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Vitrectomy and high-frequency welding-assisted endoresection of retinal vasoproliferative tumors: a case series

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Background: *The relative rarity of retinal vasoptoliferative tumors has resulted in a lack of ecidence-based consensus agreement on how best to treat these lesions. Therefore, there is a need for advanced techniques capable of more effective treatment of these tumors and allowing for the preservation of visual function.*

Purpose: *To review the results of treatment of large retinal VPTs by pars plana vitrectomy with tumor endoresection and the use of high-frequency electric welding (HFEW) for achieving hemostasis.*

Material and Methods*: We reivewed the results of surgical treatment of large retinal VPTs complicated by exudative retinal detachment, macular edema, and/or epiretinal fibrosis in 5 patients (6 eyes).*

Patients underwent a comprehensive eye examination (visual acuity, biomicroscopy, ophthalmoscopy, tonometry, perimetry) and imaging (ultrasound examination, and optical coherence tomography. Outcome measures included anatomical success (retinal re-attachment), visual acuity, the presence of intraoperative and postoperative hemorrhagic complications, resorption of subretinal exudates, restoration of retinal profile, and the absence of tumor recurrence over the 6-month follow-up period.

Results: *Total tumor removal was achieved in all cases. In addition, there was no intraoperative hemorrhage. At the 6-month follow-up examination, the best-corrected visual acuity (BCVA) ranged from 0.17 to 0.3. Over the 6-month follow-up period, the retina remained re-attached, BCVA improved, and partial resorption of hard exudates as well as restoration of the retinal profile was observed in all cases (6 eyes). Moreover, no tumor recurrence was noted.*

Conclusion*: Vitrectomy with retinal VPT endoresection results in positive anatomical and functional outcomes, making it a method of choice in the treatment of large complicated retinal VPT resistant to more eye-sparing modalities; the HFEW technique proved to be an apt choice for intraoperative hemostasis.*

Keywords:

vasoproliferartive tumor, vitrectomy, high-frequency electric welding of biolohical tissues

Introduction

Vasoproliferative tumors (VPT) of the retina are uncommon benign retinal tumors and obtained status as a distinct clinical entity in the early 1980s [1]. The first 12 cases of RVPT containing both vascular and glial components were described by Shields and colleagues (1983) [2] and termed presumed acquired retinal hemangioma. Various definitions (e.g., “angioma-like lesions” [3], “hemangioma-like masses of the retina” [4], “peripheral retinal telangiectasia” [5], “reactive retinal glioangiosis” [6], and etc.) have been proposed to describe individual peripheral vascular lesions depending of the prevalence of either vascular or glial components. In 1995 Shields and colleagues [7] reported the clinical manifestations of 103 patients with an acquired retinal tumor. They described the lesions as retinal vasoproliferative tumors, a term that has now gained acceptance in the clinical literature. VPTs may be idiopathic (74%) or secondary to a pre-existing chorioretinal disease (26%) [7]. Secondary VPTs have been described in association with a number of ocular conditions including uveitis, retinitis pigmentosa, Coats disease, retinopathy of prematurity, chronic retinal detachment, chorioretinal trauma, etc. Common denominators of these associated conditions seem to be retinal inflammation, ischemia, neovascularization and exudation. Idiopathic RVPTs are usually solitary unilateral lesions whereas secondary tumors are often bilateral multiple lesions. Honovar (2018) [8] proposed an ophthalmoscopic classification of VPTs which includes stages of severity from stage 1 (VPT with focal or diffuse exudates) to stage 5 (VPT with complications (e.g., secondary neovascular glaucoma) without visual potential).

Due to the uncommonness of the condition, no objective data on the epidemiological prevalence of VPTs have been published. VPTs may be present at any age, although the majority are present in the third and fourth decades of life. Males and females are affected equally, and patients usually have no family history of ocular disease [7].

The pathogenesis of VPT has not been fully elucidated. It is believed that histologically, such lesions are characterized by a reactive gliovascular proliferation (with the varying extent of gliosis and vascular proliferation), which develops in response to retinal ischemia, trauma and inflammation. Pathological examination of these tumors reveals that they are composed of retinal epithelial cells and glial and vascular components [6].

Ophthalmoscopically, a VPT appears as a globular or dome-shaped mass whose color varies but is mainly yellowish or pinkish or, less commonly, white or grey; this is caused by the extent of the glial component. VPTs are most commonly located in the regions between the equator and ora serrata (73%). Tumor location in the inferior temporal quadrant is also the most common (67%) [9-10]. In most cases, retinal feeder vessels, which have a normal or slightly enlarged caliber, enter the posterior aspect of the tumor. However, these vessels lack the markedly dilated and tortuous appearance of those that are found in association with capillary hemangiomas associated with von Hippel Lindau disease [7]. Possible VPT-associated complications include sub and intraretinal exudation (80%), exudative retinal detachment (50%), epiretinal fibsoris (31%), vitreous hemorrhage (26%), and cystoid macular edema (18%) [11]. Although these tumors are benign, they may lead to complete visual loss.

The diagnosis is made based on the findings of comprehensive eye examination (visual acuity, biomicroscopy, ophthalmoscopy, tonometry, perimetry) and imaging (ultrasound examination, optical coherence tomography (OCT) and fluorescein angiography (FA)). However, given the peripheral location of VPTs, it is difficult or impossible to perform FA in the eye with a VPT.

Management modalities include simple observation, laser photocoagulation or transpupillary thermotherapy, transconjunctival cryotherapy, plaque brachytherapy, photodynamic therapy, intravitreal triamcinolone, intravitreal anti-vascular endothelial growth factor (VEGF) and vitreoretinal surgery [4, 7, 8, 12–14]. Causative treatment for the underlying disease is essential in VPTs associated with uveitis.

Vitrectomy is performed for large VPTs complicated by tractional retinal detachment, unresolving vitreous hemorrhage, proliferative vitreoretinopathy, etc. Endoresection for VPT remains controversial, particularly due to the risk of hemorrhagic complications during or after the vitreoretinal procedure. High-frequency electric welding of biological tissues (HFEW) has been found beneficial for achieving an adequate homeostasis during endoresection of melanoma, hemangioma, and other malignant and benign choroidal and retinal tumors, and seems promising for the endoresection of VPT [15–17]. The welding technology boils down to electric tissue coagulation, with high-frequency electric current enabling tissue heating and subsequent coagulation of protein molecules which act as a biological glue [18].

Given the above, the purpose of the current study was to review the results of treatment of large RVPTs by pars plana vitrectomy with tumor endoresection and the use of HFEW for achieving hemostasis.

Material and Methods

This study included 5 patients (6 eyes) aged 36 to 53 years (mean age, 43.8 years) who were treated for large VPTs at the Department of Vitreoretinal Microsurgery of the Filatov Institute during 2019-2021. Of these, 3 were women and 2 were men.

The major complaint was reduced vision. Inclusion criteria were a VPT greater than three disc diameters in size, complicated by exudative retinal detachment, macular edema, and/or epiretinal fibrosis. The diagnosis was made based on the findings of comprehensive eye examination (visual acuity, biomicroscopy, ophthalmoscopy, tonometry, perimetry) and imaging (ultrasound examination, OCT and FA).

Informed consent was obtained from all patients.

A 25-G pars plana vitrectomy was performed using the Alcon Constellation vitrectomy machine (Alcon Laboratories, Inc., Fort Worth, TX). The surgical site was prepared with antiseptic solution and epibulbar anesthesia with proxymetacaine hydrochloride 0.5% as well as sub-Tenon anesthesia with 5.0 ml of lidocaine was used. In order to preserve visual function, the vitreous cavity was revised in one case, and a core and peripheral vitrectomy was performed using a wide-angle viewing system (BIOM; Oculus, Wetzlar, Germany) with cutting rates of 5,000-10,000 cuts/min, aspiration pressure of 200-650 mmHg, and irrigation pressure of 30 mmHg, in 5 cases. Thereafter, the posterior hyaloid was separated using active aspiration via the vitreous cutter over the optic disc, and the epiretinal proliferative tissue and subretinal exudates were removed after retinotomy. Prior to retinotomy and tumor endoresection, HFEW with a modified high-frequency current generator EK-300M1 and proprietary 23-G welding probe was used to minimize the risk of intraoperative hemorrhage. One electrode was secured to the blepharostat, and another was passed endovitreally. The welding voltage was set to 24–30 V, welding current, to 0.3A, welding current frequency, to 66.0 KHz, and welding time, to 1.0 s. A retinotomy around the tumor was performed under perfluorocarbon tamponade. Depending on the clinical situation, the procedure was concluded by the tamponade of the vitreous cavity with 20% C3F8 (Alcon) or 5700cSt silicone oil (Bausch & Lomb OXANE® 5700 Silicone Oil).

Outcome measures included anatomical success (retinal re-attachment), visual acuity, the presence of intraoperative and postoperative hemorrhagic complications, resorption of subretinal exudates, restoration of retinal

profile and the absence of tumor recurrence over the 6-month follow-up period.

Results

We included patients who were followed for at least 6 months after surgery. Of the 6 VPTs, 4 (66.7%) were primary RVPTs, and 2 (33.3%) were secondary VPTs associated with bilateral uveitis in remission (patient 4). The largest tumor dimension varied from 4 to 9 fisc diameters (DD). The most common tumor location was in the inferior temporal quadrant (5 tumors; 83.3%)) and one tumor was located in the superior temporal quadrant. One eye had a history of PPV for vitreous hemorrhage without VPT removal. No patient had a family history of retinal hemangioma. Of the 6 eyes with RVPTs, five had a natural lens, and one had an intraocular lens (IOL). Preoperative Maklakoff intraocular pressure (IOP) ranged from 15 mmHg to 24.0 mmHg. Preoperative complications of VPT included exudative retinal detachment (n = 6), macular edema (n = 4), and epiretinal fibsoris (n = 4) (Table 1). The best-corrected visual acuity (BCVA) at presentation varied from light perception with accurate projection of rays to 0.17.

High-frequency electric welding was used for hemostasis immediately before retinotomy and tumor. HFEW was performed with three rows around the VPT until complete cessation of retinal blood flow occurred. After removal of the tumor and subretinal exudates, the retina was flattened with perfluorocarbon liquid (6 eyes). This was followed by application of 3–4 rows of endolaser around the retinotomy site and a fluid-air exchange. Total tumor removal was achieved in all cases. The procedure was concluded by the tamponade of the vitreous cavity with 20% C3F8 (Alcon) in 2 eyes (33.3%) and 5700cSt silicone oil in 4 eyes (66.7%).

In the early preoperative period, the percentage of vitreous cavity gas fill was 85–90%, and the volume of the gas bubble was large enough to make an effective tamponade of the retinotomy. Postoperative hemorrhage, likely caused by continued oozing from the edge of the retinotomy, occurred in 3 eyes. Postoperative Maklakoff IOP ranged from 20.0 mmHg to 25.0 mmHg.

At 1 month after surgery, there was ophthalmoscopic evidence of chorioretinal scarring with pigment deposition along the edge of the retinotomy, and the retina appeared attached. At 3.5–4 months after surgery, silicone oil was removed in 2 eyes; in other 2 eyes, however, permanent silicone oil tamponade was necessary to maintain the retina re-attached. At the 6-month follow-up examination, the BCVA ranged from 0.17 to 0.3 (Table 2).

Over the 6-month follow-up period, the retina remained re-attached, BCVA improved, and partial resorption of hard exudates as well as restoration of the retinal profile was observed in all cases (6 eyes). In addition, no tumor recurrence was noted, and, consequently, there was no need for re-surgery in any eye.

Discussion

Vaeoptoliferatuve tumors of the retina are mostly primary in origin and are less commonly secondary to congenital, inflammatory, vascular, traumatic, dystrophic and degenerative ocular diseases [7]. To date, due to the relative rarity of these tumors, no unified guidelines are available for their diagnostic assessment and management. Most available methods are of limited efficacy and offer only temporary regression of tumor, necessitating multiple re-treatments or using a combination of several methods.

Of the six VPTs in the current study, four were primary tumors, and two were secondary VPTs associated with bi-

Table 1. Individual patient data at baseline

Patient	Gender	Age, years	Eye (OD or OS)	Tumor size (disc diameters)	VPT location	Tumor-associated complications	BCVA
1	Male	47	OD	5	inferior temporal quadrant	ERD ME	0.05
2	Female	42	OS	7	inferior temporal quadrant	ERD ME	Light perception with accurate projection of rays
3	Male	41	OS	4	superior temporal quadrant	ERD ERM	0.17
4	Female	36	OD	6	inferior temporal quadrant	ERD ME ERM	Light perception with accurate projection of rays
			OS	4	inferior temporal quadrant	ERD ERM	0.12
5	Female	53	OD	9	inferior temporal quadrant	ERD ME ERM	0.06

Note: BCVA, best-corrected visual acuity; ERD, exudative retinal detachment; ME, maculae edema; ERM, epiretinal membrane; VPT, vasoptoliferative tumor

Table 2. Outcomes of surgical treatment for vasoproliferative tumors at 6 months after surgery

Patient	Gender	Age (years)	Eye (OD or OS)	BCVA at baseline	Type of tamponade	BCVA at 6 months	Recurrence
1	Male	47	OD	0.05	20% C_3F_8	0.25	No
2	Female	42	OS	Light perception with accurate projection of rays	CM 5700	0.17	No
3	Male	41	OS	0.17	20% C_3F_8	0.3	No
4	Female	36	OD	Light perception with accurate projection of rays	CM 5700	0.2	No
			OS	0.12	CM 5700	0.25	No
5	Female	53	OD	0.06	CM 5700	0.2	No

Note: BCVA, best-corrected visual acuity

lateral uveitis in remission. The female patient with uveitis received causative treatment for the underlying disease, which is essential in secondary VPTs. One patient had a history of PPV for vitreous hemorrhage without RVPT removal.

The treatment strategy selected should depend on the tumor size and location, presence of complications at baseline, and extent of visual function abnormality. Smaller peripheral symptomless VPTs pose no threat to vision, and their management can be simple observation. Laser photocoagulation or transpupillary thermotherapy can be used to manage lesions ≤ 3 mm [8]. This approach is, however, somewhat limited if the tumor is located peripherally. There have been reports on the successful use of transconjunctival cryotherapy in the treatment of tumors with complications like lipid exudation, recurrent vitreous hemorrhage, and/or cystoid macular edema [4]. Others, however, noted that, because repeat treatments with cryotherapy can lead to fibrosis and exudative retinal detachment, this approach is not widely used for tumors with an apical diameter of > 2 mm as these tumors are difficult to treat in one session due to their thickness [12].

Plaque radiotherapy or photodynamic therapy may be used if the tumor does not respond to the above treatments. Both 125I and 106Ru radiotherapy plaques have been used in the management of lesions > 3 mm in thickness with mostly subretinal fluid; this resulted in tumor regression without a substantial improvement in visual function due to the development of radiation-induced complications. Anastassiou and colleagues [14] noted that there was no case of radiation-induced neuropathy, and the most common complication was epiretinal gliosis (28.6%), followed by vitreous hemorrhage (11.4%) and rhegmatogenous retinal detachment (2.9%). Photodynamic therapy is less effective in terms of eradication of the peripherally located tumor compared to other modalities [19]. Intravitreal injections of anti-VEGF agents or triamcinolone acetonide, either alone or in combinations, can facilitate the regression of exudative retinal detachment and macular edema in early phases of treatment for VPT [10]. The above modalities were not feasible in the current study due to the presence of VPT-associated complications (exudative retinal detachment, macular edema, and/or epiretinal fibrosis), tumor size (> 3.0 DD) and peripheral location of lesions (the inferior temporal quadrant in 5 eyes and superior temporal quadrant in 1 eye of the 6 eyes).

Despite its benign nature and peripheral location in the retina, progression of a VPT can lead to a complete loss of vision due to associated vitreoretinal complications. Therefore, each modality available has its strengths, but no single treatment modality can solve the issue of VPT-associated complications.

Vitrectomy is a surgery of choice for VPTs complicated by tractional retinal detachment, vitreous hemorrhage, and proliferative vitreoretinopathy irrespective of tumor location in the retina. Yeh and Wison [20] reported that, in a patient with two VPTs, surgical techniques included the use of chandelier illumination to enable bimanual manipulation of tissue, endolaser around the tumor prior to resection, endodiathermy to cauterize the tumor's feeder vessels, and long-acting gas tamponade following the retinectomy [20]. The authors observed postoperative subretinal hemorrhage at the surgical resection sites and intensive intraoperative hemorrhages.

Hyperthermic tissue welding is known to alow for adequate hemostasis and improved intraoperative visualization [18]. We believe that HFEW is a promising approach for solving the tasks [21]. Welding technology has proved to be efficient in eye cancer treatment practice. HFEW has been shown to prevent choroidal and cilary vessel bleeding and reduce the risk of intraoperative and postoperative complications in endoresection of uveal melanoma. In our study on the HFEW-assisted endoresection of uveal melanoma, the eye salvage rate was as high as 90% [16],

which demonstrated that the HFEW technique is optimal to allow for hemostasis in the resection of large uveal melanoma when other modalities cannot be used. In addition, the HFEW technique resulted in complete arrest of hemorrhage from the tumor feeder vessels in hemangioma endoresection during vitrectomy in patients with von Hippel-Lindau syndrome [17]. In the current study, VPT was removed by HFEW-assisted endoresection after vitrectomy. After HFEW was performed with three rows around the VPT, retinal vessels were obliterated, which prevented hemorrhage during retinotomy and VPT resection. Therefore, the HFEW technique allowed to optimize hemostasis, which significantly reduced surgery time and the likelihood of postoperative complications. In all study eyes (n = 6), visual acuity improved compared to baseline due to retinal re-attachment, resorption of hard exudates and restoration of the retinal profile.

Conclusion

Vitrectomy with VPT endoresection results in positive anatomical and functional outcomes, making it a method of choice in the treatment of large complicated VPT resistant to more eye-sparing modalities; the HFEW technique proved to be an apt choice for hemostasis.

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Disclosures

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Abbreviations: *BCVA – best-corrected visual acuity; DD – optic disc diameter(s); HFEW – high-frequency electric welding of biological tissues; OCT – optical coherence tomography; PFCL – perfluorocarbon liquid; VEGF – vascular endothelial growth factor; VPT – vasoproliferative tumor.*