Treatment of uncontrolled intraocular pressure secondary to uveal melanoma status post plaque radiotherapy with ab interno XEN gel stent implantation

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ABSTRACT

Purpose: To report treatment of uncontrolled intraocular pressure in a patient with uveal melanoma status post plaque radiotherapy with ab interno XEN gel stent implantation.

Observations: A 21-year-old female with a history of iris and ciliary body melanoma underwent treatment with plaque radiotherapy with subsequent elevation of intraocular pressure refractory to maximum medical therapy. In order to control the pressure, ab interno XEN gel stent implantation with mitomycin C was recommended. Preoperatively, the patient was on four topical medications and oral acetazolamide with intraocular pressure of 39 mmHg by Goldmann applanation tonometry. The patient’s intraocular pressure was reduced to 10 mmHg at her final postoperative visit on no medications. Visual acuity showed minimal degradation measuring 20/100 preoperatively and 20/150 eleven months after XEN gel stent implantation with VA improvement to 20/60 with refraction after cataract extraction at eighteen months. There were no postoperative complications and no recurrence or seeding of the uveal melanoma at follow up 18 months after her XEN gel stent implantation.

Conclusions and Importance: Ab interno XEN gel stent implantation with mitomycin C may offer an effective method to control intraocular pressure in patients with refractory intraoperative pressure control following plaque radiotherapy treatment for uveal melanoma.

1. Introduction

Ocular melanoma is the most common primary intraocular malignancy in adults, with an incidence of 4–6 cases per million in the United States.1,2 The order of frequency of uveal structures affected are choroid (90%), ciliary body (6%), and iris (4%).3 Treatment options for uveal melanoma vary depending on size and location of the malignancy and include plaque radiotherapy, proton beam radiotherapy, enucleation, and transscleral photocoagulation. A common adverse effect of plaque radiotherapy for ciliary body melanoma includes elevation of intraocular pressure (IOP), occurring in greater than 8% of eyes after treatment.4 Management of elevated IOP recalcitrant to medications following plaque radiotherapy can be challenging. Traditional surgical and laser modalities have been explored, including trabeculectomy, glaucoma drainage implant, transscleral cyclocryotherapy, and enucleation.5 More recently, a gelatin stent has been introduced into the glaucoma treatment armamentarium that offers a novel therapeutic option for consideration. The XEN gel stent (Allergan plc, Dublin, Ireland) is a six-millimeter hydrophilic tube made of porcine gelatin with a 45-μm lumen, designed to be implanted in the subconjunctival space via an ab interno approach to treat refractory glaucoma.6 To our knowledge, only one other retrospective study of 72 eyes included a single patient with treated uveal melanoma who underwent XEN gel stent implantation.7 Our case report describes the surgical technique, unique clinical course, and the outcome of ab interno XEN gel stent implantation to treat elevated IOP in one eye with uveal melanoma status post plaque radiotherapy.

2. Case report

A twenty-one-year-old female with a history of bilateral pigment dispersion and iridociliary melanoma status post plaque radiotherapy in the right eye presented to the Dean McGee Eye Institute in October 2020 for evaluation of her uncontrolled IOP. The patient was diagnosed six months prior to presentation after fine needle aspiration biopsy of an enlarging iris and angle lesion revealed atypical melanocytic...
proliferation consistent with spindle cell melanoma. Plaque radiotherapy was performed shortly thereafter, utilizing radioactive iodine-125 on a 15 mm plaque at a depth of 4 mm.

Upon presentation to our eye institute, her intraocular pressure measured 39 mmHg in the right eye (OD) by Goldmann applanation tonometry on topical latanoprost, brimonidine, and fixed-combination dorzolamide-timolol OD as well as 500mg oral acetazolamide daily. Intraocular pressure in the left eye (OS) measured 10 mmHg. Snellen visual acuity was 20/100 OD and 20/15 OS. The pupillary exam revealed a dilated, poorly reactive, relatively dyscoric pupil OD measuring approximately 7.5mm with a relative afferent pupillary defect (RAPD) by reverse. The left pupil was unremarkable, measuring 4.5mm. Corneal thickness was 531um OD and 564um OS. The conjunctiva OD was thickened and slightly scarred near the superonasal limbus but was normal in all other quadrants. Corneal exam revealed a faint Krukenburg spindle OD. Mid-peripheral iris transillumination defects could not be appreciated OD due to pupil dilation but were noted OS. Two elevated, hyperpigmented iris lesions were noted near the limbus at approximately 5:30 and 6 o’clock OD (Fig. 1). Gonioscopy revealed Shaffer grade IV angles OU, with 2+ trabecular meshwork pigmentation OD and 1+ TM pigment OS. The larger iris lesion had adjacent peripheral anterior synechia and pigment clumping (Fig. 2). Clear crystalline lenses were present bilaterally. Glaucomatous cupping was present OD with a cup-to-disc (CDR) ratio of approximately 0.9 and diffuse neuroretinal rim thinning. The CDR OS was approximately 0.6 with intact neuroretinal rim. No disc hemorrhages were noted in either eye. The remainder of the exam was unremarkable, and there was no evidence of uveal melanoma recurrence after evaluation by her ocul Oncologist. Standard automated perimetry (SAP) OD showed diffuse depression with reduced foveal threshold of 25dB, abnormal mean deviation (MD) of ~24.56dB, and abnormal pattern standard deviation (PSD) of 10.7dB; SAP OS was within normal limits. Optical coherence tomography revealed an average retinal nerve fiber layer of 62um OD and 99um OS.

Considering the glaucomatous changes OD with uncontrolled IOP despite maximum medical therapy, the patient’s young age, and the potential for localized orbital extension after filtration surgery in patients with uveal melanoma status post plaque radiotherapy, we recommended a minimally invasive, ab interno XEN gel stent implantation with adjunct mitomycin C. Other intraocular surgical options including Gonioscopy-Assisted Transluminal Trabeculotomy (GATT) or Ab-interno canoloplasty (ABIC) were not considered due to the degree of trabecular meshwork pigmentation. The larger iris lesion has adjacent peripher al anterior synechia and pigment clumping (Fig. 2).

![Slit lamp photo of the right eye depicting two elevated, hyperpigmented iris lesions near the limbus at approximately 5:30 and 6 o’clock.](image1)

Fig. 1. Slit lamp photo of the right eye depicting two elevated, hyperpigmented iris lesions near the limbus at approximately 5:30 and 6 o’clock.

Cotton-tipped applicator. Balanced salt solution was used to thoroughly wash the ocular surface. A clear corneal paracentesis was created temporally using an MVR blade, and the anterior chamber was filled with high viscosity, cohesive ophthalmic viscoelastic. Another corneal paracentesis was made in the inferotemporal cornea through which the XEN injector was inserted and docked anterior to the trabecular meshwork 180° away from the entry site under gonioscopic visualization. The needle was advanced until the entire bevel of the 27-gauge XEN needle was visualized in the subconjunctival space and the sleeve of the injector was in the angle. The XEN gel stent was delivered within the sclera and in the subconjunctival space by gentle actuation of the slider on the injector device. When the XEN gel stent was fully deployed, the inserter was removed from the anterior chamber. The gel stent was confirmed to be in good position with approximately 1mm visible with gonioscopy in the anterior chamber angle and 3mm visible in the subconjunctival space. All viscoelastic was removed from the anterior chamber using balanced salt solution irrigation. A diffuse conjunctival bleb was noted with no leaks identified.

At her postoperative day one visit, the patient’s IOP was 1 mmHg with visual acuity of 20/800. A diffuse, Seidel-negative bleb was noted. The anterior chamber was deep with trace cell, and the XEN gel stent was visible in the superonasal angle. The remainder of the exam was unremarkable. The eye remained numerically hypotonic for two months following the surgery with IOP ranging from 1 to 5 mmHg, but it displayed no corresponding anatomic findings of hypotony (corneal endothelial folds, chamber shallowing, choroidal detachments, macular folds). Visual acuity improved to 20/250, without correction, during those first two months. Intraocular pressure ranged from 6 to 14 mmHg during postoperative months 3–11. At the patient’s final postoperative visit, her BCVA was 20/150 with an IOP of 11 mmHg, and a low, diffuse
posterior bleb was noted (Fig. 3). She ultimately developed a visually significant posterior subcapsular cataract OD and underwent cataract extraction with lens implantation with a final visual acuity of 20/60 with manifest refraction and intraocular pressure of 14 eighteen months after initial presentation.

3. Discussion

In the United States, the annual incidence of uveal melanoma is approximately 4–6 cases per million.1–3 The choroid is most commonly involved (90%), followed far less frequently by the ciliary body (6%) and iris (4%).4 Intraocular pressure elevation may be found on presentation (5%) or as result of tumor treatment. Iris melanomas are most commonly associated with elevated IOP due to direct invasion of the angle by tumor and/or seeds. Ciliary body melanoma may also invade the angle directly or liberate seeds into the angle, causing secondary open angle glaucoma. Finally, choroidal melanoma may be associated with ischemic retinopathy, iris neovascularization, and secondary closed angle (neovascular) glaucoma.5

Iodine-125 plaque radiotherapy is the most common treatment for uveal melanoma in the United States. Rates of systemic metastasis and death from plaque radiotherapy are similar to those after enucleation, according to the Collaborative Ocular Melanoma Study Group.6 Reports suggest that 8.6% of eyes develop secondary open angle glaucoma following plaque radiotherapy. In a retrospective review of 374 eyes treated with Iodine-125 brachytherapy for uveal melanoma, 31 eyes (8.6%) developed secondary open angle glaucoma defined as ≥3 measurements of IOP ≥21 mmHg and an open angle on gonioscopy over a 10 year follow up period. Risk factors for open-angle IOP elevation following brachytherapy include older age, greater tumor size, iris tumor location, higher baseline IOP, tumor involvement of ciliary body, and radiotherapy combined with vitrectomy and silicone oil.7 Our patient had three of these risk factors: iris location, ciliary body involvement, and high IOP on presentation.

Medical management is often ineffectively at controlling IOP elevation after treatment of uveal melanoma. Different surgical approaches exist to treat uncontrolled IOP in eyes with treated uveal melanoma. Cycloablation and filtration surgery utilizing trabeculectomy and glaucoma drainage implants (GDI) have been described, but filtration has been associated with extrascleral extension of melanoma cells and recurrence of tumor activity. In a case report of one patient receiving trabeculectomy after treated uveal melanoma, Grossniklaus et al. found seeding of malignant melanoma cells in the filtering bleb.8 A retrospective review of 15 patients receiving trabeculectomy for control of recalcitrant IOP status post proton beam therapy for uveal melanoma achieved over a 50% reduction in IOP at six months; however, two patients developed local recurrence.9 Fatehi et al. reported a retrospective review of sixteen eyes with elevated IOP status post uveal melanoma treatment treated with glaucoma drainage devices. After one year, there was a mean IOP reduction from 30.5 to 15.9 mmHg. Although metastatic disease developed in two of these patients, none experienced local or orbital extension.10 A prospective study of eyes with treated melanoma and subsequent uncontrolled IOP receiving Baerveldt glaucoma drainage devices revealed similar pressure-lowering results and an 86% success rate defined as IOP ≤21 mmHg and 20% reduction from baseline at a mean follow up of almost 16 months without local tumor recurrence or metastases.11 Chen et al. did however identify recurrence of a uveal melanoma eight years after Baerveldt tube implantation in a single patient, with extension into the implant capsule and ultimately into the orbit with systemic metastases three years after enucleation.12

The XEN gel stent is most frequently reported in literature as a treatment modality for primary open angle glaucoma. Many studies have reported utilizing the gel stent in various forms of secondary open angle and closed angle glaucoma, but only one study of 72 eyes included a single patient with glaucoma secondary to plaque radiotherapy-treated ocular melanoma in its cumulative data without specifically discussing the patient course.7,15–18

In an eye with good visual potential, we sought a surgical option that was the least tissue-disruptive to minimize the potential risk of secondary tumor spread yet comparably effective to traditional surgery for IOP control. One potential advantage to ab interno implantation of the XEN gel stent is the elimination of conjunctival dissection. Additionally, hypotony-related complications are well known amongst traditional filtration surgeries, and cyclophotocoagulation has been associated with severe vision loss, phthisis and even sympathetic ophthalmia.19–21 Despite the initial two months of numerical hypotony, no evidence of clinical hypotony or other complications were observed in our patient. Furthermore, the stent’s 45-μm lumen provides a smaller ostium relative to traditional trabeculectomy or tube surgery, which may decrease the risk of secondary spread. However, while the lumen diameter of the XEN gel stent is 45 μm, cancer cells may have a diameter of as little as 10 μm, which does not eliminate the theoretical possibility of tumor seeding through the stent.22 As a result, 18 months of follow up for this patient may not be sufficient time to establish the safety profile of the XEN gel stent in light of reports identifying tumor seeding of GDIb 8 years after surgery.

4. Conclusions

Ab interno XEN gel stent may be considered for controlling recalcitrant pressure in eyes with uveal melanoma treated with plaque radiotherapy. Our patient achieved over a 70% reduction in intraocular pressure and remained off all medications at postoperative month 18, with excellent visual acuity postoperatively and without postoperative complications. An important limitation to this case report is that 18 months may not be sufficient time to determine if the XEN stent truly reduces the risk of tumor seeding. This is highlighted by previous studies identifying uveal melanoma recurrence in the orbit and body up to eight years after. However, in carefully selected patients, the XEN gel stent may offer an efficacious treatment modality for glaucoma secondary to radiation-treated ocular melanoma.

Patient consent

Consent to publish this case report has been obtained from the patient in writing. This case report does not contain any personal identifying information.

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