.3-A current, 66.0 kHz- frequency and, up to 1.0-s exposure time [14]. Welding burns were applied in two rows around the tumor, and resulted in retinal whitening due to coagulation changes and obliteration of the feeder artery and draining vein, with no hemorrhagic complications during retinotomy around the tumor and tumor resection. Tumor endoresection was followed by pneumohydraulic flattening of the retina and endolaser photocoagulation. Surgery was completed by using vitreous tamponade with 16% C3F8.

In the early postoperative period, the intraocular gas bubble size was 95%, retinal re-attachment was achieved, and no hemorrhagic complication was noted. The IOP was within the normal range. On day 5, the BCVA was light perception with accurate projection (due to the effect of tamponade) and the patient was discharged. One month after surgery, he received additional laser coagulation.

At the 6-month follow-up, the BCVA was 20/25 and the IOP was normal. In addition, on examination, the eye was quiescent, the cornea appeared clear, and the posterior lens capsule was diffusely opacified. Moreover, some pigment loss along the retinotomy edge and resorption of hard exudates in the macula were noted, tumor feeder vessels

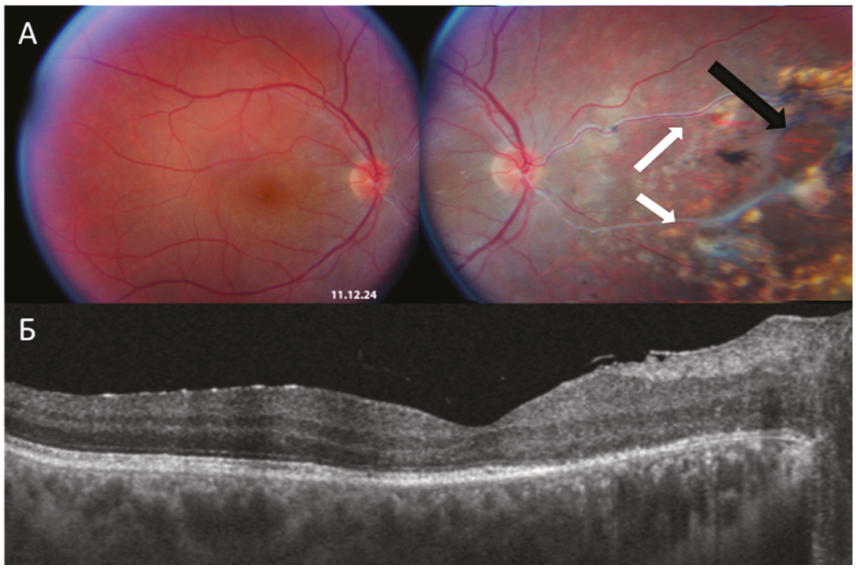

Fig. 3. Images of the right eye 6 months after vitrectomy. A: Color fundus photograph. Note resorption of macular hard exudates, obliteration of hemangioblastoma feeder vessels (white arrow), and tumor resection area (black arrow). B: Optic coherence tomography image. Note reduction of macular edema and restoration of macular profile.

appeared obliterated, and the retina reattached (Fig. 3A). There was OCT evidence of the restoration of macular profile. The retinal thickness in the macula decreased to 239 μm at the expense of subretinal fluid resorption (Fig. 3B).

Discussion

There is still no agreement on the best way to manage macular edema and exudative retinal detachment in large RHB. The literature contains reports on the successful use of anti-VEGF agents in macular edema in patients with VHL syndrome.

A case report by Otero-Marquez and colleagues [16] reported the impact of intravitreal bevacizumab on a RHB using clinical OCT angiography (OCTA). Comparison of the pre- and post-treatment OCTA at the temporal RHB showed a reduction of CME and regression of RHB. The authors concluded that anti-VEGF therapy appeared to stabilize the visual acuity and produce partial regression of RHB.

Dahr and colleagues [17] used intravitreal pegaptanib sodium in patients with juxtapapillary or large peripheral RHB secondary to VHL disease. Of the five patients enrolled in the study, the two who completed the scheduled course of at least six intravitreal injections had reductions in macular edema and retinal hard exudates. Other three patients experienced increases in macular edema and retinal hard exudates, with one of them developing a tractional retinal detach-ment. The authors concluded that intravitreal injections of anti-VEGF therapy (pegaptanib) may decrease retinal thickening minimally and reduce retinal hard exudates in some patients with advanced RHB secondary to VHL disease. They, however, noted that effective treatment may require the destruction of the tumor itself.

Wong and colleagues [18] evaluated the effect of intravitreal ranibizumab (0.5 mg) on RHBs associated with VHL disease that were not amenable or responsive to standard therapy in a case series of 5 patients. They concluded that intravitreal ranibizumab, delivered as monotherapy every 4 weeks, had minimal beneficial effects on most RHBs. However, in the smallest and least exudative of lesions (patient 5 with a lesion of about 1 disc diameter), ranibizumab monotherapy had the largest beneficial anatomic effect, with reduction in exudates and improved vision. A reduction in the macular thickness with treatment was also noted in another patient (patient 4), although her tumors were extensive [18].

In a retrospective cases series by Schlesinger and colleagurs [11], three patients with RHB were successfully managed by vitrectomy with internal en bloc resection. Retinal re-attachment was achieved in both patients that had had retinal detachment. After tumor resection, resolution of hard macular exudates was observed in two patients that had had these exudates at baseline. The authors concluded that their patients' favorable outcomes suggest that surgical resection is an option for patients with large RHBs. They, however, provided no data on tumor recurrence or long follow-up.

Gaudric and colleagues [12] evaluated the long-term success rate of vitreoretinal surgery for severe cases of RHBs caused by VHL disease. In 9 eyes, retinectomy was performed to remove the RHB. At 6 months, the retina was flat in 8 of the 9 eyes, and hard exudates resorbed in one eye [12].

Taking into account the above and that our patient was unresponsive to multiple intravitreal anti-VEGF injections and had a secondary retinal detachment, he was proposed to have vitrectomy with endoresection of RHB and our technique of HFEW of biological tissues. Of note that there were no hemorrhagic complications during tumor resection because we used HFEW of biological tissues to achieve homeostasis; this technique has been found to be effective in our previous clinical studies [13-15]. At 6 months after tumor resection, the macular edema reduced to 239 μm.

Based on the current case and a review of previous studies, we suggest that vitrectomy with endoresection of RHB is an optimal approach to the treatment of patients

with VHL syndrome and macular edema. This treatment option allows eradicating a large RHB and contributes to the restoration of the macular profile and reduction in exudation and hard exudate resorption, while HFEW of biological tissues is an effective technique for achieving intraoperative homeostasis.

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Disclosures

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Abbreviations: *BCVA, best-corrected visual acuity; IOP, intraocular pressure; FA, fluorescein angiography; HFEW, high-frequency electric welding; OCT, optic coherence tomography; RHB, retinal hemangioblastoma; US, ultrasonography; VEGF, vascular endothelial growth factor.*