Endoresection of choroidal melanoma using high-frequency electric welding of biological tissues

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Background: *The evolution of ocular oncology over the recent decades has been characterized by the emphasis on organ saving approaches, the main method requirement being the greatest degree of radicalism of tumor resection with a minimum amount of damage to surrounding tissues.*
Purpose: *To assess the efficacy of endoresection for uveal melanoma, with the high-frequency electric welding used for achievement of hemostasis.*
Materials and Methods: *Twenty patients (21 eyes; age, 51.6 (12.43) years) with choroidal melanoma were under our observation during 2010 to 2014. Prior to any treatment, the maximum tumor thickness based on ultrasound examination (Cine Scan) was 5.4 (2.6) mm (range, 1.4 mm to 10 mm), with the mean largest basal tumor diameter of 10.8 (3.7) mm (range, 7.6 mm to 15.8 mm). Patients underwent strontium-90 brachytherapy plus transpupillary thermotherapy to devitalize the tumor. Two months to 3 years thereafter, they underwent a 20-G three-port vitrectomy during which endoresection of melanoma was performed.*
Results: *In 19 eyes (90%), massive hemorrhage from uveal melanoma vessles and choroidal vessels was observed during excision of tumor tissue, and was successfully resolved with high-frequency electric welding using a unipolar endovitreal probe. All patients were still alive at the end of observation period of 2 to 6 years. Two of them underwent enucleation due to progressive tumor growth and due to subacute uveitis and phthisis bulbi, respectively.*
Conclusions: *Endoresection is an alternative technique for the treatment of uveal melanoma, with the eye salvage rate as high as 90%. The use of high-frequency electric welding of biological tissues in endoresection of uveal melanoma allowed us to avoid choroidal and ciliary hemorrhage in all cases, thus reducing the risk of intra- and post-operative complication.*

Key words:

Introduction

The evolution of ocular oncology over the recent decades has been characterized by the emphasis on organ saving approaches, the main method requirement being the greatest degree of radicalism of tumor resection with a minimum amount of damage to surrounding tissues. The most commonly used organ saving approaches for posterior uveal melanoma are radiotherapies (brachytherapy, proton beam therapy, etc.) either as monotherapy or combined with laser treatment (photodynamic therapy, transpupillary thermotherapy, photocoagulation) [1-9]. Exoresection of uveal melanoma is performed substantially less often than radiotherapies since it is a technically difficult procedure with high risk of intra- and postoperative complications and of dissemination of cancer cells. Moreover, it cannot be performed in posterior tumors (i.e., when the tumor is located near the optical nerve and fovea). In spite of advances in organ saving therapeutic approaches, enucleation still plays a role in the treatment of uveal melanoma, with enucleation rates for the disease varying from 12.3% to 59.0% [1-3, 5, 10, 11].

New eye-sparing surgical options have recently been developed. Transvitreal endoresection of uveal melanoma have been proposed and described by Linnik, Peyman and Cohen as an alternative to exoresection [12-15]. Damato and colleagues reported on 52 endoresections for choroidal melanoma, with a mean tumor thickness of 3.9 mm [16]. Patients were considered for endoresection if radiotherapy was believed to have a high risk of causing radiational optic neuropathy because of the proximity of the tumour to the optic disc. Uncontrolled choroidal and ciliary hemorrhage at the time of tumor resection and risk of metastasis due to dissemination of cancer cells is a disadvantage of this approach [17-21]. At the Filatov

Institute, we have developed in cooperation with the Paton Institute of the NAMS of Ukraine the apparatus, tools and methodology for high-frequency electric welding, which allow achieving adequate hemostasis and preventing intra- and post-operative complications in vitrectomy (UKR Patent No. 46981).

The study **purpose** was to assess the efficacy of endoresection for uveal melanoma, with the high-frequency electric welding used for achievement of hemostasis.

Materials and Methods

Twenty patients (21 eyes; age, 51.6 (12.43) years, range, 25 to 73 years) with choroidal melanoma were under our observation during 2010 to 2014. A follow-up period of two years at least after endoresection was an inclusion criterion for the study. At baseline, the maximum tumor thickness based on ultrasound examination (Cine Scan, Quantel Medical SA, Le Brezet, France) was 5.4 (2.6) mm (range, 1.4 mm to 10 mm), with the mean largest basal tumor diameter of 10.8 (3.7) mm (range, 7.6 mm to 15.8 mm). The tumor was located posteriorly, and the optic nerve as well as the ciliary body was not involved in all cases. Patients underwent brachytherapy with a strontium-90 (Sr-90) applicator (toral tumor radiation dose, 1830 to 5040 Gr) plus transpupillary thermotherapy (TTT) with 810-nm diode laser (diameter, 2000-4000 µm; power, 150 mW-1.8 W; exposure time, 60 s) to devitalize the tumor. Two months to 3 years after brachytherapy and TTT, they underwent a 20-G three-port vitrectomy, during which endoresection of melanoma was performed. Samples of excised vitreous and tumor tissue were sent for prompt cytological assessment. Upgraded high-frequency current generator EK-300M (voltage, 28-30 V; current, up to 0.3 A; frequency, 66.0 kHz; exposure time, up to 1.0 s) and proprietary tools were used to achieve homeostasis and intraoperative retinopexy.

Signs of progressive tumor growth, Bruch's membrane rupture with subsequent extension of the tumor into the vitreous, total vitreous hemorrhage and patient's refusal of enuclation were indications for endovitreal resection. Informed consent for the surgical procedure was obtained from each patient.

Preoperative examination included visual acuity assessment, comprehensive ophthalmological examination, ultrasonography with measurements of maximum tumor prominence and largest basal tumor diameter, diaphanoscopy and long-wave fundusgraphy. Thoracic and abdominal ultrasonography and MRI as well as mammography were performed to exclude metastasis. Follow-up examinations were performed daily during days 1-4 after surgery, and, subsequently, at months 1, 3 and 6. The observation period was 2 to 6 years. The number of intra- and postoperative complications, survival, presence of metastasis and the number of enucleations were assessed.

Results

With regard to the location of uveal melanoma in eyes of the study, the findings were as follows: temporal to macula was the most common location (5 eyes (23.8%)), followed by the inferior nasal quadrant (4 eyes (19%)), superior temporal quadrant (4 eyes (19%)), and inferior temporal quadrant (3 eyes (14%)). The least common locations (1 eye) for uveal melanoma were the superior nasal quadrant, nasal location, superior location, inferior location, and macula. No statistically significant change in tumor dimensions was observed after treatment for devitalization of the tumor. Thus, before this treatment and at the time of vitrectomy, the maximum tumor thickness was 5.4 (2.6) mm and 5.23 (2.51) mm, respectively (p=0.71), and the mean largest basal tumor diameter was 10.8 (3.7) mm and 11.1 (3.4) mm, respectively (p=0.52). Prior to vitrectomy, (1) the most common additional clinical signs were subtotal exudative retinal detachment (5 eyes (23.8%)) and Bruch's membrane rupture (5 eyes (23.8%)), followed by vitreous hemorrhage (4 eyes (19%)), and rhegmatogenous retinal detachment (1 eye (4.8%)), and (2) visual acuity was no light perception, light perception with accurate projection, 0.01 to 0.1, and more than 0.3 in 1 eye, 5 eyes (23.8%), 8 eyes (38.1%), and 7 eyes (33.3%), respectively. Core and peripheral vitrectomy was performed using a wide angle viewing system BIOM system (Oculus, Wetzlar, Germany) with cutting rates of 2000-5000 cuts/min, aspiration pressure of 200 mm Hg, and irrigation pressure of 30-50 mm Hg.

To prevent hemorrhage and blood dissemination of tumor cells, a unipolar endovitreal probe was used to perform high-frequency electric welding of choroidal vessels within healthy tissues surrounding the tumor, at a distance of 1.0-1.5 mm from the tumor. As a result, a grey-and-white focus of a diameter not more than that of the electrode was revealed at the site of welding electrode application, with completely stopped retinal and choroidal blood flow in each case. Retinochoroidectomy around uveal melanoma was performed subsequently, after vitreous humor was replaced with sterile air (to prevent air embolism, the air pressure was not more than 30 mmHg). At this phase, no hemorrhage from retinal vessels proper or choroidal vessels was noted. Tumor tissue was then removed with the vitreous cutter, using minimal aspiration pressure of 100 to 600 mm Hg at cutting rates of 500-1000 cuts/min. In 19 eyes (90%), massive hemorrhage from uveal melanoma vessles and choroidal vessels was observed during excision of tumor tissue. All bleeding episodes were resolved with high-frequency electric welding of the hemorrhagic vessel at the parameters above. It is important to note the fact that welding can be performed (as opposed to diathermy) during a transvitreal procedure even under conditions of air tamponade of the vitreous cavity. However, certain difficulties arose during the change-over of endovitreal instruments, when hemostatic control cannot be achieved. In 12 eyes (57%), after the entire tumor was removed with a surround of normal tissues, tumor bed tissues underwent diode endolaser photocoagulation to prevent recurrent tumor growth. Subsequently, endolaser photocoagulation was done along the retinochoroidotomy margin and, thereafter, 5700-cSt silicone oil tamponade of the vitreous cavity was performed in 16 eyes (76%), and 16% C3F8 gas tamponade of the vitreous cavity was performed in 5 eyes. Cryoretinopexy was applied to sclerotomy sites to prevent recurrent tumor growth in all patients.

In all cases, the diagnosis of uveal melanoma was confirmed histologically. The cell type of uveal melanoma was determined in 7 cases (spindle and epithelioid cell types were found in 6 eyes and 1 eye, respectively).

No hemorrhagic complications were noted early postoperatively. Mild preretinal hemorrhage at the margins of the surgical coloboma of the choroid and retina was observed in 6 eyes (28.5%). Transitory ocular hypertension was noted in 4 eyes and resolved with beta blocker therapy. Patients were discharged on postoperative day 4.

With regard to late follow-up, it is noteworthy that all patients attended follow-up visits, and were still alive at the end of observation period of 2 to 6 years. No metastasis was noted during thoracic and abdominal examinations. Progressive tumor growth was revealed in 1 case (4.8%), which required enucleation. Another patient underwent enucleation due to subacute uveitis and phthisis bulbi.

Silicone oil was removed 3 to 14 months after endoresection in 8 eyes out of 16. Rhegmatogenous retinal detachment was a serious complication that occurred in the presence of silicone oil in 5 patients (23%) and after removal of silicone oil in 4 patients, which required repeat transvitreal procedure.

In 9 patients, phacoemulsification with intraocular lens implantation was performed at different times after vitrectomy to restore media clarity.

At the last follow-up visit, visual acuity was light perception with accurate projection, 0.01 to 0.1, and more than 0.1 in 2 eyes (8.6%), 14 eyes (66.6%), and 3 eyes (14.3%), respectively.

In spite of certain intraoperative difficulties, endovitreal resection is an effective alternative to enucleation in patients with large uveal melanomas of the posterior pole, and when other treatments for uveal melanoma have failed. Without a doubt, the use of radiotherapy and laser therapy in our cases was limited due to development of retinal detachment, vitreous hemorrhage and Bruch's membrane rupture with subsequent extension of the tumor into the vitreous. All patients were offered enucleation as an alternative to our eye-saving modality, but they declined this offer. We believe that we gained promising outcomes from endoresection of uveal melanoma; namely, we managed to save 19 eyes out of 21 (more than 90%), with two of them achieving a BCVA better than 0.9.

A high risk of intraoperative hemorrhage that may lead to the need for enucleation remains a constraining factor for the wide introduction of this approach. We solved this problem by using high-frequency electric welding in biological tissues. In our study, in spite of intensive bleeding, hemostasis was achieved intraoperatively in all cases. In our opinion, laser and/or radiotherapy with the aim to devitalize the tumor should precede endovitreal resection of uveal melanoma, which would result in improved control of hemostasis and ablastics (prevention of intraoperative dissemination of tumor cells). In general, patients who had endoresection of uveal melanoma require more frequent follow-up visits than patients who had vitrectomy for the non-cancer pathology, due to the potential for the development of complications and recurrent tumor growth.

Conclusion

Endoresection is an alternative technique for the treatment of uveal melanoma, with the eye salvage rate as high as 90%. The use of high-frequency electric welding of biological tissues in endoresection of uveal melanoma allowed us to avoid choroidal and ciliary hemorrhage in all cases, thus reducing the risk of intra- and post-operative complication.

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